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As filed with the Securities and Exchange Commission on April 6, 2006

Registration No. 333-131050

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

AMENDMENT NO. 5 TO FORM S-1 REGISTRATION STATEMENT

Under
The Securities Act of 1933

TARGACEPT, INC.

(Exact name of registrant as specified in its charter)

Delaware	**2834**	**56-2020050**
(State or other jurisdiction of incorporation or organization)	**(Primary Standard Industrial Classification Code Number)**	**(I.R.S. Employer Identification Number)**

200 East First Street, Suite 300
Winston-Salem, North Carolina 27101
(336) 480-2100
(Address, including zip code, and telephone number, including area code, of registrant's principal executive offices)

J. Donald deBethizy
Chief Executive Officer
Targacept, Inc.
200 East First Street, Suite 300
Winston-Salem, North Carolina 27101
(336) 480-2100
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

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Approximate date of commencement of proposed sale of the securities to the public: As soon as practicable after the effective date of this Registration Statement.

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, as amended (the "Securities Act"), check the following box. ☐

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ☐ _____

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier registration statement for the same offering. ☐ _____

If this Form is a post-effective amendment filed pursuant to Rule 462(d) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier registration statement for the same offering. ☐ _____

The Registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the Registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

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The information in this preliminary prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is declared effective. This preliminary prospectus is not an offer to sell these securities and it is not soliciting an offer to buy these securities in any state where the offer or sale is not permitted.

Subject to Completion, Dated April 6, 2006

5,000,000 Shares
Common Stock

This is the initial public offering of Targacept, Inc. We are offering 5,000,000 shares of our common stock. We anticipate that the initial public offering price will be between $11.00 and $13.00 per share. Our common stock has been approved for listing on the NASDAQ National Market under the symbol “TRGT.”

Investing in our common stock involves risk. See “ Risk Factors” beginning on page 9.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

	Price to Public	Underwriting Discounts and Commissions	Proceeds to Targacept
Per Share	$	$	$
Total	$	$	$

We have granted the underwriters the right to purchase up to 750,000 additional shares of common stock to cover over-allotments.

Deutsche Bank Securities **Pacific Growth Equities, LLC**

CIBC World Markets **Lazard Capital Markets**

The date of this prospectus is , 2006

PROSPECTUS SUMMARY

The following summary highlights information appearing elsewhere in this prospectus. It may not contain all of the information that is important to you in deciding whether to invest in our common stock. You should read the entire prospectus carefully, including the "Risk Factors" section and the financial statements and related notes appearing at the end of this prospectus, before making an investment decision.

Targacept, Inc.

We are a biopharmaceutical company engaged in the design, discovery and development of a new class of drugs to treat multiple diseases and disorders of the central nervous system by selectively targeting neuronal nicotinic receptors, or NNRs. NNRs are found on nerve cells throughout the nervous system and serve as key regulators of nervous system activity. Our product candidates are designed to selectively target specific NNR subtypes to promote positive medical effects and limit adverse side effects.

We are developing our most advanced product candidates as treatments for target indications in three therapeutic areas: cognitive impairment, depression and anxiety, and pain. Within these areas, we have three product candidates in clinical development and two preclinical product candidates.

Cognitive Impairment

TC-1734. Our lead product candidate is a novel small molecule that we refer to as TC-1734. In December 2005, we entered into a collaborative research and license agreement with AstraZeneca AB for the development and worldwide commercialization of TC-1734 as a treatment for Alzheimer's disease, cognitive deficits in schizophrenia and potentially other conditions marked by cognitive impairment such as attention deficit hyperactivity disorder, commonly referred to as ADHD, age associated memory impairment, commonly referred to as AAMI, and mild cognitive impairment, commonly referred to as MCI. In March 2006, we completed a Phase II clinical trial of TC-1734 in AAMI designed to further assess the effects of TC-1734 on cognition in a cognitively impaired older adult population. We previously completed two other Phase II clinical trials of TC-1734, one in AAMI and one in MCI. We expect AstraZeneca to initiate two Phase II clinical trials of TC-1734 in the first half of 2007, one in mild to moderate Alzheimer's disease and one in cognitive deficits in schizophrenia.

Depression/Anxiety

Mecamylamine hydrochloride and TC-5214. Mecamylamine hydrochloride is the active ingredient in Inversine, which is our only product approved by the U.S. Food and Drug Administration for marketing. Inversine is approved for the management of moderately severe to severe essential hypertension, a high blood pressure disorder. However, we believe that Inversine is prescribed predominantly for the treatment of neuropsychiatric disorders, including Tourette's syndrome, autism and bipolar disorder. We are currently conducting a Phase II clinical trial of mecamylamine hydrochloride for depression as an add-on therapy to

citalopram hydrobromide, a commonly prescribed anti-depressant marketed as Celexa. We expect the results of this trial to be available in the fourth quarter of 2006.

TC-5214, one of the molecular components of mecamylamine hydrochloride, is a separate preclinical product candidate. If the results of our ongoing Phase II clinical trial of mecamylamine hydrochloride are favorable, we may accelerate the development of TC-5214 as an add-on therapy for depression in lieu of further advancement of mecamylamine hydrochloride. We do not expect to pursue the clinical development of both mecamylamine hydrochloride and TC-5214 for depression.

TC-2216. TC-2216 is a novel small molecule that we are developing as an oral treatment for depression and anxiety disorders. TC-2216 is currently a preclinical product candidate. We are currently conducting additional preclinical safety studies necessary to support the filing of an investigational new drug application, or IND, for clinical trials of TC-2216. We plan to file an IND for TC-2216 in the second half of 2006. We are also evaluating TC-2216 as a potential product candidate for smoking cessation or obesity instead of or in addition to depression and anxiety disorders.

Pain

TC-2696. TC-2696 is a novel small molecule that we are developing as a treatment for acute post-operative pain. Depending on clinical trial results, available resources and other considerations, we may pursue development of TC-2696 for other classes of pain in addition to or instead of acute post-operative pain. In 2004, we completed a Phase I clinical trial of TC-2696 that we conducted in France. We are currently conducting a separate Phase I clinical trial in France to further assess the safety and tolerability profile of TC-2696. We expect the full results of this trial to be available in the third quarter of 2006. We have not submitted an IND for clinical trials of TC-2696 in the United States.

Under our agreement with AstraZeneca relating to TC-1734, we and AstraZeneca have initiated a preclinical research collaboration designed to discover and develop additional compounds that, like TC-1734, act on the NNR known as $\alpha 4\beta 2$. AstraZeneca is responsible for funding the research collaboration, which has an initial term of four years and can be extended by mutual agreement. In addition to our $\alpha 4\beta 2$ research collaboration with AstraZeneca, we have a preclinical program focused on identifying and developing compounds that selectively target another NNR, known as $\alpha 7$, which we believe may have application in the treatment of conditions such as schizophrenia, cognitive impairment and inflammation. We have selected a lead compound that we refer to as TC-5619 that acts selectively on the $\alpha 7$ NNR. We are currently conducting additional preclinical studies to support the planned filing in 2007 of an IND for clinical trials of TC-5619. We have additional preclinical programs in areas in which we believe drugs that target specific NNR subtypes can be exploited for medical benefit, such as smoking cessation and obesity.

We develop product candidates using our proprietary databases and computer-based molecular design technologies, which we refer to collectively as Pentad. Pentad enables us to efficiently identify, prioritize, characterize and optimize novel compounds. We used Pentad to design or optimize TC-1734, TC-2696, TC-2216 and TC-5619.

Strategic Collaboration with AstraZeneca AB

Our agreement with AstraZeneca relating to TC-1734 became effective in January 2006. AstraZeneca paid us an initial fee of $10 million in February 2006. AstraZeneca has agreed to make an additional payment to us of $20 million if it decides to conduct a Phase II clinical trial of TC-1734 following the completion of additional safety and product characterization studies that AstraZeneca is conducting at its expense to generate further data with respect to TC-1734. We expect AstraZeneca to complete these safety and product characterization studies within approximately 12 to 15 months from January 2006. Under the agreement, we are eligible to receive other payments of up to $249 million, contingent upon the achievement of development, regulatory and first commercial sale milestones for TC-1734 for Alzheimer's disease, cognitive deficits in schizophrenia and ADHD, and royalties on future product sales. If TC-1734 is developed under the agreement for indications other than Alzheimer's disease, cognitive deficits in schizophrenia and ADHD, we would also be eligible to receive payments contingent upon the achievement of development, regulatory and first commercial sale milestones for TC-1734 for those indications. In addition, if the agreement continues in effect following AstraZeneca's completion of the additional safety and product characterization studies, we would be entitled to receive a minimum of $23.7 million in aggregate research fees over the four-year term of the a4ß2 research collaboration. Based on the current budget for the research collaboration, we expect to receive approximately $26.4 million in aggregate research fees under the agreement. However, if AstraZeneca terminates our collaboration agreement on or before April 20, 2007 based on the results of the safety and product characterization studies and all other available information with respect to TC-1734, we would be required to reimburse AstraZeneca for the amount of all research fees that it paid to us under the a4ß2 research collaboration while it conducted the studies. In that event, we would also be required to pay AstraZeneca $5 million as compensation for assigning to us the data and any intellectual property generated in the studies, but we would not be required to refund the $10 million initial fee that AstraZeneca has paid us.

AstraZeneca is responsible for the commercialization of TC-1734 and any compounds that arise out of the research collaboration that it elects to advance. We have the option to co-promote TC-1734 and any other compounds that are selected for advancement arising out of the research collaboration in the United States to specified classes of specialist physicians.

Our NNR Focus

We trace our scientific lineage to a research program initiated by R.J. Reynolds Tobacco Company in 1982 to study the activity and effects of nicotine, a compound that interacts non-selectively with all nicotinic receptors. There is a significant amount of published clinical data relating to nicotine, including studies in which individuals with Alzheimer's disease and other conditions marked by cognitive impairment showed therapeutic improvement when treated with a nicotine patch. We have used this clinical data, together with our deep understanding of the biological characteristics and functions of NNRs that we have built over more than 20 years, to validate NNRs as potential targets for drug activity. We have also developed an expertise in designing compounds of low molecular weight, referred to as small molecules, that can selectively interact with specific NNR subtypes, with the objective of eliciting a desired medical effect and limiting side effects such as those typically seen with nicotine. We have built an extensive patent estate covering the structure or therapeutic use of small molecules designed to regulate the central nervous system by selectively affecting specific NNR subtypes.

Our Business Strategy

Our goal is to become a leader in the discovery, development and commercialization of novel drugs that selectively target NNRs in order to treat diseases and disorders where there is significant medical need and commercial potential. To achieve this goal, we are pursuing the following strategies:

- Develop and commercialize drugs that selectively target specific NNR subtypes.
- Collaborate selectively to develop and commercialize product candidates.
- Remain at the forefront of the commercialization of NNR research.
- Identify and prioritize indications in which drugs that selectively target specific NNR subtypes can be exploited for medical benefit.
- Build a specialized sales and marketing organization.

Risks Associated with Our Business

Our business is subject to numerous risks, as more fully described in the section entitled “Risk Factors” immediately following this prospectus summary.

We have a limited operating history and have incurred substantial net losses since our incorporation in 1997. We expect to continue to incur substantial losses for the foreseeable future. Inversine is the only product that we have available for commercial sale, and it generates limited revenues. All of our other product candidates are undergoing clinical trials or are in early stages of development, and failure is common and can occur at any stage of development. In particular, we discontinued development of two product candidates because they failed to meet defined clinical endpoints in Phase II clinical trials that we completed in 2004. We had been developing one of these product candidates as a treatment for ADHD and the other as a treatment for ulcerative colitis. In addition, an independent statistician that we engaged to conduct an interim analysis of available data from our ongoing Phase II clinical trial of mecamylamine hydrochloride as an add-on therapy for depression recommended in March 2006 that we significantly increase the number of patients in the trial. We do not expect to implement the independent statistician’s recommendation and plan to complete the trial as designed. We believe that the independent statistician’s recommendation suggests that, when full data from the trial are available, the result on the primary efficacy endpoint for the trial may not be statistically significant. In a clinical trial for which an objective is to assess the effectiveness of a drug, the primary efficacy endpoint is the outcome variable specified in advance in the protocol for the trial that is determined to be the most important in assessing whether that objective has been achieved. If the primary efficacy endpoint for our trial of mecamylamine hydrochloride is not statistically significant, we may choose not to conduct any further development of mecamylamine hydrochloride or TC-5214 for depression. None of our product candidates, other than Inversine, has received regulatory approval for marketing and sale. Our ability to generate product revenue in the future will depend heavily on the successful development and commercialization of our product candidates. Even if we succeed in developing and commercializing one or more of our product candidates, we may never generate sufficient sales revenue to achieve and then sustain profitability.

The successful development and commercialization of our lead product candidate, TC-1734, will depend substantially on our recently established collaboration with AstraZeneca. AstraZeneca can terminate our collaboration agreement if it determines in its sole discretion on

or before April 20, 2007 not to proceed with the further development of TC-1734 based on the results of the safety and product characterization studies that AstraZeneca is conducting at its expense for TC-1734 and all other available information with respect to TC-1734. In that event, we would have the financial obligations to AstraZeneca described above under "—Strategic Collaboration with AstraZeneca AB." In addition, we have the right to offer to AstraZeneca any compound that acts on any NNR other than the α4ß2 NNR that we may in the future seek to exploit for Alzheimer's disease, cognitive deficits in schizophrenia, other conditions marked by cognitive impairment or schizophrenia. However, if we do not offer the compound to AstraZeneca, we are generally not permitted to develop or commercialize the compound for any of these indications. As a result, our ability to work in these indications outside the collaboration is substantially limited during the term of the collaboration. Furthermore, the number of compounds that we are permitted to offer to AstraZeneca is limited under the agreement. We have also granted AstraZeneca rights of first negotiation for the development and commercialization of compounds for depression, anxiety and bipolar disorder.

Company History

Our history traces back to 1982 when R.J. Reynolds Tobacco Company initiated a program to study the activity and effects of nicotine in the body. We were incorporated in Delaware in 1997 as a wholly owned subsidiary of RJR and became an independent company in August 2000. Our executive offices are located at 200 East First Street, Suite 300, Winston-Salem, North Carolina 27101, and our telephone number is (336) 480-2100. Our web site is located at www.targacept.com. Information contained on our web site is not incorporated by reference into, and does not form any part of, this prospectus. We have included our website address in this document as an inactive textual reference only. Our trademarks include Targacept® and Inversine®. Other service marks, trademarks and trade names appearing in this prospectus are the property of their respective owners. Unless the context requires otherwise, references in this prospectus to the "company," "we," "us," and "our" refer to Targacept, Inc.

	The Offering
Common stock offered by Targacept	5,000,000 shares
Common stock to be outstanding after this offering	19,104,838 shares
Over-allotment option	750,000 shares
Use of proceeds	To fund clinical trials, preclinical testing and other research and development activities, general and administrative expenses, working capital needs and other general corporate purposes. See “Use of Proceeds.”
Risk factors	You should read the “Risk Factors” section of this prospectus for a discussion of the factors to consider carefully before deciding to invest in shares of our common stock.
NASDAQ National Market symbol	TRGT

The number of shares of our common stock that will be outstanding immediately after this offering is based on 272,823 shares of common stock outstanding as of February 28, 2006 and an additional 13,832,015 shares of common stock issuable upon the conversion of all outstanding shares of our series A, series B and series C convertible preferred stock concurrently with the completion of this offering.

The number of shares of our common stock that will be outstanding immediately after this offering excludes:

- 1,631,110 shares of common stock issuable upon the exercise of options outstanding as of February 28, 2006, at a weighted average exercise price of $2.91 per share, of which options to purchase 975,545 shares were exercisable;
- 30,968 shares of common stock reserved for future grant under our 2000 equity incentive plan as of February 28, 2006; and
- 2,700,000 shares of common stock that will become reserved for future grant under our 2006 stock incentive plan concurrently with the completion of this offering.

Unless otherwise indicated, all information in this prospectus assumes:

- no exercise by the underwriters of their over-allotment option to purchase up to 750,000 shares of our common stock;
- the conversion of all outstanding shares of our convertible preferred stock into 13,832,015 shares of common stock concurrently with the completion of this offering; and
- no exercise of an outstanding warrant exercisable for 215,054 shares of common stock at an exercise price of $14.63 per share that will expire if not exercised concurrently with the completion of this offering.

Summary Financial Data

The following tables summarize our financial data. You should read the following summary financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section and other financial information included in this prospectus.

The pro forma net loss attributable to common stockholders per share information is computed using the weighted average number of common shares outstanding, after giving pro forma effect to the conversion of all outstanding shares of our convertible preferred stock into 13,832,015 shares of common stock concurrently with the completion of this offering, as if the conversion had occurred at the dates of the original issuances.

	Year ended December 31,		
	2003	2004	2005
	(in thousands, except share and per share data)		
Statement of Operations Data:			
Net revenue	$ 2,458	$ 3,738	$ 1,180
Operating expenses:			
Research and development	18,179	22,771	24,252
General and administrative .	3,600	5,163	6,388
Cost of product sales	743	198	481
Total operating expenses	22,522	28,132	31,121
Loss from operations	(20,064)	(24,394)	(29,941)
Interest and dividend income	791	505	1,174
Interest expense .	(122)	(132)	(225)
Loss on disposal of fixed assets	—	(4)	—
Net loss .	(19,395)	(24,025)	(28,992)
Deemed dividend—beneficial conversion feature for Series C redeemable convertible preferred stock issued December 2004	—	(10,312)	—
Preferred stock accretion	(8,341)	(8,744)	(11,238)
Net loss attributable to common stockholders .	$ (27,736)	$ (43,081)	$ (40,230)
Basic and diluted net loss per share applicable to common stockholders.	$ (254.33)	$ (196.53)	$ (153.54)
Shares used to compute basic and diluted net loss per share	109,053	219,213	262,013
Pro forma basic and diluted net loss per share applicable to common stockholders (unaudited)			$ (2.06)
Shares used to compute pro forma basic and diluted net loss per share (unaudited)			14,068,182

The pro forma balance sheet information gives effect to the conversion of all outstanding shares of our convertible preferred stock into 13,832,015 shares of common stock concurrently with the completion of this offering. The pro forma as adjusted balance sheet information gives further effect to our sale of 5,000,000 shares of common stock in this offering at an assumed initial public offering price of $12.00 per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us.

	As of December 31, 2005		
	Actual	Pro forma	Pro forma as adjusted
		(unaudited) (in thousands)	
Balance Sheet Data:			
Cash and cash equivalents	$ 24,851	$ 24,851	$ 79,690
Working capital	20,531	20,531	75,271
Total assets	28,001	28,001	82,741
Long-term debt, net of current portion	1,409	1,409	1,409
Redeemable convertible preferred stock	183,628	—	—
Accumulated deficit	(174,983)	(138,486)	(138,258)
Total stockholders' equity (deficit)	(162,481)	21,147	75,887

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this prospectus before deciding to invest in our common stock. If any of these risks actually occurs, our business, business prospects, financial condition, results of operations or cash flows would likely suffer, maybe materially. This could cause the trading price of our common stock to decline, and you could lose part or all of your investment.

Risks Related to Our Financial Results and Need for Additional Financing

We have incurred losses since our inception and anticipate that we will continue to incur substantial losses for the foreseeable future. We may never achieve or sustain profitability.

We were incorporated in 1997 and operated as a wholly owned subsidiary of R.J. Reynolds Tobacco Company until August 2000. We have a limited operating history and have incurred substantial net losses since our inception. As of December 31, 2005, we had an accumulated deficit of $175.0 million. Our net loss was $19.4 million for the year ended December 31, 2003, $24.0 million for the year ended December 31, 2004 and $29.0 million for the year ended December 31, 2005. Our losses have resulted principally from costs incurred in connection with our research and development activities, including clinical trials, and from general and administrative expenses associated with our operations. We expect to continue to incur substantial losses for the foreseeable future. We expect our research and development expenses to increase substantially following the completion of this offering as we expand our clinical trial activity and as our product candidates advance through the development cycle. We also expect our general and administrative expenses to increase substantially as we expand our infrastructure. As a result, we will need to generate significant revenues to pay these expenses and achieve profitability.

Inversine is our only current source of product revenue. We acquired the rights to Inversine in August 2002. Sales of Inversine generated revenues of only $815,000 for the year ended December 31, 2003, $767,000 for the year ended December 31, 2004 and $681,000 for the year ended December 31, 2005. Inversine is approved in the United States for the management of moderately severe to severe essential hypertension, a high blood pressure disorder. However, we believe that the substantial majority of Inversine sales are derived from prescriptions written by a very limited number of physicians for the treatment of neuropsychiatric disorders, including Tourette's syndrome, autism and bipolar disorder, in children and adolescents. If any of these physicians were to change their prescribing habits, Inversine sales would suffer. We do not expect that sales of Inversine will increase substantially in the future.

If we are unable to develop and commercialize any of our product candidates, if development is delayed or if sales revenue from any product candidate that receives marketing approval is insufficient, we may never become profitable. Even if we do become profitable, we may not be able to sustain or increase our profitability on a quarterly or annual basis.

We will require substantial additional financing and our failure to obtain additional funding when needed could force us to delay, reduce or eliminate our product development programs or commercialization efforts.

We will require substantial future capital in order to continue to conduct the research and development and clinical and regulatory activities necessary to bring our product candidates to

market and to establish marketing and sales capabilities. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and cost of preclinical development and laboratory testing and clinical trials;
- the costs, timing and outcomes of regulatory reviews;
- the number and characteristics of product candidates that we pursue;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the costs of establishing sales and marketing functions and of establishing arrangements for manufacturing;
- the rate of technological advancements for the indications that we target;
- our ability to establish strategic collaborations and licensing or other arrangements on terms favorable to us;
- the costs to satisfy our obligations under existing and potential future collaborations;
- the timing, receipt and amount of milestone and other payments from AstraZeneca and potential future collaborators;
- the timing, receipt and amount of sales or royalties, if any, from our potential products; and
- the extent and scope of our general and administrative expenses.

In addition, we may seek additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, your ownership interest will be diluted and the terms may include liquidation or other preferences that adversely affect your rights as a stockholder. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through collaboration and licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates or grant licenses on terms that are not favorable to us.

Our current operating plan provides for us to continue, either alone or with a collaborator, to advance our product candidates through the development process. It is also our objective to continue to invest in our preclinical programs and to file at least one investigational new drug application, or IND, or foreign equivalent each year beginning in 2006. Our net cash used in operating activities for 2005 was $26.2 million, or approximately $2.2 million per month.

We do not expect our existing capital resources and the net proceeds from this offering to be sufficient to enable us to fund the completion of the development of any of our product candidates. We expect that our existing capital resources and the net proceeds from this offering will enable us to maintain currently planned operations through mid-2008. However, our operating plan may change as a result of many factors, including those described above, and we may need additional funds sooner than planned to meet operational needs and capital requirements for product development and commercialization.

We currently have no credit facility or committed sources of capital other than from AstraZeneca for research and development expenses under our collaboration agreement, which

we could be required to refund. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available on a timely basis, we may:

- terminate or delay clinical trials for one or more of our product candidates;
- delay our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates; or
- curtail significant drug development programs that are designed to identify new product candidates.

If AstraZeneca does not proceed with a Phase II clinical trial of TC-1734 and terminates our collaboration agreement, we may need additional capital sooner than planned.

Our collaboration agreement with AstraZeneca provides for AstraZeneca to conduct additional safety and product characterization studies of TC-1734 before deciding whether to proceed with planned Phase II clinical trials to evaluate the efficacy of TC-1734 in mild to moderate Alzheimer's disease and cognitive deficits in schizophrenia. Upon completion of any or all of the safety and product characterization studies, AstraZeneca has the right to terminate our agreement. In that event, we would be required to reimburse AstraZeneca for the amount of all research fees that it paid to us under the a4ß2 research collaboration that we and AstraZeneca have initiated under the agreement while AstraZeneca conducted the studies. We would also be required to pay AstraZeneca $5 million as compensation for assigning to us the data and any intellectual property generated in the studies, but we would not be required to refund the $10 million initial fee that AstraZeneca has paid us. If AstraZeneca terminates our agreement, we may need additional capital sooner than planned.

The safety and product characterization studies that AstraZeneca is conducting consist of:

- in vitro studies to assess whether TC-1734, when administered at a therapeutically relevant dose, activates a particular protein that can activate an enzyme known as CYP1A1 that is considered by some scientists to increase susceptibility to cancer;
- a clinical trial to characterize the cardiovascular effects of various doses of TC-1734 in persons who break down and eliminate, or metabolize, TC-1734 at varying rates;
- a single-dose study in dogs to further assess TC-1734's cardiovascular effects; and
- small clinical trials to evaluate the interaction and combined effects of TC-1734 with paroxetine, a known inhibitor of a key enzyme involved in TC-1734's primary metabolic pathway, and with multiple commonly prescribed treatments for schizophrenia.

In a study in rats conducted by a former collaborator of ours, TC-1734 was found to activate the enzyme CYP1A1, but at a dose substantially higher than the doses at which we and AstraZeneca plan to pursue development of TC-1734 for Alzheimer's disease and cognitive deficits in schizophrenia. If AstraZeneca determines that TC-1734 also activates CYP1A1 in humans at a therapeutically relevant dose, AstraZeneca may terminate our agreement.

In addition, the study design for the single-dose cardiovascular study of TC-1734 in dogs that we expect AstraZeneca to conduct is substantially similar to a study previously conducted by a former collaborator of ours as part of the preclinical evaluation of TC-1734 in which cardiovascular effects were observed. However, we believe that the cardiovascular effects observed in the prior study were not related to TC-1734, but resulted from the presence of a

substance that was used to facilitate the administration and delivery of TC-1734 and that is now known to cause cardiovascular effects in dogs. We do not expect that AstraZeneca will use that substance in its study. We did not observe cardiovascular effects in subsequent studies that we conducted in dogs in which we administered TC-1734 over 90 days and 180 days. If the results of the single-dose study in dogs that we expect AstraZeneca to conduct are not favorable, AstraZeneca may terminate our agreement.

Risks Related to the Development and Regulatory Approval of Our Product Candidates

Our success depends substantially on our most advanced product candidates, which are still under development. If we are unable to bring any or all of these product candidates to market, or experience significant delays in doing so, our ability to generate product revenue and our likelihood of success will be harmed.

We and AstraZeneca have agreed to develop TC-1734 for Alzheimer's disease and cognitive deficits in schizophrenia. However, TC-1734 has not yet been evaluated in any clinical trial in patients suffering from Alzheimer's disease or cognitive deficits in schizophrenia. In March 2006, we independently completed a Phase II clinical trial of TC-1734 in age associated memory impairment, commonly referred to as AAMI, designed to further assess the effects of TC-1734 on cognition in a cognitively impaired older adult population. The clinical data from this trial have only recently become available. New information may arise from our continuing analysis of the data that may be less favorable than currently anticipated. Our ability to generate product revenue in the future will depend heavily on the successful development and commercialization of TC-1734.

Inversine is our only approved product and generates limited revenues. We are currently conducting a Phase II clinical trial of mecamylamine hydrochloride, the active ingredient in Inversine, as an add-on therapy for depression.

Mecamylamine hydrochloride is our only product candidate in an ongoing Phase II clinical trial. We have completed a Phase I single rising dose clinical trial for TC-2696, our product candidate for the treatment of pain and are currently conducting a Phase I multiple rising dose clinical trial for TC-2696. In a single rising dose clinical trial, each subject in a dose group receives a dosage of the drug being evaluated only one time, with subjects in each subsequent dose group receiving a pre-determined higher dosage than subjects in the preceding dose group. In a multiple rising dose clinical trial, each subject in a dose group receives a dosage of the drug being evaluated multiple times, with subjects in each subsequent dose group receiving a pre-determined higher dosage than subjects in the preceding dose group. Our other product candidates are in various stages of preclinical development.

Any of our product candidates could be unsuccessful if it:

- does not demonstrate acceptable safety and efficacy in preclinical studies or clinical trials or otherwise does not meet applicable regulatory standards for approval;
- does not offer therapeutic or other improvements over existing or future drugs used to treat the same conditions;
- is not capable of being produced in commercial quantities at acceptable costs; or
- is not accepted in the medical community and by third-party payors.

We do not expect any of our current product candidates to be commercially available for at least the next several years, if at all. If we are unable to make our product candidates commercially available, we will not generate substantial product revenues and we will not be successful.

If safety studies conducted by AstraZeneca demonstrate that TC-1734 is not safe for individuals that metabolize the drug slowly or when the primary means by which the body metabolizes TC-1734 is blocked, AstraZeneca could cease development of TC-1734 and terminate its agreement with us. Poor results from these safety studies or termination of our agreement with AstraZeneca would make it more difficult for us to advance development and obtain the regulatory approvals required to market and sell TC-1734.

Metabolism of a drug refers to a process in which a drug is broken down and then eliminated from the body. The means by which the body metabolizes a drug is referred to as the metabolic pathway. Due to genetic differences, individuals can metabolize drugs through the same metabolic pathway at different rates. For any particular metabolic pathway, an individual can be a poor, intermediate or extensive metabolizer. Drugs that are metabolized through a particular metabolic pathway may remain in the body at higher concentrations and for longer periods of time in people who are poor metabolizers than in people who are intermediate or extensive metabolizers through that metabolic pathway. As a result, a drug that is determined to be safe when metabolized efficiently by an extensive metabolizer may not be safe or may not be as safe when metabolized inefficiently by a poor metabolizer.

As discussed in greater detail above under "—Risks Related to Our Financial Results and Need for Additional Financing," our agreement with AstraZeneca provides for AstraZeneca to conduct additional safety and product characterization studies of TC-1734 before deciding whether to proceed with further development of TC-1734. In particular, our agreement with AstraZeneca provides that AstraZeneca will assess the safety of TC-1734 in both extensive metabolizers and poor metabolizers, as well as in combination with another drug that may block TC-1734's primary metabolic pathway. We expect AstraZeneca to conduct a clinical trial to characterize the cardiovascular effects of TC-1734 at doses of up to 200mg in both extensive metabolizers and poor metabolizers. The highest dose at which we have assessed the safety of TC-1734 in persons over the age of 65 is 150mg, in the first Phase II clinical trial in AAMI that we conducted. In that trial, three out of eight subjects treated with 150mg of TC-1734 while fasting experienced side effects such as headache, lightheadedness, dizziness and vomiting and dropped out of the trial. However, in a Phase I clinical trial of TC-1734 that we conducted, TC-1734 was well tolerated at a dose of up to 320mg in young adults. We also expect AstraZeneca to conduct a small clinical trial to characterize the cardiovascular effects of TC-1734 when administered in combination with paroxetine, a known inhibitor of a key enzyme involved in TC-1734's primary metabolic pathway.

If the safety studies conducted by AstraZeneca demonstrate that TC-1734 is not safe in poor metabolizers or is not safe when the primary metabolic pathway for TC-1734 is blocked, AstraZeneca could decide not to conduct a Phase II clinical trial of TC-1734 and terminate its agreement with us. If AstraZeneca terminates our agreement, it would delay our development of TC-1734. In addition, poor results from these studies would make it more likely that we would not receive the regulatory approvals required to market and sell TC-1734. Even if we were to receive the required regulatory approvals, the regulatory authorities could limit the patient population for which TC-1734 is approved to those who are extensive or intermediate metabolizers through TC-1734's primary metabolic pathway. If regulatory authorities limit the patient population for which TC-1734 is approved in this manner, it would have an adverse effect on TC-1734's commercial potential.

If the combination of TC-1734 administered together with other drugs that are commonly prescribed for schizophrenia is not considered to be safe, the commercial potential of TC-1734 would be adversely affected.

A drug that is generally safe when taken alone may not be safe or may not be as safe when taken together with other drugs. We expect AstraZeneca to conduct a small clinical trial of TC-1734 administered together with multiple commonly prescribed treatments for schizophrenia in healthy volunteers to evaluate the interaction of the drugs and the combined effects on metabolism and safety. If the interaction of TC-1734 and any or all of the commonly prescribed treatments for schizophrenia adversely affects the metabolism of TC-1734 such that TC-1734 and any of those treatments are determined to be unsafe together, it could limit TC-1734's commercial potential as a treatment for cognitive deficits in schizophrenia. Moreover, AstraZeneca could decide not to advance TC-1734 as a treatment for cognitive deficits in schizophrenia, which would limit TC-1734's overall commercial potential. Furthermore, if the interaction of TC-1734 with any of these commonly prescribed treatments adversely affects the metabolism of TC-1734, AstraZeneca could decide not to conduct any Phase II clinical trials of TC-1734 and terminate its agreement with us. If AstraZeneca terminates our agreement, it would delay our development of TC-1734.

If we do not obtain the regulatory approvals required to market and sell our product candidates, our ability to generate product revenue will be materially impaired and our business will not be successful.

The preclinical laboratory testing, development, manufacturing and clinical trials of product candidates that we develop, whether independently or in collaboration with a third party, as well as their distribution, sale and marketing, are regulated by the FDA and other federal, state and local governmental authorities in the United States and by similar agencies in other countries. We must receive regulatory approval of each product candidate before we can market and sell it. We have only limited experience in pursuing regulatory approvals. Securing FDA approval requires the submission of extensive preclinical and clinical data and information about the chemistry and manufacture of, and control procedures for, each potential product. In addition, the supporting information submitted to the FDA must establish the safety and efficacy of the product candidate for each indicated use. The marketing approval process takes many years, requires the expenditure of substantial resources, is subject to delays and can vary substantially based upon the type, complexity and novelty of the product candidates involved. In addition to the time and expense involved, the process is uncertain and we may never receive the required regulatory approvals. In addition, the FDA, the U.S. Congress and foreign regulatory authorities may from time to time change approval policies or adopt new laws or regulations, either of which could prevent or delay our receipt of required approvals. Even if we receive regulatory approval to market a particular product candidate, the approval will be subject to limitations on the indicated uses for which it may be marketed and may not permit labeling claims that are necessary or desirable for its promotion.

According to the FDA, a Phase I clinical trial program typically takes several months to complete, a Phase II clinical trial program typically takes several months to two years to complete and a Phase III clinical trial program typically takes one to four years to complete. Industry sources report that the preparation and submission of a new drug application, or NDA, which is required for regulatory approval in the United States, generally takes six months to one year to complete after completion of a pivotal clinical trial. Industry sources also report that approximately 10% to 15% of all NDAs accepted for filing by the FDA are not approved and that FDA approval, if granted, usually takes approximately one year after submission, although it may take longer if additional information is required by the FDA. In addition, the Pharmaceutical Research and Manufacturers of America reports that only one out of five product candidates that enter clinical trials will ultimately be approved by the FDA for commercial sale.

The FDA may delay, limit or deny approval of any of our product candidates for many reasons. For example:

- clinical trial results may indicate that the product candidate is not safe or effective;
- the FDA may interpret our clinical trial results to indicate that the product candidate is not safe or effective, even if we interpret the results differently; or
- the FDA may deem the processes and facilities that we, our collaborative partners or our third-party manufacturers propose to use in connection with the manufacture of the product candidate to be unacceptable.

In particular, because drugs that target NNRs are a new class of drugs, the FDA and other applicable regulatory authorities may require more preclinical or clinical data for our product candidates or more time to evaluate that data than we currently anticipate. If we obtain the requisite regulatory approval for a particular product candidate, the approval may not extend to all indications for which we have sought approval, which could limit the use of the product and adversely impact our potential revenues.

Even if the FDA approves a product candidate for marketing and sale in the United States, applicable regulatory authorities in other countries may not approve the product candidate or may subject their approval to conditions such as additional product testing or otherwise cause delays. The regulatory approval process varies among countries, but generally includes all of the risks associated with obtaining FDA approval. In addition, many countries require a separate review process prior to marketing to determine whether their respective national health insurance schemes will pay for newly approved products, as well as the price that may be charged for a product. This process will cause delays in the marketing of any of our product candidates that receives marketing approval and could adversely impact our revenues and results of operations.

If clinical trials for our product candidates are not successful, we will not obtain the regulatory approvals required to market and sell them.

To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate, through extensive preclinical studies and clinical trials, that the product candidate is safe and effective in humans. The number of clinical trials required to obtain approval varies depending on the particular product candidate, the disease or condition for which it is in development and the regulations applicable to it. Preclinical studies and clinical trials are lengthy and expensive, difficult to design and implement and subject to a historically high rate of failure. The development of each of our product candidates involves significant risks at each stage of testing. A failure of one or more of our clinical trials could occur at any stage of testing. In 2004, we completed Phase II clinical trials for product candidates that we had been developing for attention deficit hyperactivity disorder and ulcerative colitis. Because we determined that these product candidates failed to meet defined endpoints of the Phase II clinical trials, we discontinued the development of these product candidates. If we experience similar difficulties or failures in our ongoing or future clinical trials, or if we are not able to design our clinical trials with clear criteria to determine the efficacy of our product candidates, our product candidates may never be approved for sale or become commercially available.

We may not be able to obtain authority or approval from the FDA, other applicable regulatory authorities or the institutional review boards at our intended investigational sites to commence or complete our clinical trials. Before a clinical trial may commence in the United States, we must submit an IND containing preclinical studies, chemistry, manufacturing, control and other information and a study protocol to the FDA. If the FDA does not object within 30 days

after submission of the IND, then the trial may commence. If commenced, we, the FDA, other applicable regulatory authorities or institutional review boards may delay, suspend or terminate clinical trials of a product candidate at any time if, among other reasons, we or they believe the subjects or patients participating in the clinical trials are being exposed to unacceptable health risks or for other reasons.

If we do not prove in clinical trials that our product candidates are safe and effective, we will not obtain marketing approvals from the FDA and other applicable regulatory authorities. In particular, one or more of our product candidates may not exhibit the expected medical benefits in humans, may cause harmful side effects or may have other unexpected characteristics that preclude regulatory approval for any or all indications of use or limit commercial use if approved. For example, in the 100mg dose group of our Phase I multiple rising dose trial of TC-2696, our product candidate for pain, we suspended further dosing after two of three volunteers discontinued participation in the trial due to dizziness, nausea and, in one case, vomiting. Both of these volunteers had received a single dose of TC-2696 prior to discontinuing participation in the trial. We did not see comparable effects at 100mg in our completed single rising dose trial of TC-2696. Based on in vitro metabolism studies of TC-2696 that we subsequently conducted, we currently believe that the different effects of 100mg in our single rising dose trial and our multiple rising dose trial may be due to genetic differences in the primary metabolic pathway of TC-2696. We have not yet determined definitively the dose range in which positive medical effects, if any, are achieved with TC-2696. If following further evaluation we determine that the different effects observed are in fact due to the primary metabolic pathway of TC-2696, that TC-2696 is not safe in poor metabolizers or is not safe when the primary metabolic pathway for TC-2696 is blocked and that 100mg of TC-2696 is within the dose range in which positive medical effects are achieved with TC-2696, we may not receive the regulatory approvals required to market and sell TC-2696. Even if we do receive the required regulatory approvals, the regulatory authorities may limit the patient population for which TC-2696 is approved to those who are extensive or intermediate metabolizers through TC-2696's primary metabolic pathway.

We engaged an independent statistician to conduct an interim analysis and to make a recommendation as to whether it would be advisable to increase the number of patients in our ongoing Phase II clinical trial of mecamylamine hydrochloride as an add-on therapy for depression. The independent statistician reviewed available data from the first 105 patients who completed the trial. In March 2006, the independent statistician recommended that we increase the number of patients by 607 patients per dose group based on his interim analysis of data relating to the primary efficacy endpoint of the trial. This recommendation is consistent with a prior recommendation from the same independent statistician based on available data from the first 50 patients who had completed the trial. We do not expect to implement the independent statistician's recommendation and plan to complete the trial as designed. We believe that the independent statistician's recommendation suggests that, when data from all subjects who complete the trial become available, the result on the primary efficacy endpoint for the trial may not be statistically significant. If the primary efficacy endpoint for the trial is not statistically significant, we may choose not to conduct any further development of mecamylamine hydrochloride or TC-5214 for depression. If we do conduct further development of mecamylamine hydrochloride or TC-5214 for depression, the results of future clinical trials may not provide sufficient evidence that either product candidate is effective in treating depression. If we are unable to demonstrate in clinical trials that mecamylamine hydrochloride or TC-5214 is effective in treating depression, we will not receive the regulatory approvals required to market and sell either product candidate for depression.

We and AstraZeneca have agreed to develop TC-1734 as a treatment for Alzheimer's disease and for cognitive deficits in schizophrenia. We and AstraZeneca may also in the future

develop TC-1734 as a treatment for AAMI. AAMI is a condition that is characterized by gradual memory loss or other cognitive impairment that generally occurs with normal aging. Because AAMI accompanies normal aging, is not a disease state and does not prevent a person from functioning on a daily basis, the FDA or foreign regulatory authorities may require that we establish that TC-1734 meets a higher threshold of safety than the FDA or foreign regulatory authorities would require for diseases and more severe disorders. If we or AstraZeneca is unable to demonstrate that TC-1734 meets this higher safety threshold, the FDA or foreign regulatory authorities may not grant approval to market TC-1734 for the treatment of AAMI.

Our research and preclinical programs and product candidates target diseases or disorders that are not well understood. For example, there is only limited scientific understanding of the causes of Alzheimer's disease, AAMI, schizophrenia, including cognitive deficits in schizophrenia, and depression and anxiety. In addition, there are no approved drugs that target NNRs to treat these diseases, and there is only limited scientific understanding of the relationships between these diseases and the neurological pathways targeted by our product candidates and research and preclinical programs. These uncertainties increase the risk that one or more of our clinical trials will not be successful.

If positive results of our completed clinical trials of TC-1734 in AAMI and MCI are not replicated in future clinical trials in Alzheimer's disease, cognitive deficits in schizophrenia or other indications, we and AstraZeneca will not obtain the regulatory approvals required to market and sell TC-1734.

Positive findings in preclinical studies of a product candidate may not be predictive of similar results in clinical trials in humans. In addition, positive results in early clinical trials of a product candidate may not be replicated in later clinical trials. In particular, we completed a Phase II clinical trial of TC-1734 in AAMI in March 2006. We previously completed two other Phase II clinical trials of TC-1734, one in AAMI and one in mild cognitive impairment, commonly referred to as MCI. In those trials, TC-1734 demonstrated positive effects on cognition. However, our findings in those trials on cognition may not be replicated in future clinical trials of TC-1734 in Alzheimer's disease, cognitive deficits in schizophrenia or other indications that involve a large number of subjects and a long duration of dosing. In addition, although TC-1734 demonstrated positive effects on cognition at some dose levels with respect to some measures of cognition tested in the first Phase II clinical trial in AAMI that we conducted, TC-1734 did not demonstrate positive effects as to all measures at all dose levels and placebo showed superior effects to TC-1734 as to some measures at some dose levels in that trial.

Like most drugs, the active component of TC-1734 must be combined with an inactive component to form a powder, known as a salt, that is suitable for commercialization as a pharmaceutical product. We have developed a salt form of TC-1734 that is different from the salt form of TC-1734 that we used in our completed trials. We anticipate that we or AstraZeneca may use the alternate salt form of TC-1734 in the planned Phase II trials in mild to moderate Alzheimer's disease and cognitive deficits in schizophrenia and in future clinical trials of TC-1734. The results of our completed clinical trials of TC-1734 in the initial salt form may not be replicated in any future clinical trials of TC-1734 in the alternate salt form.

In our completed clinical trials of TC-1734 in AAMI and MCI, we used a battery of tests developed by CDR Ltd. to assess each subject's cognitive function. However, if we or AstraZeneca use an additional or a different test battery for any future AAMI or MCI trials, there would be a greater risk that the results of our completed Phase I and Phase II clinical trials of TC-1734 will not be replicated in those future clinical trials and that the future trials will not provide a sufficient basis for further development or regulatory approval.

If we and AstraZeneca do not have success in clinical trials of TC-1734 for Alzheimer's disease or cognitive deficits in schizophrenia, we and AstraZeneca will not obtain the regulatory approvals required to market TC-1734 for Alzheimer's disease or cognitive deficits in schizophrenia notwithstanding positive results in clinical trials of TC-1734 in other indications.

We and AstraZeneca have agreed to develop TC-1734 for Alzheimer's disease and cognitive deficits in schizophrenia. We and AstraZeneca may in the future also seek to develop TC-1734 for other conditions marked by various degrees of cognitive impairment, such as ADHD, AAMI or MCI. Successful results in clinical trials of TC-1734 in a condition marked by one degree of cognitive impairment may not be predictive of successful results in clinical trials of TC-1734 in a condition marked by more severe cognitive impairment or in cognitive impairment resulting from a different condition. Neither we nor AstraZeneca has conducted any clinical trial of TC-1734 in Alzheimer's disease or cognitive deficits in schizophrenia. The findings in any of our completed Phase II trials of TC-1734 in AAMI or MCI may not be predictive of the effect of TC-1734 in Alzheimer's disease or cognitive deficits in schizophrenia.

The CDR test battery that we have used in our clinical trials of TC-1734 is different from the Alzheimer's Disease Assessment Scale-cognitive subscale, or ADAS-Cog, the test battery that is most often used to assess the efficacy of drugs for Alzheimer's disease. ADAS-Cog is designed to measure improvement in persons who are severely impaired and is generally less sensitive than the CDR test battery in measuring improvement in persons who are less impaired. We and AstraZeneca plan to use ADAS-Cog, and not the CDR test battery, as the primary endpoint in our clinical trials of TC-1734 in Alzheimer's disease. The findings in our completed trials as to the effect of TC-1734 on various aspects of cognition as measured by the CDR test battery may not be predictive of the effect of TC-1734 on cognition as measured by ADAS-Cog. If future clinical trials of TC-1734 in Alzheimer's disease are not successful, we and AstraZeneca will not obtain the regulatory approvals required to market TC-1734 for Alzheimer's disease.

If clinical trials for our product candidates are prolonged or delayed, we would be unable to commercialize our product candidates on a timely basis, which would require us to incur additional costs and delay our receipt of any revenues from potential product sales.

We cannot predict whether we will encounter problems with any of our completed, ongoing or planned clinical trials that will cause us or any regulatory authority to delay or suspend those clinical trials or delay the analysis of data derived from them. A number of events, including any of the following, could delay the completion of our ongoing and planned clinical trials and negatively impact our ability to obtain regulatory approval for, and to market and sell, a particular product candidate:

- conditions imposed on us by the FDA or any foreign regulatory authority regarding the scope or design of our clinical trials;
- delays in recruiting and enrolling patients or volunteers into clinical trials;
- delays in obtaining, or our inability to obtain, required approvals from institutional review boards or other reviewing entities at clinical sites selected for participation in our clinical trials;
- insufficient supply or deficient quality of our product candidates or other materials necessary to conduct our clinical trials;
- lower than anticipated retention rate of subjects and patients in clinical trials;
- negative or inconclusive results from clinical trials, or results that are inconsistent with earlier results, that necessitate additional clinical study;

- serious and unexpected drug-related side effects experienced by subjects and patients in clinical trials; or
- failure of our third-party contractors to comply with regulatory requirements or otherwise meet their contractual obligations to us in a timely manner.

Clinical trials require sufficient patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the trial protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial. Delays in patient enrollment can result in increased costs and longer development times. We previously experienced delays in patient enrollment for our Phase II clinical trial of TC-1734 in persons with MCI. In that trial, we limited the eligible patient population to persons whose condition was sufficiently severe to qualify for a diagnosis of MCI, but not severe enough to qualify for a diagnosis of dementia. Similarly, we expect that the eligible patient population for the Phase II clinical trial of TC-1734 for mild to moderate Alzheimer's disease to be conducted by AstraZeneca will be limited to Alzheimer's disease patients for whom the disease has not yet progressed to the severe stage. As a result of these inclusion limits, there could be delays in recruitment for this trial similar to those that we experienced in our MCI trial. In addition, this trial would require some of the Alzheimer's disease patients to be assigned randomly into a dosing group that would receive placebo instead of TC-1734. Those patients would not receive any medication for the duration of the trial. As a result, Alzheimer's disease patients or their caregivers may be unwilling or unable to give informed consent to participate in the trial, which would result in delays in patient enrollment. The failure to enroll patients in a clinical trial could delay the completion of the clinical trial beyond our current expectations. In addition, the FDA could require us and AstraZeneca to conduct clinical trials with a larger number of subjects than we have projected for any of our product candidates. We and AstraZeneca may not be able to enroll a sufficient number of patients in a timely or cost-effective manner. Furthermore, enrolled patients may drop out of clinical trials, which could impair the validity or statistical significance of those clinical trials.

Prior to commencing clinical trials in the United States, we must submit an IND to the FDA and the IND must become effective. We conducted our completed Phase I clinical trial for our product candidate TC-2696 outside the United States and we are conducting our ongoing Phase I multiple rising dose clinical trial of TC-2696 outside the United States. We have not submitted an IND to enable us to conduct clinical trials of TC-2696 in the United States.

We do not know whether our clinical trials will begin as planned, will need to be restructured or will be completed on schedule, if at all. Delays in our clinical trials will result in increased development costs for our product candidates. In addition, if our clinical trials are delayed, our competitors may be able to bring products to market before we do and the commercial viability of our product candidates could be limited.

If we are unable to successfully develop and manufacture a salt form of TC-2696 acceptable for use as a pharmaceutical product, clinical development may be delayed and we will not be able to commercialize TC-2696.

In our completed Phase I single rising dose trial of TC-2696 and in our ongoing Phase I multiple rising dose trial of TC-2696, we used a particular salt form of TC-2696 that we refer to as the hemigalactarate salt. We do not expect that the hemigalactarate salt form of TC-2696 will ultimately be viable for marketing as a pharmaceutical product because it accumulates moisture. If the results of our ongoing Phase I multiple rising dose clinical trial of TC-2696 are favorable, we plan to conduct additional work to develop a salt form of this product candidate that is acceptable for use as a pharmaceutical product. If we are unable to develop a pharmaceutically acceptable salt form of TC-2696, we may have to terminate or substantially delay development of this product candidate.

If the FDA or foreign regulatory authorities do not consider AAMI or MCI to be a clinical indication appropriate for the approval of a drug, we and AstraZeneca will not receive the regulatory approvals required to market and sell TC-1734 for AAMI or MCI.

We and AstraZeneca have agreed to develop TC-1734 for Alzheimer's disease and cognitive deficits in schizophrenia. In addition, we and AstraZeneca may in the future pursue development of TC-1734 for other conditions, such as one or both of AAMI and MCI. Neither the FDA nor, to our knowledge, any foreign regulatory authority has approved a drug indicated for use in the treatment of AAMI or MCI. Furthermore, neither AAMI nor MCI is listed in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, or DSM-IV, the manual published by the American Psychiatric Association to establish diagnostic criteria. We do not know if the FDA or any foreign regulatory authority will be willing to recognize AAMI or MCI as a distinct clinical condition, or in the FDA's terminology, a clinical entity, for which approval of a drug is possible. If neither the FDA nor any foreign regulatory authority recognizes AAMI or MCI as a clinical entity, we and AstraZeneca will not obtain the regulatory approval required to market TC-1734 for AAMI or MCI even if our clinical trials show that TC-1734 is safe and provides a medical benefit for the persons treated.

When the FDA assesses whether a proposed clinical entity justifies labeling, it generally requires that the existence of the clinical entity be broadly accepted by medical experts in the relevant clinical discipline and that the clinical entity can be defined in practice. This means that the clinical entity must be able to be diagnosed using valid and reliable criteria that are widely accepted by those medical experts. The FDA imposes these requirements to assure that both the population for whom a drug is intended and the effects of the drug in that population can be adequately described in labeling for the drug. The FDA has informed us that it believes it is questionable whether AAMI satisfies these criteria. In three letters that we have received from the FDA in connection with the protocol submission for the Phase II trial of TC-1734 for the treatment of AAMI that we completed in March 2006 and subsequent protocol amendment submissions, the FDA informed us that, in its view, because varying methodologies and criteria have historically been used by medical experts to define AAMI, the requisite consensus in the medical community has not been established. The FDA also informed us that it is not clear that our Phase II clinical trial design and efficacy endpoints are appropriate for measuring the clinical effect of TC-1734 in AAMI. In particular, the FDA characterized it as unclear whether the power of attention factor of the CDR test battery, which we used as one of our co-primary endpoints for that AAMI trial, is an appropriate outcome measure to use for assessing the effect of a drug on AAMI, in which the only claimed deficit is an impairment of memory. In addition, the FDA indicated that we would need to demonstrate statistically significant improvement on a global measure of overall cognitive improvement to show that the effects of TC-1734 in AAMI are clinically meaningful. We do not have, and we do not believe that AstraZeneca has, any current plan to pursue the development of TC-1734 for the treatment of AAMI beyond the Phase II clinical trial that we completed in March 2006. However, if in the future we and AstraZeneca pursue the development of TC-1734 for the treatment of AAMI and are unable to establish to the satisfaction of the FDA or foreign regulatory authorities that AAMI can be identified using criteria that are accepted in the medical community, that both the deficit in cognitive performance associated with the condition and its subsequent improvement can be measured and that the improvement is clinically meaningful, we and AstraZeneca will not obtain the regulatory approval required to market TC-1734 for AAMI.

Our product candidates will remain subject to ongoing regulatory review even if they receive marketing approval. If we fail to comply with continuing regulations, we could lose these approvals and the sale of our products could be suspended.

Even if we receive regulatory approval to market a particular product candidate, the approval could be conditioned on us conducting additional costly post-approval studies or could

limit the indicated uses included in our labeling. Moreover, the product may later cause adverse effects that limit or prevent its widespread use, force us to withdraw it from the market or impede or delay our ability to obtain regulatory approvals in additional countries. In addition, the manufacturer of the product and its facilities will continue to be subject to FDA review and periodic inspections to ensure adherence to applicable regulations. After receiving marketing approval, the manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping related to the product will remain subject to extensive regulatory requirements. We may be slow to adapt, or we may never adapt, to changes in existing regulatory requirements or adoption of new regulatory requirements.

If we fail to comply with the regulatory requirements of the FDA and other applicable U.S. and foreign regulatory authorities or previously unknown problems with our products, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions, including:

- restrictions on the products, manufacturers or manufacturing processes;
- warning letters;
- civil or criminal penalties;
- fines;
- injunctions;
- product seizures or detentions;
- import bans;
- voluntary or mandatory product recalls and publicity requirements;
- suspension or withdrawal of regulatory approvals;
- total or partial suspension of production; and
- refusal to approve pending applications for marketing approval of new drugs or supplements to approved applications.

Because we have a number of compounds and are considering a variety of target indications, we may expend our limited resources to pursue a particular product candidate or indication and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have limited financial and managerial resources, we must focus on research programs and product candidates for the specific indications that we believe are the most promising. As a result, we may forego or delay pursuit of opportunities with other product candidates or other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Through 2004, we spent managerial and financial resources on clinical trials for two product candidates that we have ceased developing. We may in the future spend our resources on other research programs and product candidates for specific indications that ultimately do not yield any commercially viable products. Furthermore, if we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights.

We may not be successful in our efforts to identify or discover additional product candidates.

A key element of our strategy is to develop and commercialize drugs that selectively target specific NNR subtypes. We seek to do so through our understanding of the role of specific NNRs in the nervous system, our scientific expertise and the use of Pentad.

Other than TC-1734, TC-2696 and mecamylamine hydrochloride, all of our product candidates are at a preclinical stage. A significant portion of the research that we are conducting involves new and unproven compounds. Research programs to identify new product candidates require substantial technical, financial and human resources. These research programs may initially show promise in identifying potential product candidates, yet fail to yield product candidates for clinical development for a number of reasons, including:

- the research methodology used may not be successful in identifying potential product candidates; or
- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be effective products.

If we are unable to develop suitable product candidates through internal research programs, we will not be able to increase our revenues in future periods, which could result in significant harm to our financial position and adversely impact our stock price. Any additional product candidates that we are able to develop through our internal research programs will require the commitment of substantial time and financial resources for further preclinical research and clinical development.

Risks Related to Our Dependence on Third Parties

The successful development and commercialization of our lead product candidate, TC-1734, depends substantially on our recently established collaboration with AstraZeneca. If AstraZeneca is unable to further develop or commercialize TC-1734, or experiences significant delays in doing so, our business will be materially harmed.

In December 2005, we entered into our collaborative research and license agreement with AstraZeneca for the development and worldwide commercialization of TC-1734 for the treatment of Alzheimer's disease, cognitive deficits in schizophrenia and potentially other indications marked by cognitive impairment. We do not have a history of working together with AstraZeneca and cannot predict the success of the collaboration. The collaboration involves a complex allocation of rights, provides for milestone payments to us based on the achievement of specified development, regulatory and first commercial sale milestones and provides us with royalty-based revenue if TC-1734 or another product candidate is successfully commercialized. AstraZeneca has decision-making authority for most matters in our collaboration. AstraZeneca is also generally responsible for conducting and funding substantially all future development and regulatory approval activities for TC-1734 and will have significant control over the conduct and timing of development efforts with respect to TC-1734. Although we have had discussions with AstraZeneca regarding its current plans and intentions, AstraZeneca may change its development plans for TC-1734. We have little control over the amount and timing of resources that AstraZeneca devotes to the development of TC-1734. If AstraZeneca fails to devote sufficient financial and other resources to the development plan for TC-1734, the development and potential commercialization of TC-1734 would be delayed. This would result in a delay in milestone payments and, if regulatory approval to market and sell TC-1734 is obtained, royalties that we could receive on commercial sales.

If we lose AstraZeneca as a collaborator in the development or commercialization of TC-1734 at any time, it would materially harm our business.

Our agreement with AstraZeneca provides for AstraZeneca to conduct additional safety and product characterization studies of TC-1734 before deciding whether to proceed with planned Phase II clinical trials to evaluate the efficacy of TC-1734 in mild to moderate Alzheimer's disease and cognitive deficits in schizophrenia. AstraZeneca can terminate our collaboration agreement if it determines in its sole discretion on or before April 20, 2007 not to proceed with

the further development of TC-1734 based on the results of the studies and all other available information with respect to TC-1734.

In addition, in January 2006, we and AstraZeneca initiated preclinical research under our agreement that is designed to identify and develop additional compounds that act on the a4ß2 NNR and enhance cognitive function. The agreement provides for a four-year research term. AstraZeneca will have the right to terminate the a4ß2 research collaboration upon at least six months notice effective three years after the research term begins. AstraZeneca will have the right to terminate the agreement upon 90 days notice after the earlier of the end of the research term or four years after the research term begins.

If AstraZeneca terminates our agreement at any time, whether on the basis of any of the safety and product characterization studies of TC-1734 or for any other reason, it would delay our development of TC-1734 and materially harm our business and could accelerate our need for additional capital. In particular, we would have to fund the clinical development and commercialization of TC-1734 on our own, seek another collaborator or licensee for clinical development and commercialization or abandon the development and commercialization of TC-1734.

We will depend on collaborations with third parties for the development and commercialization of some of our product candidates. If these collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates.

In addition to our collaboration with AstraZeneca, we intend to selectively enter into collaboration agreements with leading pharmaceutical and biotechnology companies where our potential collaborator has particular therapeutic expertise in a target indication or where the target indication represents a large, primary care market. We will have limited control over the amount and timing of resources that our collaborators dedicate to the development of our licensed product candidates. Our ability to generate revenues from our collaborators will depend on our collaborators' abilities to establish the safety and efficacy of our product candidates, to obtain regulatory approvals and to achieve market acceptance.

Strategic collaborations involving our product candidates, including our collaboration with AstraZeneca, pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;
- collaborators may not pursue further development and commercialization of our product candidates or may elect not to continue or renew research and development programs based on preclinical or clinical trial results, changes in their strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive;
- a collaborator with marketing and distribution rights to one or more products may not commit enough resources to their marketing and distribution;

- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- disputes may arise between us and the collaborators that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development of the applicable product candidates.

Collaboration agreements may not lead to development of product candidates in the most efficient manner or at all. For example, a collaborative research and development agreement that we entered into with Aventis Pharma SA for the development of our compounds for the treatment or prevention of Alzheimer's disease terminated effective January 2, 2005. None of our compounds were advanced into clinical development under the agreement.

In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development program could be delayed, diminished or terminated.

If we do not establish additional collaborations, we may have to alter our development plans.

Our drug development programs and potential commercialization of our product candidates will require substantial additional cash to fund expenses. Our strategy includes selectively collaborating with leading pharmaceutical and biotechnology companies to assist us in furthering development and potential commercialization of some of our product candidates. We intend to do so especially for target indications in which our potential collaborator has particular therapeutic expertise or that involve a large, primary care market that must be served by large sales and marketing organizations.

We are entitled to offer to AstraZeneca the right to develop and commercialize any compound that acts on any NNR other than the a4ß2 NNR that we may in the future seek to exploit for Alzheimer's disease, cognitive deficits in schizophrenia, other conditions marked by cognitive impairment or schizophrenia. However, if we do not offer the compound to AstraZeneca, we are generally not permitted to develop or commercialize the compound for any of these indications. As a result, our ability to seek additional collaborations for these indications is substantially limited during the term of our collaboration with AstraZeneca. We have also granted AstraZeneca rights of first negotiation for the development and commercialization of compounds for depression, anxiety and bipolar disorder.

We face significant competition in seeking appropriate collaborators. Collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on acceptable terms, or at all. If that were to occur, we may have to curtail the development of a particular product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of our sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we will not be able to bring our product candidates to market and generate product revenue.

If our contract manufacturers fail to devote sufficient resources to our concerns, or if their performance is substandard, our clinical trials and product introductions may be delayed or there may be a shortage of commercial supply.

Our product candidates require precise, high quality manufacturing. We have limited internal manufacturing capability. We have historically manufactured our product candidates only in small quantities for preclinical testing and have contracted with third parties to manufacture, in collaboration with us, our product candidates for clinical trials and, in the case of Inversine, for commercial sale. If any of our product candidates is approved by the FDA or by foreign regulatory authorities for marketing and sale, it will need to be manufactured in substantially larger, commercial quantities. Our experience in the manufacture of drugs in commercial quantities is limited to our contractual arrangements with third parties to manufacture Inversine and its active ingredient.

We currently rely on various third-party contract manufacturers, including Siegfried Ltd., for our product candidates and we intend to continue to rely on third-party manufacturers to supply, store and distribute our product candidates for our clinical trials and to manufacture commercial supplies of any product candidate that is approved for sale. Our reliance on third-party manufacturers will expose us to risks that could delay or prevent the initiation or completion of our clinical trials, the submission of applications for regulatory approvals, the approval of our products by the FDA or the commercialization of our products or result in higher costs or lost product revenues. In particular, contract manufacturers:

- could encounter difficulties in achieving volume production, quality control and quality assurance and suffer shortages of qualified personnel, which could result in their inability to manufacture sufficient quantities of drugs to meet our clinical schedules or to commercialize our product candidates;
- could terminate or choose not to renew the manufacturing agreement, based on their own business priorities, at a time that is costly or inconvenient for us;
- could fail to establish and follow FDA-mandated current good manufacturing practices, or cGMPs, required for FDA approval of our product candidates or fail to document their adherence to cGMPs, either of which could lead to significant delays in the availability of material for clinical study and delay or prevent filing or approval of marketing applications for our product candidates; and
- could breach, or fail to perform as agreed under, the manufacturing agreement.

We expect to rely initially on a single contract manufacturer for each of our product candidates. Currently, we have separate arrangements with third-party manufacturers, each of which is a sole supplier to us, for mecamylamine hydrochloride, the active ingredient of Inversine, and for the finished tablets of Inversine. Changing these or any manufacturer that we subsequently engage for a particular product or product candidate may be difficult, as the number of potential manufacturers is limited and we will have to compete with third parties for access to those manufacturing facilities. cGMP manufacturing processes and procedures typically must be reviewed and approved by the FDA and changing manufacturers may require re-validation of any new facility for cGMP compliance, which would likely be costly and time-consuming. We may not be able to engage replacement manufacturers on acceptable terms quickly or at all. In addition, our contract manufacturers located in foreign countries may be subject to import limitations or bans. As a result, if any of our contract manufacturers is unable, for whatever reason, to supply the contracted amounts of Inversine or any other product that we successfully bring to market, a shortage would result which would have a negative impact on our revenues.

Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the United States Drug Enforcement Agency and corresponding state and foreign agencies to ensure strict compliance with cGMPs, other government regulations and corresponding foreign standards. While we are obligated to audit the performance of third-party contractors, we do not have control over our third-party manufacturers' compliance with these regulations and standards. Failure by our third-party manufacturers or us to comply with applicable regulations could result in sanctions being imposed on us, including fines, injunctions, civil penalties, failure of the government to grant pre-market approval of drugs, delays, suspension or withdrawal of approvals, seizures or recalls of product, operating restrictions and criminal prosecutions.

If third parties on which we rely for clinical trials do not perform as contractually required or as we expect, we may not be able to obtain regulatory approval for or commercialize our product candidates.

We do not have the ability to independently conduct the clinical trials required to obtain regulatory approval for our product candidates. We depend on independent clinical investigators and, in some cases, contract research organizations and other third-party service providers to conduct the clinical trials of our product candidates and expect to continue to do so. We rely heavily on these parties for successful execution of our clinical trials, but we do not control many aspects of their activities. Nonetheless, we are responsible for confirming that each of our clinical trials is conducted in accordance with its general investigational plan and protocol. Moreover, the FDA requires us to comply with regulations and standards, commonly referred to as good clinical practices, for conducting and recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the trial participants are adequately protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements. Third parties may not complete activities on schedule or may not conduct our clinical trials in accordance with regulatory requirements or the respective trial plans and protocols. The failure of these third parties to carry out their obligations could delay or prevent the development, approval and commercialization of our product candidates or result in enforcement action against us.

Risks Related to Our Intellectual Property

If we are unable to protect our intellectual property effectively, our competitors may develop and market similar products and the value of our technology and our ability to compete would be damaged.

Our continued success depends significantly on our ability to obtain and maintain meaningful intellectual property protection for our product candidates, technology and know-how. We generally seek to protect our compounds and technologies by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology that is important to the development of our business. We file patent applications directed to our product candidates in an effort to establish intellectual property positions regarding new chemical entities and uses in the treatment of disease.

The patent positions of companies like ours are generally uncertain and involve complex legal and factual questions. Our ability to maintain and solidify our proprietary position for our technology will depend on our success in obtaining effective patent claims and enforcing claims that are granted. We do not know whether any of our patent applications or those patent applications that we license will result in the issuance of any patents. Moreover, our issued patents and those that may issue in the future, or those licensed to us, may be challenged, invalidated, rendered unenforceable or circumvented, any of which could limit our ability to stop competitors from marketing related products. In addition, the rights granted under any issued

patents may not provide us with competitive advantages against competitors with similar compounds or technologies. Furthermore, our competitors may independently develop similar technologies in a manner that does not infringe our patents or other intellectual property.

Although we own or otherwise have rights to a number of patents, these patents may not effectively exclude competitors from engaging in activities that compete with us. Furthermore, the issuance of a patent is not conclusive as to its validity or enforceability, and third parties may challenge the validity or enforceability of our patents. Because patent applications in the United States and many foreign countries are confidential for a period of time after filing, and because publications of discoveries in the scientific literature often lag behind actual discoveries, we cannot be certain that we were the first to make the inventions claimed in our issued U.S. patents or pending patent applications, or that we were the first to file for protection of the inventions set forth in the foreign patents or patent applications. It is possible that a competitor may successfully challenge our patents or that challenges will result in the elimination or narrowing of patent claims and, therefore, reduce our patent protection.

Because of the extensive time required for development, testing and regulatory review of a new drug, it is possible that any related patent may expire before any of our product candidates can be commercialized or remain in force for only a short period following commercialization. In either case, this would reduce any advantages of the patent. The patent laws of various foreign countries in which we intend to compete may not protect our intellectual property to the same extent as the laws of the United States. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection.

If we are unable to protect the confidentiality of our proprietary information and know-how, the commercial value of our technology and product candidates could be reduced.

In addition to patents, we rely on protection of trade secrets, know-how and confidential and proprietary information to maintain our competitive position. To maintain the confidentiality of trade secrets and proprietary information, we generally enter into confidentiality agreements with our employees, consultants, contractors and collaborative partners upon the commencement of our relationship with them. These agreements typically require that all confidential information developed by the individual or made known to the individual by us during the course of the individual's relationship with us be kept confidential and not disclosed to third parties. However, we may not obtain these agreements in all circumstances, and individuals with whom we have these agreements may not comply with their terms. Even if obtained, these agreements may not provide meaningful protection for our trade secrets or other proprietary information or an adequate remedy in the event of their unauthorized use or disclosure. The loss or exposure of our trade secrets or other proprietary information could impair our competitive position.

We also typically enter into agreements with employees that provide inventions conceived by them in the course of rendering services to us are our exclusive property and, where appropriate, we enter into similar agreements with consultants and contractors. To the extent that our employees, consultants or contractors use technology or know-how owned by others in their work for us, disputes may arise as to the rights in related inventions.

If we fail to comply with our obligations in our intellectual property licenses with third parties, we could lose license rights that are important to our business.

We are a party to various license agreements. In particular, we license patent rights for a method of use of our product candidate for pain, TC-2696, and two of our product candidates for depression, mecamylamine hydrochloride and one of its molecular components, TC-5214. We

may enter into additional licenses in the future. Our existing licenses impose, and we expect future licenses will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we might not be able to market any product that is covered by the licensed patents.

Our patent protection for mecamylamine hydrochloride is, and our patent protection for any other particular compound may be, limited to a specific method of use or indication. If a third party were to obtain approval of mecamylamine hydrochloride or other particular compound for use in another indication, we could be subject to competition arising from off-label use.

Although we generally seek the broadest patent protection available for our proprietary compounds, we may not be able to obtain patent protection for the actual composition of any particular compound and may be limited to protecting a new method of use for the compound or otherwise restricted in our ability to prevent others from exploiting the compound. For example, we currently rely on method of use patent coverage in the United States for mecamylamine hydrochloride. If we are unable to obtain patent protection for the actual composition of any compound that we seek to develop and commercialize and must rely on method of use patent coverage, we would likely be unable to prevent others from manufacturing or marketing that compound for any use that is not protected by our patent rights. We are aware of one company, Athenagen Inc., that has announced plans to initiate a clinical trial of mecamylamine hydrochloride as a treatment for age-related macular degeneration, a condition characterized by degeneration of the retina in the eye. If a third party were to receive marketing approval for mecamylamine hydrochloride or any other compound for which we rely on method of use patent coverage for another use, physicians could nevertheless prescribe it for indications that are not described in the product's labeling or approved by the FDA or other regulatory authorities. Even if we have patent protection for the prescribed indication, as a practical matter, we would have little recourse as a result of this off-label use. In that event, our revenues from the commercialization of the compound would likely be adversely affected.

If the development of mecamylamine hydrochloride for depression as an add-on therapy to citalopram hydrobromide infringes the intellectual property of a third party, we may be required to pay license fees or cease our development activities, which could significantly harm our business.

We are currently conducting a Phase II clinical trial of mecamylamine hydrochloride for depression as an add-on therapy to citalopram hydrobromide, a commonly prescribed anti-depressant. We are aware of a patent application that has been filed internationally that, if issued as a patent, could be infringed by our continued development and commercialization of mecamylamine hydrochloride for depression as an add-on therapy to citalopram hydrobromide. We believe that, even if this patent application issues as a patent, the development or commercialization of mecamylamine hydrochloride for depression as an add-on therapy to citalopram hydrobromide by the patent holder or any other third party would infringe our intellectual property rights. However, if this patent application issues as a patent, we could be required to obtain a license if we continue to develop and commercialize mecamylamine hydrochloride for depression as an add-on therapy to citalopram hydrobromide. We may not be able to obtain a license on acceptable terms, or at all. If we are unable to obtain a license on acceptable terms, we may be required to cease further development or commercialization of mecamylamine hydrochloride for depression as an add-on therapy to citalopram hydrobromide, which could significantly harm our business.

We may be involved in lawsuits to protect or enforce our patents that could be expensive and time-consuming.

We may initiate patent litigation against third parties to protect or enforce our patent rights and we may be similarly sued by third parties. We may also become subject to interference or opposition proceedings conducted in the patent and trademark offices of various countries to determine our entitlement to patents. The defense and prosecution of intellectual property suits, interference proceedings and related legal and administrative proceedings, if necessary, would be costly and divert our technical and management personnel from conducting our business. Moreover, we may not prevail in any of these suits. An adverse determination of any litigation or proceeding could put our patents at risk of being invalidated or narrowly interpreted and our patent applications at risk of not being issued and could prevent us from protecting our rights, particularly in countries where the laws may not protect such rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that disclosure of some of our confidential information could be compelled and the information compromised. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments that, if perceived as negative by securities analysts or investors, could have a substantial adverse effect on the trading price of our common stock.

Claims by third parties that we infringe their proprietary rights may result in liability for damages or prevent or delay our development and commercialization efforts.

Our success depends in part on avoiding the infringement of other parties' patents and proprietary rights. Patents may issue from patent applications of which we are unaware, and avoiding patent infringement may be difficult. We may infringe or it may be alleged that we infringe third-party patents. If a third party were to file a patent infringement suit against us, we could be forced to stop or delay research, development, manufacturing or sales of any infringing product in the country or countries covered by the patent infringed, unless we can obtain a license from the patent holder. Any necessary license may not be available on acceptable terms or at all, particularly if the third party is developing or marketing a product competitive with the infringing product. Even if we are able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property.

We also may be required to pay substantial damages to the patent holder in the event of an infringement. These damages could in some circumstances be triple the actual damages the patent holder incurs. If we have supplied infringing products to third parties for marketing or have licensed third parties to manufacture, use or market infringing products, we may be obligated to indemnify these third parties for any damages they may be required to pay to the patent holder and for any losses they may sustain themselves as a result.

Any successful infringement action brought against us may also adversely affect marketing of the infringing product in other markets not covered by the infringement action, as well as our marketing of other products based on similar technology. Furthermore, we may suffer adverse consequences from a successful infringement action against us even if the action is subsequently reversed on appeal, nullified through another action or resolved by settlement with the patent holder. The damages or other remedies awarded, if any, may be significant. As a result, any infringement action against us would likely delay the regulatory approval process, harm our competitive position, be very costly and require significant time and attention of our key management and technical personnel.

Risks Related to Commercialization

Even if approved for marketing, our product candidates may not gain market acceptance and may fail to generate significant revenues.

The commercial success of any of our product candidates for which we may obtain marketing approval from the FDA or other regulatory authorities will depend upon their acceptance by the medical community and third-party payors as clinically useful, cost-effective and safe. Many of the product candidates that we are developing are based upon technologies or methods of treatment that are relatively new and unproven. As a result, it may be more difficult for us to achieve market acceptance of our products.

The degree of market acceptance of any drug depends on a number of factors, such as:

- its demonstration of efficacy and safety in clinical trials;
- its superior efficacy as compared to alternative treatment methods and its side effect profile;
- its cost-effectiveness and the availability of insurance or other third-party reimbursement;
- its convenience and ease of administration;
- the timing of its market entry relative to competitive treatments;
- the extent and success of marketing and sales efforts; and
- the product labeling or product insert required by the FDA or regulatory authorities in other countries.

In addition, perceptions about the relationship or similarity between our product candidates and nicotine could limit their market potential. Our product candidates derive their medical effects by interacting with NNRs. Nicotine, which can have significantly negative health effects, also interacts with NNRs. Accordingly, our product candidates may be perceived by some to be nicotine or to be closely related to nicotine, particularly in light of the shared derivative names, “nicotine” and neuronal “nicotinic” receptors, and the fact that our company was launched originally as a research group within, and then as a subsidiary of, R.J. Reynolds Tobacco Company. This potential perception could result in a reluctance by patients to take, or by physicians to prescribe, any of our product candidates that receives marketing approval, which would affect our revenues.

We currently have limited sales, marketing and distribution experience and no internal sales or distribution capabilities. If we are unable to enter into collaborations or other arrangements with third parties to market and sell our product candidates or to develop our own internal marketing capability, we may not be successful in commercializing our products.

We currently have limited sales, marketing and distribution experience. Our experience is limited to a contractual arrangement with a third party to distribute Inversine, which we acquired in 2002 and which generates only limited sales. We currently have no internal sales or distribution capabilities. Although we intend to build an internal sales force and expand our marketing capabilities in areas where specialists heavily influence our target markets, such as neurology and psychiatry, we also intend to seek to further augment our sales, marketing and distribution capabilities through arrangements with third parties. In particular, our strategy includes selectively entering into collaborations and other strategic alliances with respect to product candidates for disease indications with sales and distribution characteristics requiring a

large sales force. There are risks involved with establishing our own sales force and marketing and distribution capabilities, as well as in entering into arrangements with third parties to perform these services. Developing our own sales force will be expensive and time-consuming and could delay any product launch. We may not be successful in entering into arrangements with third parties on terms that are favorable to us or at all. Also, we would have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell, market or distribute our products effectively. If we do not establish sales and distribution capabilities successfully, either on our own or in collaboration with third parties, we may not successfully commercialize our products.

Unfavorable pricing regulations, third-party reimbursement practices or healthcare reform initiatives applicable to our product candidates could limit our potential product revenue.

The regulations governing drug pricing and reimbursement vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed and, in many of these countries, the pricing review period begins only after approval is granted. In some countries, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Although we monitor these regulations, our product candidates are currently in the development stage and we will not be able to assess the impact of price regulations for at least several years. As a result, we may obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay the commercial launch of the product and may negatively impact the revenues we are able to derive from sales in that country.

Successful commercialization of our products will also depend in part on the extent to which coverage and adequate payment for our products will be available from government health administration authorities, private health insurers and other third-party payors. If we succeed in bringing a product candidate to the market, it may not be considered cost-effective and reimbursement to the patient may not be available or sufficient to allow us to sell it at a satisfactory price. Because our product candidates are in the development stage, we are unable at this time to determine their cost-effectiveness. We may need to conduct expensive studies in order to demonstrate cost-effectiveness. Moreover, third-party payors frequently require that drug companies provide them with predetermined discounts from list prices and are increasingly challenging the prices charged for medical products. Because our product candidates are in the development stage, we do not know the level of reimbursement, if any, we will receive for any products that we are able to successfully develop. If the reimbursement for any of our product candidates is inadequate in light of our development and other costs, our ability to achieve profitability could be affected.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory proposals to change the healthcare system in the United States and other major healthcare markets have been proposed and adopted in recent years. For example, the U.S. Congress has enacted a limited prescription drug benefit for Medicare recipients as part of the Medicare Prescription Drug, Improvement and Modernization Act of 2003. While the program established by this statute may increase demand for any products that we are able to successfully develop, if we participate in this program, our prices will be negotiated with drug procurement organizations for Medicare beneficiaries and are likely to be lower than prices we might otherwise obtain. If successfully developed, TC-1734, our product candidate for Alzheimer’s disease, cognitive deficits in schizophrenia and other conditions marked by cognitive impairment, could be particularly

affected by this law because Alzheimer's disease is a disease that affects the elderly. Non-Medicare third-party drug procurement organizations may also base the price they are willing to pay on the rate paid by drug procurement organizations for Medicare beneficiaries. In addition, ongoing initiatives in the United States have and will continue to increase pressure on drug pricing. The announcement or adoption of any such initiative could have an adverse effect on potential revenues from any product candidate that we may successfully develop.

If our competitors develop and market drugs that are less expensive, more effective or safer than ours, if they develop and market products faster than we do, or if they have better sales and marketing capabilities than we do, any products we are able to commercialize may not generate initial or ongoing revenues.

The development and commercialization of new drugs is highly competitive. Our business is characterized by extensive research efforts and rapid developments. We expect intense competition in our target markets as new products and advanced technologies become available. Our competitors include large pharmaceutical, biotechnology and other companies and research institutions, many of which have greater financial, technical and other resources and personnel and more experience in research, clinical development, regulatory and drug commercialization than we have. Our competitors may:

- develop products that are more effective, safer, more convenient or less costly than our product candidates;
- obtain FDA or other regulatory approval for their products more rapidly than we do;
- adapt more quickly to new technologies and scientific advances;
- initiate or withstand substantial price competition more successfully than we can;
- have greater success in recruiting skilled scientific workers from the limited pool of available talent;
- obtain more effective intellectual property protection than we have;
- negotiate third-party licensing and collaboration arrangements more effectively than we do; and
- take advantage of acquisition or other opportunities more readily than we do.

Competitive products may render our product candidates obsolete or noncompetitive before we can recover our development or commercialization expenses.

We also face substantial competition from therapies designed to target NNRs. We believe that several prominent pharmaceutical companies have product candidates that target NNRs in development, including Pfizer, with a compound for which it has filed an NDA for smoking cessation, Sanofi-Aventis, with a compound that has completed a Phase II clinical trial for smoking cessation, and Abbott Laboratories, with one compound in Phase I for pain and another in Phase II for Alzheimer's disease, ADHD and schizophrenia. We expect that we will face increased competition in the future if therapies that target NNRs are further validated and companies initiate or expand programs focused on NNRs, whether independently or by collaboration or acquisition.

Any products that we are able to successfully develop and commercialize in the future could be subject to competition from lower priced generic drugs. The manufacturer of a generic product could challenge our patents as invalid or not infringed and subject us to expensive

litigation. We do not know if we would prevail in litigation and succeed in keeping the generic product out of the market until our patent protection expires.

If we successfully develop and obtain approval for our product candidates, we will face competition based on the safety and effectiveness of our products, the timing and scope of regulatory approvals, the availability and cost of supply, marketing and sales capabilities, reimbursement coverage, price, patent position and other factors. Our competitors may develop or commercialize more effective or more affordable products, or obtain more effective patent protection, than we do. Accordingly, our competitors may commercialize products more rapidly or effectively than we do.

If approved, our product candidates will compete for a share of the existing market with numerous approved products. There is currently no approved product for cognitive deficits in schizophrenia. We believe that the primary competitive products for use in indications that we are currently targeting include:

- for mild to moderate Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer/Eisai, Reminyl from Johnson & Johnson and Exelon from Novartis and for moderate to severe Alzheimer's disease, Namenda from Forest Laboratories, which acts by regulating the neurotransmitter glutamate;
- for pain, non-steroidal anti-inflammatory drugs such as Celebrex from Pfizer and opioids such as OxyContin from Purdue Pharma;
- for depression, selective serotonin reuptake inhibitors such as Prozac from Eli Lilly, Paxil from GlaxoSmithKline, Zoloft from Pfizer, Celexa and Lexapro from Forest Laboratories and the dual uptake inhibitor Effexor from Wyeth;
- for schizophrenia, anti-psychotics such as Seroquel from AstraZeneca, Zyprexa from Eli Lilly, Risperdal from Johnson & Johnson, Geodon from Pfizer and Abilify from Bristol-Myers Squibb; and
- for smoking cessation, Zyban from GlaxoSmithKline.

We may have substantial exposure to product liability claims and may not have adequate insurance to pay them.

We face an inherent business risk of exposure to product liability claims if the use of our products is alleged to have resulted in harm to others. This risk exists for product candidates in clinical trials, whether or not the product candidate is subsequently approved for commercial sale, as well as for products in commercial distribution. Any product liability claim arising in the future against us or any third party that we have agreed to indemnify, regardless of its merit or eventual adjudication, could be costly and significantly divert management's attention from conducting our business or adversely affect our reputation and the demand for our products.

We have secured product liability insurance coverage with limits of $8 million per occurrence and $8 million in the aggregate. Our current insurance coverage may not reimburse us or may not be sufficient to reimburse us for any expenses or losses we may incur. We intend to expand our coverage with respect to any products for which we obtain marketing approval. However, additional insurance may not be available to cover our potential liabilities fully or may be prohibitively expensive. In addition, some potential product liability claims may be excluded from coverage under the terms of the policy. Our inability to obtain adequate insurance coverage at an acceptable cost could prevent or impede the commercialization of our product candidates.

Our business activities involve hazardous materials, which could subject us to significant liability.

Our research and development activities involve, and any future manufacturing processes that we conduct may involve, the use of hazardous materials, including hazardous chemicals and radioactive materials. Accordingly, we are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of these materials. We incur significant costs to comply with these laws and regulations. Moreover, despite precautionary procedures that we implement, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident or environmental discharge, we may be held liable for any resulting damages. We do not carry insurance against the risk of contamination or injury from hazardous materials.

If our promotional activities fail to comply with the regulations and guidelines of the FDA and other applicable regulatory authorities, we may be subject to warnings or enforcement actions that could harm our business.

Physicians may prescribe drugs for uses that are not described in the product's labeling or for uses that differ from those tested in clinical studies and approved by the FDA or similar regulatory authorities in other countries. Regulatory authorities generally do not regulate the behavior of physicians in their choice of treatments. Regulatory authorities do, however, restrict communications on the subject of off-label use. Companies cannot actively promote approved drugs for off-label uses but, in some countries outside of the European Union, they may under specified conditions disseminate articles published in peer-reviewed journals that discuss off-label uses of approved products to physicians. To the extent allowed, we may in the future disseminate peer-reviewed articles on our products to physicians. We do not currently promote Inversine for off-label use in the treatment of any neuropsychiatric disorder. However, if we undertake any promotional activities in the future for Inversine or any other product candidate that we are able to commercialize and our activities fail to comply with these regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities.

Risks Related to Employees and Managing Growth

If we lose our key personnel or are unable to attract and retain additional skilled personnel, we may be unable to successfully develop and commercialize our product candidates or effectively compete in our industry.

Our performance depends substantially on the performance of our senior management and key scientific, technical and managerial personnel, including our Chief Executive Officer and President, J. Donald deBethizy, and our Vice President, Clinical Development and Regulatory Affairs, Geoffrey C. Dunbar. Our executive officers, including these individuals, can terminate their employment agreements with us at any time. The loss of the services of any of our executive officers may significantly delay or prevent the achievement of product research and development and other business objectives. We maintain key man life insurance policies on Dr. deBethizy and Dr. Dunbar, among other executive officers. We also rely on consultants and advisors to assist us in formulating our research and development strategy. All of our consultants and advisors are either self-employed or employed by other organizations, and they may have other commitments, including consulting or advisory contracts with other organizations, that may affect their ability to contribute to us.

Our ability to operate successfully and manage our potential future growth will depend on our ability to identify, recruit and retain additional qualified scientific, technical, financial and

managerial personnel. There is currently a shortage of skilled executives in our industry, and we face intense competition for such personnel. We may not be able to continue to attract and retain personnel with the advanced qualifications necessary for the growth of our business.

We may encounter difficulties in managing our growth, which could increase our losses.

We expect the number of our employees and the scope of our operations to grow following the completion of this offering. Continued growth may place a significant strain on our managerial, operational and financial resources, in particular as we expand our focus beyond drug discovery and development to commercialization. To manage our anticipated growth, we must continue to implement and improve our managerial, operational and financial systems and controls and reporting processes and procedures, to expand our facilities and to continue to recruit and train additional qualified personnel. We may not be able to manage our growth effectively. Moreover, we may discover deficiencies in existing systems and controls that could expose us to an increased risk of incurring financial or accounting irregularities or fraud.

Risks Related to Our Common Stock and this Offering

The market price of our common stock may be highly volatile. You may not be able to resell your shares at or above the initial public offering price.

There has been no public market for our common stock prior to this offering, and it is possible that no active trading market for our common stock will develop or continue following this offering. You may not be able to sell your shares quickly or at the market price if trading in our common stock is not active. The initial public offering price for the shares will be determined by negotiation with representatives of the underwriters and may not be indicative of prices that will prevail in the trading market. Please see “Underwriters” for more information regarding our arrangements with the underwriters and the factors to be considered in setting the initial public offering price.

We expect that the trading price of our common stock is likely to be highly volatile in response to factors that are beyond our control. The stock market in general has previously experienced extreme price and volume fluctuations. The market prices of securities of pharmaceutical and biotechnology companies have been extremely volatile and have experienced fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. These broad market fluctuations could result in extreme fluctuations in the price of our common stock, which could cause a decline in the value of your shares.

If you purchase shares of our common stock in this offering, you will experience immediate and substantial dilution of your investment.

The offering price of our common stock will be substantially higher than the net tangible book value of approximately $(602.73) per share, based on our existing capital stock as of December 31, 2005. As a result, based on an assumed initial public offering price of $12.00 per share, purchasers of our common stock in this offering will incur immediate and substantial dilution of $8.05 per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the assumed initial public offering price, and will incur $0.08 additional dilution if outstanding stock options and warrants with exercise prices below the public offering price are exercised. See “Dilution” for a more detailed discussion of the dilution new investors will incur in this offering.

If our operating results fluctuate significantly, our stock price may decline and result in losses to you.

Our operating results are likely to fluctuate significantly from quarter to quarter and year to year. These fluctuations could cause our stock price to decline. Some of the factors that could cause our operating results to fluctuate include:

- our inability, or the inability of AstraZeneca or any of our potential future collaborators, to successfully complete preclinical studies and clinical trials in a timely manner or at all, resulting in a delay in receiving, or a failure to receive, the required regulatory approvals to commercialize our product candidates;
- the timing of regulatory approvals or other regulatory actions;
- general and industry-specific economic conditions that may affect the research and development expenditures of AstraZeneca or any of our potential future collaborators;
- the timing of receipt of milestone payments from AstraZeneca or any of our potential future collaborators; and
- the expiration or termination of agreements with AstraZeneca or any of our potential future collaborators or the execution of new agreements.

Due to fluctuations in our operating results, a period-to-period comparison of our results of operations may not be a good indication of our future performance. In any particular quarter or quarters, our operating results could be below the expectations of securities analysts or investors and our stock price could decline.

If our existing stockholders sell a substantial number of shares of our common stock in the public market, our stock price may decline.

Sales of a substantial number of shares of our common stock in the public market following this offering could cause the market price to decline. Such sales also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. After this offering, we will have 19,104,838 shares of common stock outstanding based on the number of shares outstanding as of February 28, 2006. If there are more shares of our common stock offered for sale than buyers are willing to purchase, the market price of our common stock may decline to a market price at which buyers are willing to purchase the offered shares and sellers remain willing to sell the shares. The number of shares of our common stock available for sale in the public market is limited by restrictions under federal securities laws and under lock-up agreements that substantially all of our current stockholders have entered into with the underwriters. Except in limited circumstances, these lock-up agreements restrict our stockholders from selling or otherwise disposing of their shares for a period of 180 days after the date of this prospectus, subject to a possible extension, without the prior written consent of Deutsche Bank Securities Inc. on behalf of the underwriters. However, Deutsche Bank Securities may, in its sole discretion, release all or any portion of the common stock from the restrictions of the lock-up agreements. Deutsche Bank Securities does not have any pre-established conditions to waiving the terms of the lock-up agreements. Any determination to release any shares subject to the lock-up agreements would be based on a number of factors at the time of determination, including but not necessarily limited to the market price of the common stock, the liquidity of the trading market for the common stock, general market conditions, the number of shares proposed to be sold and the timing, purpose and terms of the proposed sale.

Additionally, of the 1,631,110 shares of our common stock that may be issued upon the exercise of options outstanding as of February 28, 2006, approximately 1,199,029 shares will be vested and eligible for sale 180 days after the date of this prospectus. For a further description of the eligibility of shares for sale into the public market following the offering, see “Shares Eligible for Future Sale.” In the future, we may issue additional shares to our employees, directors or consultants, in connection with corporate alliances or acquisitions or to raise capital. Accordingly, sales of a substantial number of shares of our common stock in the public market could occur at any time.

Management may invest or spend the proceeds of this offering in ways in which you may not agree or in ways that may not yield a favorable return to our stockholders.

Management will retain broad discretion over the use of the net proceeds from this offering. Stockholders may not agree with such uses, and our use of the proceeds may not yield a significant return or any return at all for our stockholders. We intend to use the proceeds from this offering for research and development and other general corporate purposes. Because of the number and variability of factors that will determine our use of the proceeds from this offering, their ultimate use may vary substantially from their currently intended use.

Concentration of ownership among our existing executive officers, directors and principal stockholders may prevent new investors from influencing significant corporate decisions.

Following the completion of this offering, our executive officers, directors and their affiliates will beneficially own or control approximately 38.3% of the outstanding shares of our common stock, excluding any shares that any of our directors or their affiliates may purchase in this offering. Accordingly, our current executive officers, directors and their affiliates will have substantial control over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transactions, as well as our management and affairs. The concentration of ownership may also delay or prevent a change of control of us at a premium price if these stockholders oppose it, even if it would benefit our other stockholders.

Provisions of our charter, bylaws and Delaware law may make an acquisition of us or a change in our management more difficult.

Provisions of our certificate of incorporation and bylaws that will be in effect upon the completion of this offering could discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which you might otherwise receive a premium for your shares. These provisions also could limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. Stockholders who wish to participate in these transactions may not have the opportunity to do so. Furthermore, these provisions could prevent or frustrate attempts by our stockholders to replace or remove our management. These provisions:

- allow the authorized number of directors to be changed only by resolution of our board of directors;
- establish a classified board of directors, providing that not all members of the board be elected at one time;
- authorize our board of directors to issue without stockholder approval blank check preferred stock that, if issued, could operate as a “poison pill” to dilute the stock

ownership of a potential hostile acquirer to prevent an acquisition that is not approved by our board of directors;

- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit stockholder action by written consent;
- establish advance notice requirements for stockholder nominations to our board of directors or for stockholder proposals that can be acted on at stockholder meetings;
- limit who may call stockholder meetings; and
- require the approval of the holders of 66 2/3% of the outstanding shares of our capital stock entitled to vote in order to amend certain provisions of our certificate of incorporation and bylaws.

In addition, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, which may, unless certain criteria are met, prohibit large stockholders, in particular those owning 15% or more of our outstanding voting stock, from merging or combining with us for a prescribed period of time.

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

Some of the statements under “Prospectus Summary,” “Risk Factors,” “Management’s Discussion and Analysis of Financial Condition and Results of Operations,” “Business” and elsewhere in this prospectus constitute forward-looking statements. These statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, levels of activity, performance or achievements to be materially different from the information expressed or implied by these forward-looking statements. While we believe that we have a reasonable basis for each forward-looking statement contained in this prospectus, we caution you that these statements are based on a combination of facts and factors currently known by us and projections of the future, about which we cannot be certain. Many important factors affect our ability to achieve our objectives, including the following:

- the success of our collaboration with AstraZeneca;
- the size and growth potential of the potential markets for our product candidates and our ability to serve those markets;
- the rate and degree of market acceptance of our product candidates;
- our plans to research, develop and commercialize our product candidates;
- the success of our clinical trials;
- the success of non-clinical studies conducted to further characterize our clinical stage product candidates;
- our ability to obtain and maintain regulatory approval for our product candidates;
- our use of the proceeds from this offering;
- the accuracy of our estimates regarding expenses, future revenues, capital requirements and needs for additional financing, and our ability to obtain additional financing;
- our ability to attract and to establish collaborations with pharmaceutical and biotechnology companies with development, regulatory and commercialization expertise;
- our ability to obtain and maintain intellectual property protection for our product candidates;
- the successful development of our marketing capabilities;
- the success of competing therapies that are or become available; and
- the performance of third-party manufacturers with which we contract to provide a supply of our product candidates.

In addition, you should refer to the “Risk Factors” section of this prospectus for a discussion of other important factors that may cause our actual results to differ materially from those expressed or implied by our forward-looking statements. As a result of these factors, we cannot assure you that the forward-looking statements in this prospectus will prove to be accurate. Furthermore, if our forward-looking statements prove to be inaccurate, the inaccuracy may be material. In light of the significant uncertainties in these forward-looking statements, you should not regard these statements as a representation or warranty by us or any other person that we will achieve our objectives and plans in any specified time frame, or at all. The Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act of 1933 do not protect any forward-looking statements that we make in connection with this offering.

You should read this prospectus completely. In some cases, you can identify forward-looking statements by the following words: “may,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “ongoing” or the negative of these terms or other comparable terminology, although not all forward-looking statements contain these words. We may not update these forward-looking statements even though our situation may change in the future. We qualify all the forward-looking statements contained in this prospectus by the foregoing cautionary statements.

USE OF PROCEEDS

We estimate that our net proceeds from the sale of 5,000,000 shares of our common stock in this offering will be approximately $54.7 million, or approximately $63.1 million if the underwriters exercise their over-allotment option in full, assuming an initial public offering price of $12.00 per share and after deducting estimated underwriting discounts and commissions and offering expenses payable by us. A $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share would increase (decrease) our net proceeds from this offering by approximately $4.7 million, or approximately $5.3 million if the underwriters exercise their over-allotment option in full, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions.

We currently estimate that we will use these net proceeds as follows:

- approximately $10 million to complete our ongoing Phase I clinical trial, to conduct Phase II clinical trials and to conduct formulation activities for TC-2696, our product candidate for acute post-operative pain;
- approximately $9 million to conduct the additional preclinical safety studies necessary to support an IND for clinical trials, to conduct Phase I and Phase II clinical trials of TC-2216, our product candidate for depression and anxiety disorders;
- approximately $6 million to conduct the additional preclinical safety studies necessary to support an IND for clinical trials and, unless licensed by us to AstraZeneca under the terms of our collaboration agreement, to conduct Phase I clinical trials of TC-5619;
- approximately $4 million to fund preclinical testing and other research and development activities in one or more of the areas of smoking cessation, obesity and inflammation;
- approximately $2 million to complete our ongoing Phase II clinical trial of mecamylamine hydrochloride as an add-on therapy for depression; and
- the remainder to fund general and administrative expenses, other research and development expenses, working capital needs and other general corporate purposes.

We may also use a portion of the net proceeds for the potential acquisition of, or investment in, technologies, products or companies that complement our business, although we have no current understandings, commitments or agreements to do so.

The amounts and timing of our actual expenditures may vary significantly depending upon numerous factors, including the progress and status of our development and commercialization efforts, the amount of proceeds actually raised in this offering, the amount of cash generated through our existing strategic collaboration with AstraZeneca, any additional strategic collaborations into which we may enter and sales of Inversine, and our operating costs and capital expenditures. Accordingly, our management will have significant flexibility in applying the net proceeds of this offering. We may change the allocation of use of these proceeds as a result of contingencies such as the progress and results of our clinical trials and other research and development activities, product development timelines and the status of our intellectual property position, a decision by us to conduct a Phase III clinical trial of mecamylamine hydrochloride or to accelerate the development of TC-5214 as an add-on therapy for depression in lieu of further advancement of mecamylamine hydrochloride, any decision by us to offer TC-5619 or any other compound to AstraZeneca and by AstraZeneca to license the compound under the terms of our collaboration agreement, the establishment of collaborations, the results of our commercialization efforts, our manufacturing requirements and regulatory or competitive

developments. In particular, if AstraZeneca terminates our collaboration agreement following the completion of the additional safety and product characterization studies of TC-1734 that AstraZeneca is conducting and we choose to fund the clinical development of TC-1734 on our own, we would need to use a substantial portion of the net proceeds of this offering for that purpose or seek additional funds from external sources.

Under our collaboration agreement, AstraZeneca will assume substantially all development costs for TC-1734. As a result, we do not expect to use any of the net proceeds of this offering in the development of TC-1734. We do not expect our existing capital resources and the net proceeds from this offering to be sufficient to enable us to fund the completion of the development of any of our other product candidates. We expect that the net proceeds from this offering will be sufficient to enable us to: complete our ongoing Phase II clinical trial of mecamylamine hydrochloride; conduct the additional preclinical safety studies necessary to support an IND for clinical trials, conduct Phase I and Phase II clinical trials of TC-2216; complete our ongoing Phase I clinical trial and conduct Phase II clinical trials of TC-2696; and conduct the additional preclinical safety studies necessary to support an IND for clinical trials and conduct Phase I clinical trials of TC-5619. It is possible that we will not make the progress that we expect because the actual costs and timing of drug development, particularly clinical trials, are highly uncertain, are subject to substantial risk and often change depending on the target indication, the particular development strategy and the results of earlier clinical trials. It is also possible that we will not make the progress that we expect because we change the allocation of use of the net proceeds of this offering as a result of contingencies, including any termination of our collaboration agreement by AstraZeneca or any of the other contingencies described in the preceding paragraph. As a result, we may need to raise additional funds from external sources to make the development progress described in this paragraph.

Until the funds are used as described above, we intend to invest the net proceeds from this offering in short-term interest-bearing, investment grade securities.

DIVIDEND POLICY

We have never declared or paid cash dividends on any of our shares of capital stock. We currently intend to retain future earnings, if any, to finance the expansion and growth of our business and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements and other factors that our board of directors deems relevant. In addition, the terms of any future debt or credit facility may preclude us from paying dividends.

CAPITALIZATION

The following table sets forth our capitalization at December 31, 2005:

- on an actual basis;
- on a pro forma basis to give effect to the conversion of all outstanding shares of our convertible preferred stock into 13,832,015 shares of common stock concurrently with the completion of this offering; and
- on a pro forma as adjusted basis to give further effect to our sale of 5,000,000 shares of common stock in this offering at an assumed initial public offering price of $12.00 per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us.

You should read this table together with our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section and other financial information included in this prospectus.

	As of December 31, 2005		
	Actual	Pro Forma	Pro Forma As Adjusted
		(in thousands, except share and per share data)	
Total long-term obligations	$ 2,193	$ 2,193	$ 2,193
Redeemable convertible preferred stock, $0.001 par value; 93,309,532 shares authorized, 88,505,565 shares issued and outstanding actual; no shares authorized, issued or outstanding pro forma and pro forma as adjusted	183,628	—	—
Stockholders' equity (deficit):			
Common stock, $0.001 par value; 16,666,666 shares authorized actual and pro forma; 100,000,000 shares authorized pro forma as adjusted; 270,427 issued and outstanding actual; 14,102,442 shares issued and outstanding pro forma; 19,102,442 shares issued and outstanding pro forma as adjusted	—	14	19
Preferred stock, $0.001 par value; no shares authorized, issued or outstanding actual and pro forma; 5,000,000 shares authorized and no shares issued and outstanding pro forma as adjusted	—	—	—
Capital in excess of par value (1)	12,288	159,405	214,126
Common stock warrants	214	214	—
Accumulated deficit	(174,983)	(138,486)	(138,258)
Total stockholders' equity (deficit) (1)	(162,481)	21,147	75,887
Total capitalization (1)	$ 23,340	$ 23,340	$ 78,080

(1) A $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share would increase (decrease) each of capital in excess of par value, total stockholders' equity (deficit) and total capitalization by approximately $4.7 million, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same

and after deducting estimated underwriting discounts and commissions. The pro forma information discussed above is illustrative only and following the completion of this offering will be adjusted based on the actual initial public offering price and other terms of this offering determined at pricing.

The table above does not include:

- 1,610,009 shares of common stock issuable upon exercise of options outstanding as of December 31, 2005, at a weighted average exercise price of $2.88 per share, of which options to purchase 979,784 shares were exercisable; and
- 54,465 shares of common stock reserved for future grant under our 2000 equity incentive plan as of December 31, 2005.

DILUTION

If you invest in our common stock, your interest will be diluted immediately to the extent of the difference between the initial public offering price per share of our common stock and the pro forma net tangible book value of our common stock immediately after completion of this offering.

The historical net tangible book value of our common stock as of December 31, 2005 was approximately $(163.0) million, or approximately $(602.73) per share, based on 270,427 shares of common stock outstanding as of December 31, 2005. Historical net tangible book value per share represents our total tangible assets less total liabilities divided by the actual number of shares of our common stock outstanding.

As of December 31, 2005, the pro forma net tangible book value of our common stock was approximately $20.6 million, or approximately $1.46 per share. Pro forma net tangible book value per share represents our total tangible assets less total liabilities divided by the pro forma number of shares of our common stock outstanding, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into 13,832,015 shares of common stock concurrently with the completion of this offering.

Assuming the sale of the 5,000,000 shares of our common stock offered by this prospectus at an assumed initial public offering price of $12.00 per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us, our pro forma net tangible book value as of December 31, 2005 would have been $75.4 million, or $3.95 per share. This represents an immediate increase in pro forma net tangible book value of $2.49 per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of $8.05 per share to new investors purchasing in this offering at the initial public offering price. The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share		$12.00
Historical net tangible book value per share	$(602.73)	
Increase attributable to the conversion of convertible preferred stock	604.19	
Pro forma net tangible book value per share before this offering	1.46	
Increase per share attributable to new investors	2.49	
Pro forma net tangible book value per share after this offering		3.95
Dilution per share to new investors		$ 8.05

A $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share would increase (decrease) our pro forma net tangible book value per share after this offering by approximately $0.24 and dilution per share to new investors by approximately $0.76, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same and after deducting estimated underwriting discounts and commissions.

The following table summarizes, on a pro forma basis as of December 31, 2005, the total number of shares of common stock purchased from us, the total consideration paid and the average price per share paid by existing stockholders and by new investors purchasing shares in this offering at an assumed initial public offering price of $12.00 per share, before deducting estimated underwriting discounts and commissions and offering expenses payable by us.

	Shares Purchased		Total Consideration		
	Number	Percent	Amount	Percent	Average Price per Share
Existing stockholders	14,102,442	73.8%	$149,092,000	71.3%	$ 10.57
New investors	5,000,000	26.2	60,000,000	28.7	12.00
Total	19,102,442	100.0%	$209,092,000	100.0%	

A $1.00 increase (decrease) in the assumed initial public offering price of $12.00 per share would increase (decrease) the total consideration paid by new investors by $5.0 million and increase (decrease) the percent of total consideration paid by new investors by approximately 1.7%, assuming that the number of shares offered by us, as set forth on the cover page of this prospectus, remains the same.

The share data in the table above is based on shares outstanding as of December 31, 2005, counting as outstanding 13,832,015 shares of common stock underlying all outstanding convertible preferred stock.

The share data in the table above excludes:

- 1,610,009 shares of common stock issuable upon the exercise of options outstanding as of December 31, 2005, at a weighted average exercise price of $2.88 per share, of which options to purchase 979,784 shares were exercisable;
- 54,465 shares of common stock reserved for future grant under our 2000 equity incentive plan as of December 31, 2005; and
- 215,054 shares of common stock subject to an outstanding warrant with an exercise price of $14.63 per share that will expire if not exercised concurrently with the completion of this offering.

If the underwriters exercise their over-allotment in full, the following will occur:

- the number of shares of our common stock held by existing stockholders would decrease to approximately 71% of the total number of shares of our common stock outstanding after this offering; and
- the number of shares of our common stock held by new investors would increase to 5,750,000 shares, or approximately 29% of the total number of our common stock outstanding after this offering.

SELECTED FINANCIAL DATA

You should read the following selected financial data together with our financial statements and the related notes appearing at the end of this prospectus and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section and other financial data included in this prospectus.

We have derived the statement of operations data for the years ended December 31, 2003, 2004 and 2005 and the balance sheet data as of December 31, 2004 and 2005 from our audited financial statements included in this prospectus. We have derived the statement of operations data for the years ended December 31, 2001 and 2002 and the balance sheet data as of December 31, 2001 and 2002 from our audited financial statements not included in this prospectus. We became an independent company in August 2000, prior to which we were a wholly owned subsidiary of R.J. Reynolds Tobacco Company. Our historical results for any prior period are not necessarily indicative of the results to be expected for any future period.

The pro forma net loss attributable to common stockholders per share information is computed using the weighted average number of common shares outstanding, after giving pro forma effect to the conversion of all outstanding shares of our convertible preferred stock into 13,832,015 shares of common stock concurrently with the completion of this offering, as if the conversion had occurred at the date of the original issuance.

	Year ended December 31,				
	2001	2002	2003	2004	2005
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Net revenue	$ 1,703	$ 2,286	$ 2,458	$ 3,738	$ 1,180
Operating expenses:					
Research and development	8,152	16,244	18,179	22,771	24,252
General and administrative	2,302	4,135	3,600	5,163	6,388
Cost of product sales	—	244	743	198	481
Purchased in-process research and development	—	2,666	—	—	—
Total operating expenses	10,454	23,289	22,522	28,132	31,121
Loss from operations	(8,751)	(21,003)	(20,064)	(24,394)	(29,941)
Interest and dividend income	1,449	88	791	505	1,174
Interest expense	—	(103)	(122)	(132)	(225)
Loss on disposal of fixed assets	—	(54)	—	(4)	—
Net loss	(7,302)	(21,072)	(19,395)	(24,025)	(28,992)
Deemed dividend—beneficial conversion feature for Series C redeemable convertible preferred stock issued December 2004	—	—	—	(10,312)	—
Preferred stock accretion	(3,808)	(4,173)	(8,341)	(8,744)	(11,238)
Net loss attributable to common stockholders	$ (11,110)	$(25,245)	$ (27,736)	$ (43,081)	$ (40,230)
Basic and diluted net loss per share applicable to common stockholders	$(200.97)	$(339.63)	$ (254.33)	$ (196.53)	$ (153.54)
Shares used to compute basic and diluted net loss per share	55,283	74,332	109,053	219,213	262,013
Pro forma basic and diluted net loss per share applicable to common stockholders (unaudited)					$ (2.06)
Shares used to compute pro forma basic and diluted net loss per share (unaudited)					14,068,182

	As of December 31,				
	2001	2002	2003	2004	2005
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 21,180	$ 49,361	$ 42,977	$ 53,075	$ 24,851
Working capital	20,371	46,685	40,526	50,079	20,531
Total assets	24,396	54,379	47,390	58,204	28,001
Long-term debt, net of current portion	—	2,088	1,462	3,443	1,409
Redeemable convertible preferred stock	58,365	108,026	130,134	171,778	183,628
Accumulated deficit	(38,691)	(63,936)	(91,672)	(134,754)	(174,983)
Total stockholders' equity (deficit)	(38,268)	(63,335)	(90,796)	(122,966)	(162,481)

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes appearing at the end of this prospectus. Some of the information contained in this discussion and analysis or set forth elsewhere in this prospectus, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. You should read the "Risk Factors" section of this prospectus for a discussion of important factors that could cause actual results to differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Overview

We are a biopharmaceutical company engaged in the design, discovery and development of a new class of drugs to treat multiple diseases and disorders of the central nervous system by selectively targeting a class of receptors known as neuronal nicotinic receptors, or NNRs. We are developing our most advanced product candidates as treatments for target indications in three therapeutic areas: cognitive impairment, depression and anxiety, and pain. Within these areas, we have three product candidates in clinical development and two preclinical product candidates. Our lead product candidate is a novel small molecule that we refer to as TC-1734. In December 2005, we entered into a collaborative research and license agreement with AstraZeneca AB for the development and worldwide commercialization of TC-1734 as a treatment for Alzheimer's disease, cognitive deficits in schizophrenia and potentially other conditions marked by cognitive impairment such as attention deficit hyperactivity disorder, commonly referred to as ADHD, age associated memory impairment, commonly referred to as AAMI, and mild cognitive impairment, commonly referred to as MCI. In March 2006, we completed a Phase II clinical trial of TC-1734 in AAMI that we conducted at our own expense to further assess the effects of TC-1734 on cognition in a cognitively impaired older adult population. Mecamylamine hydrochloride, our product candidate currently in a Phase II clinical trial as an add-on therapy for depression, is the active ingredient in Inversine, our product approved in the United States for moderately severe to severe essential hypertension.

We trace our scientific lineage to a research program initiated by R.J. Reynolds Tobacco Company in 1982 to study the activity and effects of nicotine in the body and the function of nicotinic receptors. We were incorporated in Delaware in 1997 as a wholly owned subsidiary of RJR. In August 2000, we became an independent company when we issued shares of our series B convertible preferred stock to outside investors.

We have devoted substantially all of our resources to the discovery and development of our product candidates and technologies, including the design, conduct and management of preclinical and clinical studies and related manufacturing, regulatory and clinical affairs, and intellectual property prosecution. Through 1998, we received all of our funding from RJR. At the end of 1998, we entered into a collaboration agreement with the predecessor company to Aventis Pharma SA. Aventis Pharma SA is now controlled by Sanofi-Aventis. We received an upfront license fee and research support payments under this agreement which, together with a modest amount of additional financial support from RJR, funded our activities through August 2000. Since August 2000, we have funded our operations primarily through the private placement of equity securities and, to a much lesser extent, through payments we received from our collaborators, equipment and building lease incentive financing, sales of our product Inversine and government grants.

We have never been profitable. As of December 31, 2005, we had an accumulated deficit of $175.0 million. We expect to continue to incur substantial losses for the foreseeable future. We expect our research and development expenses to increase substantially following the completion of this offering as we expand our clinical trial activity, as our product candidates advance through the development cycle and as we invest in additional product opportunities and research programs. We also expect our general and administrative expenses to increase substantially due to costs associated with being a public company. Clinical trials and preclinical studies are time-consuming, expensive and may never yield a product that will generate revenue. A substantial portion of our revenue for the next several years will depend on the conduct of research and the successful achievement of milestone events in the development of TC-1734 under our agreement with AstraZeneca. Our revenue may vary substantially from quarter to quarter and year to year. We believe that period-to-period comparisons of our results of operations are not meaningful and should not be relied upon as indicative of our future performance.

We currently have one FDA approved product, Inversine. We acquired rights to Inversine in August 2002. Inversine is approved for the management of moderately severe to severe essential hypertension, a high blood pressure disorder with an unknown cause. However, we believe that Inversine is prescribed predominantly for the treatment of neuropsychiatric disorders, including Tourette's syndrome, autism and bipolar disorder, in children and adolescents. Sales of Inversine generated revenue of $767,000 for the year ended December 31, 2004 and $681,000 for the year ended December 31, 2005.

Our agreement with AstraZeneca relating to TC-1734 became effective in January 2006. AstraZeneca paid us an initial fee of $10 million in February 2006. AstraZeneca has agreed to make an additional payment to us of $20 million if it decides to conduct a Phase II clinical trial of TC-1734 following the completion of additional safety and product characterization studies that AstraZeneca is conducting at its expense to generate further data with respect to TC-1734. We expect AstraZeneca to complete these safety and product characterization studies within approximately 12 to 15 months from January 2006. We are eligible to receive other payments of up to $249 million, contingent upon the achievement of development, regulatory and first commercial sale milestones for TC-1734 for Alzheimer's disease, cognitive deficits in schizophrenia and ADHD, and royalties on future product sales. If TC-1734 is developed under the agreement for indications other than Alzheimer's disease, cognitive deficits in schizophrenia and ADHD, we would also be eligible to receive payments contingent upon the achievement of development, regulatory and first commercial sale milestones for TC-1734 for those indications. Under the terms of a sponsored research agreement and a subsequent license agreement between us and the University of Kentucky Research Foundation, or UKRF, we are required to pay to UKRF a low single digit percentage of any of these payments, including royalties, that we receive from AstraZeneca.

If AstraZeneca decides to initiate a Phase II clinical trial of TC-1734 following the completion of the additional safety and product characterization studies, we would be entitled under the agreement to receive a minimum of approximately $23.7 million in aggregate research fees over the four-year term of an a4ß2 research collaboration that we and AstraZeneca have initiated under the agreement. Based on the current budget for the research collaboration, we expect to receive approximately $26.4 million in aggregate research fees under the agreement. However, AstraZeneca can terminate our agreement if it determines in its sole discretion on or before April 20, 2007 not to proceed with the further development of TC-1734 based on the results of the additional safety and product characterization studies and all other available information with respect to TC-1734. In that event, we would be required to reimburse AstraZeneca for the amount of all research fees that it paid to us under the a4ß2 research collaboration while

AstraZeneca conducted the studies, which we expect to be approximately $2.5 million. We would also be required to pay to AstraZeneca an additional $5 million as compensation for assigning to us the data and any intellectual property generated in the studies, but we would not be required to refund the $10 million initial fee that AstraZeneca has paid us.

We previously entered into two collaboration agreements with Aventis. One of those collaboration agreements with Aventis terminated effective January 2, 2005. The research term for the other collaboration agreement with Aventis expired on December 31, 2004. As of December 31, 2005, we had received a total of $8.0 million in upfront license fees and payments for research and development services under the two agreements. We will not receive any additional amounts under the agreements.

In December 2004, we entered into a development agreement with The Stanley Medical Research Institute relating to the development of one of our compounds for the treatment of cognitive deficits in schizophrenia. Upon effectiveness of the agreement, The Stanley Medical Research Institute paid us $1.3 million in return for our issuance of a convertible promissory note in an equal principal amount. In August 2005, we repaid the promissory note in full. We and The Stanley Medical Research Institute terminated the development agreement in December 2005 in anticipation of our collaboration agreement with AstraZeneca.

In January 2001, we entered into a collaboration agreement with Dr. Falk Pharma GmbH covering the development and commercialization of one of our compounds for the treatment of ulcerative colitis and other gastrointestinal and liver diseases. Upon effectiveness of the collaboration agreement, Dr. Falk Pharma paid us a $1.0 million upfront license fee and purchased $1.0 million of our common stock. We and Dr. Falk Pharma shared the development costs for the lead compound subject to the collaboration agreement. We and Dr. Falk Pharma discontinued the development of the lead compound in the fourth quarter of 2004 and have terminated this agreement.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets, liabilities, revenues and expenses. On an ongoing basis, we evaluate these estimates and judgments, including those described below. We base our estimates on historical experience and on various other assumptions that we believe to be reasonable under the circumstances. These estimates and assumptions form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results and experiences may differ materially from these estimates.

While our significant accounting policies are more fully described in Note 2 to our financial statements included at the end of this prospectus, we believe that the following accounting policies are the most critical to aid you in fully understanding and evaluating our reported financial results and affect the more significant judgments and estimates that we use in the preparation of our financial statements.

Revenue Recognition

Our collaboration agreements contain multiple elements, including upfront fees, research fees for ongoing research and development, payments associated with achieving development, regulatory and commercialization milestones and royalties to be paid based on specified

percentages of net product sales or net profits, if any. We consider a variety of factors in determining the appropriate method of revenue recognition under these arrangements such as whether the elements are separable, whether there are determinable fair values and whether there is a unique earnings process associated with a particular element of an agreement.

We recognize research fee revenue from research services performed under our collaboration agreements as research is performed and related expenses are incurred. We defer upfront fees and amortize them over the estimated research and development period. All revenue to date under collaboration agreements, or under government grants, is non-refundable. We recognize revenue based on the achievement of development and regulatory milestones that carry substantive performance risk upon achievement of the milestone event. As of December 31, 2005, we have not received payment of any milestone-based revenues. We record product sales revenues when goods are shipped, at which point title has passed, and we establish an allowance for estimated returns at that time.

We are eligible to receive future research fees, license fees and milestone payments under our collaboration agreement with AstraZeneca. The amount of research fees, license fees and milestone payments will depend on the extent of our research activities and the timing and achievement of development, regulatory and first commercial sale milestone events. AstraZeneca paid us an initial fee of $10 million in February 2006. Based on the agreement terms, we allocated $5 million of the initial fee to the a4ß2 research collaboration, which we expect to recognize as revenue over the four-year term of the research collaboration. We deferred recognition of the remaining $5 million of the initial fee, which we allocated to the TC-1734 license grants, until AstraZeneca makes a determination whether to conduct Phase II clinical development of TC-1734 following the completion of additional safety and product characterization studies that AstraZeneca is conducting. If AstraZeneca decides to conduct a Phase II clinical trial of TC-1734 following the completion of the safety and product characterization studies, we would recognize the deferred $5 million of the initial fee as revenue over the expected development period for TC-1734. We expect to recognize any revenue based on the achievement of milestones under the collaboration agreement upon achievement of the milestone event, if we determine that the revenue satisfies the revenue recognition requirements of generally accepted accounting principles and Securities and Exchange Commission Staff Accounting Bulletin, or SAB 101, *Revenue Recognition in Financial Statements*, as amended by SAB No. 104, *Revenue Recognition (replacement of SAB 101)*. SAB 101 requires that four basic criteria must be met before revenue can be recognized: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed and determinable; and collectibility is reasonably assured. We will record research fees that we receive from AstraZeneca while it is conducting the safety and product characterization studies on TC-1734 as deferred revenue. If the agreement continues in effect following the completion of the additional safety and product characterization studies that AstraZeneca is conducting, we will recognize all research fees previously recorded as deferred revenue and recognize future research fee revenues as the research is performed and related expenses are incurred.

Accrued Expenses

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates

of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. To date, we have not adjusted our estimate at any particular balance sheet date in any material amount. Examples of estimated accrued expenses include:

- fees paid to contract research organizations in connection with preclinical and toxicology studies and clinical trials;
- fees paid to investigative sites in connection with clinical trials;
- fees paid to contract manufacturers in connection with the production of clinical trial materials and Inversine; and
- professional service fees.

We base our expenses related to clinical trials on our estimates of the services received and efforts expended pursuant to contracts with multiple research institutions and clinical research organizations that conduct and manage clinical trials on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. Payments under some of these contracts depend on factors such as the successful enrollment of patients and the completion of clinical trial milestones. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we will adjust the accrual accordingly. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates.

Stock-Based Compensation

Effective January 1, 2005, we adopted Statement of Financial Accounting Standard No. 123(R), *Share-Based Payment*, or SFAS 123R. Under SFAS 123R, we recognize the grant-date fair value of stock options and other stock-based compensation issued to employees and non-employee directors over the requisite service periods, which are typically the vesting periods. We currently use the Black-Scholes formula to estimate grant-date fair value and expect to continue to use this valuation model in the future. We have adopted SFAS 123R using the modified-prospective-transition method, which requires us to record compensation expense for the non-vested portion of previously issued awards that were outstanding at January 1, 2005, and any awards issued or modified after January 1, 2005. We recorded stock-based compensation expense related to stock options granted to employees and directors of $690,000 in 2005. As of December 31, 2005, we had $989,000 in total unrecognized compensation cost related to non-vested stock-based compensation arrangements, which we expect to recognize over a weighted average period of 3.3 years.

The fair value of our common stock underlying stock options and other stock-based compensation granted to employees and non-employee directors has historically been determined by our board of directors based upon information available as of the grant dates. We engaged an independent valuation firm in January 2006 to perform a retrospective analysis to determine the deemed fair market value of our common stock as of March 31, 2005 for accounting purposes in light of the potential initial public offering of our common stock. This retrospective analysis relied on income-based and market-based valuation methodologies. The independent valuation firm determined the fair market value of our common stock as of March 31, 2005 to be $1.60 per share.

For all periods prior to January 1, 2005, we accounted for our employee stock-based compensation using the intrinsic value method in accordance with Accounting Principles Board Opinion No. 25 and related interpretations, or APB 25. Under APB 25, we recognized compensation expense for stock options granted to employees and non-employee directors only if the exercise price was below the fair market value of the underlying common stock on the date of grant. We recognized this compensation expense over the vesting periods of the shares purchasable upon exercise of options. We recorded deferred stock-based compensation related to stock options granted to employees and directors of $65,000 in 2003 and $51,000 in 2004. We amortized our deferred stock-based compensation on a straight-line basis over the related option vesting periods, which range from immediate vesting to four years.

As required by Statement of Financial Accounting Standards No. 123, *Accounting for Stock-Based Compensation,* or SFAS 123, as amended by SFAS No. 148, *Accounting for Stock-Based Compensation—Transition and Disclosure*, our financial statement footnotes disclose on a pro forma basis the amount of compensation expense that we would have recorded for periods prior to January 1, 2005, had we applied the fair value option methodology described in SFAS 123. Had we recorded all of our stock-based compensation using the SFAS 123 fair value methodology, our compensation expense would have been approximately $866,000 greater and our diluted net loss per share attributable to common stockholders would have been approximately $3.96 greater in 2004. For more information, you should refer to Note 2 to our financial statements included at the end of this prospectus.

Financial Operations Overview

Revenue

Inversine is our only approved product generating revenue. Sales of Inversine generated revenue of $815,000 for the year ended December 31, 2003, $767,000 for the year ended December 31, 2004 and $681,000 for the year ended December 31, 2005. We have an exclusive distribution agreement with Cord Logistics, Inc., a Cardinal Health company, for the distribution of Inversine. We do not have or use a sales force or actively promote Inversine. Accordingly, we do not anticipate any significant increase in Inversine sales. If any of the very limited number of physicians that most often prescribe Inversine were to cease to do so, revenue generated by Inversine sales would likely be substantially less. We have no other commercial products for sale and do not anticipate that we will have any other commercial products for sale for at least the next several years.

Our collaboration agreement with AstraZeneca became effective in January 2006. AstraZeneca paid us an initial fee of $10 million in February 2006. AstraZeneca has agreed to make an additional payment to us of $20 million if it decides to conduct a Phase II clinical trial of TC-1734 following the completion of the additional safety and product characterization studies that AstraZeneca is conducting at its expense to generate further data with respect to TC-1734. We expect AstraZeneca to complete these safety and product characterization studies within approximately 12 to 15 months from January 2006. We are eligible to receive other payments of up to $249 million, contingent upon the achievement of development, regulatory and first commercial sale milestones for TC-1734 for Alzheimer's disease, cognitive deficits in schizophrenia and ADHD, and royalties on future product sales. If TC-1734 is developed under the agreement for indications other than Alzheimer's disease, cognitive deficits in schizophrenia and ADHD, we would also be eligible to receive payments contingent upon the achievement of development, regulatory and first commercial sale milestones for TC-1734 for those indications. Under the terms of a sponsored research agreement and a subsequent license agreement between us and UKRF, we are required to pay to UKRF a low single digit percentage of any of these amounts that we may receive from AstraZeneca. If AstraZeneca terminates our agreement

upon completion of any or all of the safety and product characterization studies, we would be required to reimburse AstraZeneca for the amount of all research fees that it paid to us under the a4ß2 research collaboration while it conducted the studies. In that event, we would also be required to pay AstraZeneca an additional $5 million as compensation for assigning to us the data and any intellectual property generated in the studies, but we would not be required to refund the $10 million initial fee that AstraZeneca has paid us.

Upon effectiveness of our collaboration agreement, we and AstraZeneca initiated preclinical research designed to discover and develop additional compounds that, like TC-1734, act on the a4ß2 NNR. During the period that AstraZeneca is conducting the safety and product characterization studies, AstraZeneca has agreed to pay us research fees equal to 50% of our research expenses. If our agreement with AstraZeneca continues in effect following the completion of the safety and product characterization studies, AstraZeneca has agreed to pay us the remaining 50% of our research expenses incurred while those studies were conducted and thereafter research fees equal to 100% of our research expenses in the collaboration, subject to specified limits. In that event, we would be entitled to receive a minimum of $23.7 million in aggregate research fees over the four-year term of the a4ß2 research collaboration. Based on the current budget for the research collaboration, we expect to receive approximately $26.4 million in aggregate research fees under the agreement. The research fees that AstraZeneca has agreed to pay us are based on a negotiated rate designed to approximate our personnel costs to conduct the research.

Other revenue has consisted primarily of amounts earned for providing research and development services under our two collaboration agreements with Aventis and non-refundable upfront license fees that we received in connection with our first agreement with Aventis and our collaboration agreement with Dr. Falk Pharma. We received research support payments from Aventis of $1.3 million for the year ended December 31, 2003 and $338,000 for the year ended December 31, 2004. We did not receive any research support payments from Aventis in 2005. The research term of our continuing agreement with Aventis ended in December 2004. We will not receive additional research support payments from Aventis under the agreement.

In 2003, we were awarded a cooperative agreement from the National Institute of Standards and Technology through its Advanced Technology Program. The terms of the agreement provide for us to receive up to $1.9 million over a three-year period to help fund the development of sophisticated new computer simulation software designed to more accurately predict biological and toxicological effects of drugs. The agreement provides for reimbursement of costs that we incur to perform specified work that is designed to meet the objectives of the agreement. We recognize grant revenue as we perform the work and incur reimbursable costs. Funding for awards under this program is subject to the availability of funds as determined annually in the federal appropriations process.

Research and Development Expense

Since our inception, we have focused our activities on our drug discovery and development programs. We expense research and development expenses as they are incurred. Research and development expenses represented approximately 81% of our total operating expenses for each of the years ended December 31, 2003 and 2004 and 78% of our total operating expenses for the year ended December 31, 2005.

Research and development expense includes expenses associated with:

- the employment of personnel involved in our drug discovery and development activities;
- research and development facilities and equipment;

- the screening, identification and optimization of product candidates;
- the development and enhancement of Pentad;
- formulation and process synthesis;
- production of clinical materials, including fees paid to contract manufacturers;
- preclinical animal studies, including the costs to engage third-party research organizations;
- clinical trials, including fees paid to contract research organizations to monitor and oversee some of our trials;
- quality assurance activities;
- compliance with FDA regulatory requirements;
- consulting, license and sponsored research fees paid to third parties;
- depreciation of capital assets used to develop our products; and
- stock options or other stock-based compensation granted to personnel in research and development functions.

We use our employee and infrastructure resources across several projects. Consistent with our focus on the development of a class of drugs with potential uses in multiple indications, many of our costs are not attributable to a specifically identified project. Instead, these costs are directed to broadly applicable research efforts. Accordingly, we do not account for internal research and development costs on a project-by-project basis. As a result, we cannot state precisely the total costs incurred for each of our clinical and preclinical projects on a project-by-project basis.

The following table shows, for the periods presented, total payments that we made to third parties for preclinical study support, clinical supplies and clinical trial services for TC-1734, mecamylamine hydrochloride, TC-2216 and TC-2696:

	Year ended December 31,		
Product Candidate	**2003**	**2004**	**2005**
		(in thousands)	
TC-1734	$3,557	$4,135	$6,713
Mecamylamine hydrochloride	—	—	1,067
TC-2216	—	—	903
TC-2696	893	1,145	879
	$4,450	$5,280	$9,562

At the end of 2004, we discontinued the development of two product candidates following the completion of Phase II clinical trials. We made total payments to third parties of $2.1 million for the year ended December 31, 2003, $4.3 million for the year ended December 31, 2004 and $83,000 for the year ended December 31, 2005 in connection with these discontinued programs.

Our expenditures on current and future preclinical and clinical development programs are subject to numerous uncertainties in timing and cost to completion. We test compounds in numerous preclinical studies for safety, toxicology and efficacy. We then conduct clinical trials for those product candidates that we determine to be the most promising. If we do not establish a collaboration covering the development of a particular product candidate, we fund these trials

ourselves. As we obtain results from clinical trials, we may elect to discontinue or delay trials for some product candidates in order to focus our resources on more promising product candidates. Completion of clinical trials by us or our collaborators may take several years or more, but the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product candidate. The cost of clinical trials may vary significantly over the life of a project as a result of a variety of factors, including:

- the number of patients who participate in the trials;
- the number of sites included in the trials;
- the length of time required to enroll trial participants;
- the duration of patient follow-up;
- the costs of producing supplies of the product candidates needed for clinical trials and regulatory submissions;
- the efficacy and safety profile of the product candidate; and
- the costs and timing of, and the ability to secure, regulatory approvals.

We have not received FDA or foreign regulatory marketing approval for any of our product candidates that are in development. In order to achieve marketing approval, the FDA or foreign regulatory agencies must conclude that our or our collaborators' clinical data establishes the safety and efficacy of the product candidates. Furthermore, our strategy includes entering into collaborations with third parties to participate in the development and commercialization of some of our product candidates. In situations in which third parties have control over the preclinical development or clinical trial process for a product candidate, the estimated completion date is largely under control of that third party and not under our control. We cannot forecast with any degree of certainty which of our product candidates will be subject to future collaborations or how such arrangements would affect our development plans or capital requirements.

As a result of the uncertainties discussed above, we are unable to determine the duration and completion costs of our research and development projects or when and to what extent we will generate revenues from the commercialization and sale of any of our development stage product candidates.

General and Administrative Expense

General and administrative expense consists principally of salaries and other related costs for personnel in executive, finance, accounting, business development and human resource functions. Other general and administrative expenses include expenses associated with stock options and other stock-based compensation granted to personnel in those functions, facility costs not otherwise included in research and development expense, patent related costs, and professional fees for consulting, legal and accounting services.

Cost of Product Sales

Cost of product sales are those costs related directly to the sale of Inversine and are principally comprised of cost of goods sold, FDA product license fees, distribution expenses, product royalty obligations and product liability insurance.

Interest and Dividend Income

Interest and dividend income consists of interest and dividends earned on our cash, cash equivalents and short-term investments.

Interest Expense

Interest expense consists of interest incurred to finance equipment, office furniture and fixtures.

Income Taxes

We have incurred net operating losses since our incorporation in 1997 and consequently have not paid federal, state or foreign income taxes in any period. We had net operating loss carryforwards of approximately $98.3 million for each of federal and state income tax purposes as of December 31, 2005. We also had $2.1 million in research and development federal income tax credits as of December 31, 2005. Utilization of the net operating loss carryforwards and credits may be subject to a substantial annual limitation due to ownership change limitations provided by Section 382 of the Internal Revenue Code of 1986, as amended, and similar state provisions. As a result of a series of stock issuances, we had such an ownership change on November 30, 2002 and we could experience additional ownership changes as a result of this offering or in the future. When an ownership change, as defined by Section 382, occurs, an annual limitation is imposed on a company's use of net operating loss and credit carryforwards attributable to periods before the change. For financial reporting purposes, we have recorded a valuation allowance to fully offset the deferred tax asset related to these carryforwards because realization of the benefit was uncertain.

Results of Operations

Years ended December 31, 2005 and December 31, 2004

Revenue

Revenue decreased by $2.6 million, or 68%, to $1.2 million for the year ended December 31, 2005, from $3.7 million for 2004. The decrease was primarily attributable to our recognition in 2004 of $1.9 million in license fee revenue. Because we concluded our research obligations under our collaboration agreements with both Aventis and Dr. Falk Pharma in the fourth quarter of 2004, we recognized the remaining unamortized deferred upfront license fee balance at that time and recognized no license fee revenue for 2005. The decrease in revenue for 2005 was also attributable in part to the conclusion at the end of 2004 of our research activities under our collaboration agreement with Aventis, from which we derived $338,000 in research fees in 2004 and no research fee revenue in 2005.

In future periods, we are eligible to receive research fees, license fees and milestone payments under our collaboration agreement with AstraZeneca. The amount of research fees, license fees and milestone fees will depend on the extent of our research activities and the timing and achievement of development, regulatory and first commercial sale milestone events.

Grant revenue decreased to $499,000 in 2005, from $717,000 for 2004. The grant revenue in both periods resulted from work performed under a cooperative agreement awarded to us in the third quarter of 2003 by the National Institute of Standards and Technology through its Advanced Technology Program to fund the development of sophisticated molecular simulation software. The award was structured to provide a greater amount of funding in 2004 to enable us

to purchase hardware and software required to carry out the cooperative agreement activities. The term of the award expires September 30, 2006. As of December 31, 2005, we were eligible to receive up to an additional $710,000 of funding under the award. In addition, we are a named subcontractor under a grant awarded by the National Cooperative Drug Discovery Group, a National Institutes of Health program, to a university to fund the characterization of specified neuronal nicotinic receptor subtypes as potential targets in the development of therapies for smoking cessation. We have applied to receive a permit from the Office of Laboratory Animal Welfare. If we receive the permit, we expect to receive approximately $1.0 million over five years in connection with this grant, beginning in 2006.

Net sales of Inversine decreased by $85,000 to $681,000 for the year ended December 31, 2005, from $767,000 for 2004. This decrease resulted from a reduction in the volume of sales of Inversine. We believe that the substantial majority of Inversine sales are derived from prescriptions written by a very limited number of physicians. If any of these physicians were to change their prescribing habits, it would likely cause sales of Inversine to decrease. We do not promote sales of Inversine.

Research and Development Expense

Research and development expense increased by $1.5 million, or 7%, to $24.3 million for the year ended December 31, 2005, from $22.8 million for 2004. The increase was principally attributable to an increase of $2.6 million in expenses related to the clinical development, formulation and manufacturing of TC-1734, an increase of $1.1 million in clinical development expenses for mecamylamine hydrochloride, an increase of $608,000 in expenses related to the preclinical development of TC-2216 and other preclinical programs and an increase of $1.7 million in salaries and infrastructure costs for 2005 as compared to 2004. The increase in research and development salaries and infrastructure costs includes $458,000 of non-cash stock-based employee compensation charges attributable to our adoption of SFAS 123R as of January 1, 2005. There were no stock-based employee compensation charges included in our research and development expense for 2004. These increases were partially offset by a decrease in external costs resulting from our discontinuation in the fourth quarter of 2004 of clinical programs for two of our product candidates. One of these candidates, which was in development for the treatment of ADHD, resulted in a decrease in external costs of $2.3 million for 2005 as compared to 2004. The other product candidate, which was in development for the treatment of ulcerative colitis, resulted in a decrease in external costs of $1.9 million for 2005 as compared to 2004.

For the year ended December 31, 2005, we estimate that approximately 28% of our total research and development expenses were payments made to third parties in connection with our development of TC-1734, 4% were payments made to third parties in connection with our development of mecamylamine hydrochloride, 7% were payments made to third parties in connection with our development of TC-2216 and 4% were payments made to third parties in connection with our development of TC-2696. We spent the remaining 57% of our total research and development expenses on salaries, benefits and infrastructure costs associated with our internal research and development capabilities, including clinical programs, preclinical programs and research efforts, and on payments to third parties in connection with preclinical programs.

We expect to continue to incur substantial research and development expenses for the foreseeable future. We anticipate that these expenses will increase substantially as we continue to advance our clinical stage product candidates through the development process, to advance additional product candidates into clinical trials, to invest in promising product opportunities in

our research programs and to grow our research and development organization and infrastructure. Because we have licensed TC-1734 to AstraZeneca and AstraZeneca will assume substantially all future development costs for TC-1734, we expect generally to focus our future research and development efforts on our other clinical stage product candidates and preclinical programs.

General and Administrative Expense

General and administrative expense increased by $1.2 million, or 24%, to $6.4 million for the year ended December 31, 2005, from $5.2 million for 2004. This increase resulted primarily from the recognition of $1.6 million in 2005 for expenses incurred in connection with a public offering that we terminated in the first quarter of 2005. We did not incur any similar expenses in 2004. We also incurred an additional $182,000 in non-cash stock-based compensation charges in 2005 attributable to our adoption of SFAS 123R as of January 1, 2005. These increases were partially offset by lower infrastructure and personnel costs for our general and administrative activities, along with lower professional fees and travel costs in connection with business development pursuits in 2005 as compared to 2004. We expect that general and administrative expense will increase in 2006 and subsequent years due to increased payroll, expanded infrastructure and increased consulting, legal, accounting and investor relations expenses associated with being a public company.

Cost of Product Sales

Cost of product sales increased by $282,000 to $481,000 for the year ended December 31, 2005, from $198,000 for 2004. Cost of product sales for each of 2005 and 2004 reflects our costs related to sales of Inversine, net of the amount of FDA product and establishment fees refunded to us in that year. Product and establishment fees for marketed products are assessed by the FDA each year and paid by companies in the year in which they are assessed. We have historically requested a waiver of the FDA fees that we have paid for Inversine. If a waiver is granted, the FDA fees are refunded, typically in the year following the year in which they are paid. Our requests for waivers of the FDA fees for 2002 and 2003 were granted in 2004, resulting in a refund to us in 2004 of $505,000 in 2002 and 2003 fees. Our request for a waiver of the FDA fees for 2004 was granted in 2005, resulting in a refund to us in 2005 of $304,000 in 2004 fees. The lower cost of product sales for 2004 resulted primarily from the refund in 2004 of the FDA fees for both 2003 and 2002 as compared to the refund in 2005 of the FDA fees for only 2004. We have again petitioned the FDA for a waiver of the product and establishment fees that were assessed by the FDA and paid by us in 2005 and plan to petition again in future years. In previous years, the award that we received from the National Institute of Standards and Technology through its Advanced Technology Program to fund the development of sophisticated molecular simulation software was significant in supporting our waiver requests. Our funding under the award concludes in the third quarter of 2006, and there is no assurance that our pending or future fee waiver requests will be allowed.

Interest and Dividend Income

Interest and dividend income increased by $669,000 to $1.2 million for the year ended December 31, 2005, from $505,000 for 2004. The increase was attributable to substantially higher short-term interest rates and higher average levels of cash and short-term investments during 2005 resulting from the issuance and sale of shares of our convertible preferred stock on December 6, 2004 for net proceeds of $32.9 million.

Interest Expense

Interest expense increased by $92,000 to $225,000 for the year ended December 31, 2005, from $133,000 for 2004. This increase is attributable to higher indebtedness under a credit facility used to finance capital equipment purchases, primarily laboratory equipment. The higher indebtedness resulted from our borrowing an additional $973,000 under this facility in December 2004.

Years ended December 31, 2004 and December 31, 2003

Revenue

Revenue increased by $1.3 million, or 52%, to $3.7 million for the year ended December 31, 2004, from $2.5 million for 2003. The increase resulted principally from the acceleration in recognition of $1.6 million of deferred license fee revenue and an increase in grant revenue of $646,000, partially offset by a decrease in research fee revenue of $965,000.

The acceleration in recognition of $1.6 million of deferred license fee revenue represented the remaining unamortized balance of upfront payments that we received when we entered into collaboration agreements with Aventis and Dr. Falk Pharma and were amortizing over the period of our expected research obligations under the agreements. In the fourth quarter of 2004, we concluded our research obligations under our collaboration agreement with Aventis and our collaboration agreement with Dr. Falk Pharma.

Grant revenue increased by $646,000 to $717,000 for 2004 as a result of a full year of work performed under a cooperative agreement awarded to us in the third quarter of 2003 by the National Institute of Standards and Technology through its Advanced Technology Program to fund the development of sophisticated molecular simulation software.

Research fee revenue decreased to $338,000 in 2004, from $1.3 million in 2003. The decrease of $965,000 resulted from less activity in 2004 under our collaboration agreement with Aventis relating to Aventis compounds as we completed the research requested by Aventis. The research term of that collaboration agreement with Aventis expired on December 31, 2004.

Net sales of Inversine decreased by $48,000 to $767,000 for the year ended December 31, 2004, from $815,000 for 2003. This decrease resulted from a reduction in the volume of sales of Inversine. We do not promote sales of Inversine.

Research and Development Expense

Research and development expense increased by $4.6 million, or 25%, to $22.8 million for the year ended December 31, 2004, from $18.2 million for 2003. The increase was primarily attributable to the costs associated with having four product candidates in clinical trials for most of 2004, compared to only two product candidates in clinical trials for most of 2003.

For the year ended December 31, 2004, we estimate that approximately 18% of our total research and development expenses were payments made to third parties in connection with our development of TC-1734, 5% were payments made to third parties in connection with our development of TC-2696 and 19% were made to third parties in connection with the two discontinued clinical development programs. We spent the remaining 58% of our total research and development expenses on salaries, benefits, and infrastructure costs associated with our internal research and development capabilities, including clinical programs, preclinical

programs and research efforts, and on payments to third parties in connection with preclinical programs.

General and Administrative Expense

General and administrative expense increased by $1.6 million, or 43%, to $5.2 million for the year ended December 31, 2004, from $3.6 million for 2003. This increase resulted from our investment in development of the administrative infrastructure necessary to enable us to expand our operations, to support our development efforts and to fulfill the additional reporting and regulatory requirements applicable to a public company. The increase was principally attributable to increased expenses of $705,000 related to expansion of our business development staff and an increase in spending on business development pursuits, $431,000 of additional patent related expenses and increases in our legal and other professional fees.

Cost of Product Sales

Cost of product sales decreased by $545,000 to $198,000 for the year ended December 31, 2004, from $743,000 for 2003. All of these costs related to sales of Inversine. The decrease in cost of product sales resulted from a successful outcome in 2004 of our request for a waiver of FDA product and establishment fees that had been assessed by FDA in 2003 and 2002. In July 2004, the FDA informed us that our fee waiver request had been granted in full. We had accrued the costs for these FDA fees in our financial statements since our acquisition of Inversine in August 2002, as there was no assurance that our fee waiver request would be granted.

Interest and Dividend Income

Interest and dividend income decreased by $286,000 to $505,000 for the year ended December 31, 2004, from $791,000 for 2003. The decrease was primarily attributable to lower levels of cash and short-term investments.

Interest Expense

Interest expense increased to $133,000 for the year ended December 31, 2004, from $123,000 in 2003.

Liquidity and Capital Resources

Sources of Liquidity

Since we became an independent company in 2000, we have financed our operations and internal growth primarily through private placements of convertible preferred stock. As of December 31, 2005, we had derived aggregate net proceeds of $121.8 million from these private placements. We have received additional funding from upfront license fees and payments for research and development services under collaboration agreements, equipment and building lease incentive financing, government grants and interest income. As of December 31, 2005, we had received $9.9 million under collaboration agreements that were terminated or under which we had ceased conducting research as of the end of 2004.

In December 2005, we entered into a collaboration agreement with AstraZeneca relating to TC-1734. In January 2006, the agreement became effective and we began conducting research for which we are eligible to receive research fees. AstraZeneca paid us an initial fee of $10 million in February 2006. AstraZeneca has agreed to make an additional payment to us of $20.0

million if it decides to conduct a Phase II clinical trial of TC-1734 following the completion of additional safety and product characterization studies that AstraZeneca is conducting at its expense to generate further data with respect to TC-1734. We expect AstraZeneca to complete these safety and product characterization studies within approximately 12 to 15 months from January 2006.

If AstraZeneca terminates our agreement upon completion of any or all the additional safety and product characterization studies, we would be required to reimburse AstraZeneca for the amount of all research fees that it paid to us under the a4ß2 research collaboration that we and AstraZeneca have initiated under the agreement while AstraZeneca conducted the studies. In addition, we would be required to pay AstraZeneca an additional $5.0 million as compensation for assigning to us the data and any intellectual property generated in the studies.

On December 31, 2004, we received loan proceeds of $1.3 million from The Stanley Medical Research Institute in connection with a development agreement relating to the development of one of our compounds for the treatment of the cognitive deficits in schizophrenia. In August 2005, we repaid the loan in full in anticipation of entering into our strategic collaboration agreement with AstraZeneca. We and The Stanley Medical Research Institute terminated the development agreement in December 2005 in anticipation of our collaboration agreement with AstraZeneca.

We began generating revenues from product sales of Inversine in December 2002. To date, the net contribution from Inversine sales has not been a significant source of cash and we do not expect it to be a significant source in the future.

Our cash, cash equivalents and short-term investments were $43.0 million as of December 31, 2003, $53.1 million as of December 31, 2004 and $24.9 million as of December 31, 2005.

Cash Flows

Net cash used for operating activities was $26.2 million for the year ended December 31, 2005, primarily reflecting our net loss of $29.0 million partially offset by a decrease of $999,000 in prepaid expenses primarily attributable to our recognition of payments made in 2004 in connection with a public offering that we terminated in the first quarter of 2005, $803,000 in depreciation and amortization expense and $690,000 in stock-based employee compensation expense. Net cash used for operating activities was $25.0 million for the year ended December 31, 2004. Net cash used for operating activities for 2004 consisted primarily of a net loss of $24.0 million, which included acceleration of recognition of deferred license fee revenue of $1.6 million representing the unamortized portion of the upfront payments that we received when we entered into collaboration agreements with Aventis and Dr. Falk Pharma. Net cash used for operating activities was $19.3 million for the year ended December 31, 2003, primarily reflecting a net loss occurring for this period of $19.4 million.

Net cash used in investing activities was $250,000 for the year ended December 31, 2005, $622,000 for the year ended December 31, 2004 and $545,000 for the year ended December 31, 2003. These amounts exclude cash flows from the purchase and sale of investments and were primarily to purchase equipment for use in expanding our internal research and development activities.

Net cash used in financing activities was $1.7 million for the year ended December 31, 2005 and consisted principally of the repayment of a $1.3 million convertible promissory note to The Stanley Medical Research Institute and $1.1 million in principal repayments on an equipment

financing loan facility, partially offset by $612,000 in proceeds from the issuance of shares of our series C convertible preferred stock in May 2005. Net cash provided by financing activities was $35.9 million for the year ended December 31, 2004 and consisted principally of $32.9 million in net proceeds from the issuance of shares of our series C convertible preferred stock in December 2004, $2.0 million received under an equipment financing loan facility and $1.3 million received from The Stanley Medical Research Institute in return for our issuance of a convertible promissory note in an equal principal amount, partially offset by $731,000 of principal repayments on equipment financing. As of December 31, 2004, we did not have any borrowing facility or line of credit. Net cash provided by financing activities for the year ended December 31, 2003 was $13.4 million and consisted principally of net proceeds of $13.8 million from the issuance of shares of our series C convertible preferred stock and proceeds of $239,000 received in connection with the purchase of our common stock upon the exercise of stock options, partially offset by $637,000 of principal repayments on equipment financing.

In May 2002, we borrowed $2.5 million from R.J. Reynolds Tobacco Holdings, Inc. to finance equipment and other fixed assets that we had previously purchased. The borrowing bears a fixed interest rate of 6.6%, is payable in 48 equal monthly installments and matures in May 2006. In January 2004, we amended the terms of our loan facility to permit us to borrow up to an additional $2.0 million in 2004 in up to three separate borrowings. Each borrowing would bear a fixed interest rate equal to a theoretical four-year U.S. Treasury Rate on the disbursement date plus 3.5%, be payable in 48 equal monthly installments and be secured by specified tangible fixed assets determined sufficient by the lender at the time of disbursement. We borrowed $1.0 million in April 2004 and $973,000 in December 2004 under the amended loan facility to finance equipment. The April 2004 borrowing bears a fixed interest rate of 5.87%, is payable in 48 equal monthly installments and matures in April 2008. The December 2004 borrowing bears a fixed interest rate of 6.89%, is payable in 48 monthly installments and matures in January 2009. All borrowings under the loan facility are secured by specified tangible fixed assets. As of December 31, 2005, the outstanding principal balance under the loan facility was $1.7 million. We are currently in discussions with R.J. Reynolds regarding a potential amendment to the terms of the loan facility to provide up to $2.0 million in new borrowing capacity to finance equipment.

On December 6, 2004, we sold 27,272,728 shares of convertible preferred stock to 11 of our existing stockholders for net proceeds of $32.9 million. On May 13, 2005, we sold an additional 496,132 shares of convertible preferred stock to another of our existing stockholders for net proceeds of $612,000. On December 15, 2004, we entered into a development agreement with The Stanley Medical Research Institute, a nonprofit organization that supports the research and development of treatments for schizophrenia. In connection with this agreement, we issued a $1.3 million convertible promissory note to The Stanley Medical Research Institute. In August 2005, we repaid the promissory note in full. We and The Stanley Medical Research Institute terminated the development agreement in December 2005 in anticipation of our collaboration agreement with AstraZeneca.

Funding Requirements

We have incurred significant losses since our inception. As of December 31, 2005, we had an accumulated deficit of $175.0 million. We expect to continue to incur substantial operating losses for the foreseeable future. Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the scope, progress, results and cost of preclinical development and laboratory testing and clinical trials;

- the timing, receipt and amount of milestone and other payments from AstraZeneca and potential future collaborators;
- the costs, timing and outcome of regulatory review;
- the number and characteristics of product candidates that we pursue;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the costs of establishing sales and marketing functions and of establishing arrangements for manufacturing;
- the rate of technological advancements for the indications that we target;
- our ability to establish strategic collaborations and licensing or other arrangements on terms favorable to us;
- the costs to satisfy our obligations under existing and potential future collaborations;
- the timing, receipt and amount of sales or royalties, if any, from our potential products; and
- the extent and scope of our general and administrative expenses.

We anticipate that implementing our strategy will require substantial increases in our capital expenditures and other capital commitments as we expand our clinical trial activity, as our product candidates advance through the development cycle, and as we invest in additional product opportunities and research programs and expand our infrastructure. Because we have licensed TC-1734 to AstraZeneca and AstraZeneca will assume substantially all development costs for TC-1734, we expect generally to focus our future research and development efforts on our other clinical stage product candidates and preclinical programs. We do not expect our existing capital resources and the net proceeds from this offering to be sufficient to enable us to fund the completion of the development of any of our other product candidates. We expect that our existing capital resources, together with the net proceeds from this offering, will be sufficient to fund our operations through mid-2008. However, our operating plan may change as a result of many factors, including those described above. In particular, our operating plan may change if AstraZeneca decides not to proceed with the further development of TC-1734 following its completion of any or all of the safety and product characterization studies that it is conducting and terminates our agreement. In that event, we would be required to reimburse AstraZeneca for the amount of all research fees that it paid to us under the a4ß2 research collaboration while it conducted the studies. We would also be required to pay to AstraZeneca an additional $5.0 million as compensation for assigning to us the data and any intellectual property generated in the studies, but we would not be required to refund the $10.0 million initial fee that AstraZeneca has paid us. We may need additional funds sooner than planned to meet operational needs and capital requirements for product development.

We do not expect to generate sufficient cash from our operations to sustain our business for the foreseeable future. We expect our continuing operating losses to result in increases in our cash required to fund operations over the next several quarters and years. To the extent our capital resources are insufficient to meet future capital requirements, we will need to finance future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements. Additional equity or debt financing, or corporate collaboration and licensing arrangements, may not be available on acceptable terms, if at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our research and development programs, reduce our planned commercialization efforts, or

obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain drug candidates that we might otherwise seek to develop or commercialize independently. Additionally, any future equity funding may dilute the ownership of our equity investors.

We cannot estimate the completion dates and costs of our current internal research and development programs due to inherent uncertainties in outcomes of clinical trials and regulatory approvals of our product candidates. We cannot be certain that we will be able to successfully complete our research and development projects or successfully find collaboration or distribution partners for our product candidates. Our failure to complete our research and development projects could have a material adverse effect on our financial position or results of operations.

To date, inflation has not had a material effect on our business.

Contractual Obligations

The following table summarizes our significant contractual obligations and commercial commitments as of December 31, 2005:

	Payments Due by Period				
Contractual Obligations	**Total**	**Less Than 1 Year**	**1-3 Years**	**3-5 Years**	**More Than 5 Years**
Long-term debt obligations	$ 2,193,297	$ 783,895	$ 1,048,883	$ 224,479	$ 136,040
Operating lease obligations	2,328,374	1,470,552	857,822	—	—
Other contractual obligations	3,013,958	3,006,939	7,019	—	—
Total contractual obligations	$ 7,535,629	$ 5,261,386	$ 1,913,724	$ 224,479	$ 136,040

The amounts of other contractual obligations reflected in the above table include obligations to purchase product candidate material contingent on the delivery of the material and to compensate clinical investigators and clinical trial sites contingent on the performance of services in connection with clinical trials. The amount of other contractual obligations for 2006 reflected in the above table also includes annual maintenance fees or other fixed payments required under our technology license agreements. Our technology license agreements are generally terminable by us on short notice. As a result, the annual maintenance fees or other fixed payments under those agreements are not included in other contractual obligations in the above table after 2006. The amounts of other contractual obligations for all periods reflected in the above table exclude contingent royalty payments that we may be required to pay under our technology license agreements and other contingent payments that we may become required to make under our technology license agreements upon achievement of specified development, regulatory or commercial milestones.

Quantitative and Qualitative Disclosures about Market Risk

The primary objective of our investment activities is to preserve our capital to fund operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of cash equivalents and short-term investments in a variety of securities of high credit quality. As of December 31, 2005, we had cash and cash equivalents of $24.9 million consisting of cash deposited in a highly rated financial institution in the United States. A portion of our investments may be subject to interest rate risk and could fall in value if market interest rates increase. However, because our investments are short-term in duration, we believe that our exposure to interest rate risk is not

significant and a 1% movement in market interest rates would not have a significant impact on the total value of our portfolio. We actively monitor changes in interest rates.

We contract for the conduct of some of our clinical trials and other research and development and manufacturing activities with contract research organizations, investigational sites and manufacturers in Europe and India. We may be subject to exposure to fluctuations in foreign exchange rates in connection with these agreements. We do not hedge our foreign currency exposures. We have not used derivative financial instruments for speculation or trading purposes.

Recent Accounting Pronouncements

In June 2005, the Financial Accounting Standards Board issued Statement No. 154, *Accounting Changes and Error Corrections, a replacement of APB Opinion No. 20, Accounting Changes, and FASB Statement No. 3, Reporting Accounting Changes in Interim Financial Statements,* or SFAS 154. SFAS 154 requires retrospective application to prior periods' financial statements for all voluntary changes in accounting principle, unless impracticable. SFAS 154 is effective for accounting changes and corrections of errors made in fiscal years beginning after December 15, 2005. SFAS 154 will have no immediate impact on our financial statements, though it would impact our presentation of future voluntary accounting changes if such changes occur.

BUSINESS

Overview

We are a biopharmaceutical company engaged in the design, discovery and development of a new class of drugs to treat multiple diseases and disorders of the central nervous system by selectively targeting neuronal nicotinic receptors, or NNRs. NNRs are found on nerve cells throughout the nervous system and serve as key regulators of nervous system activity. We trace our scientific lineage to a research program initiated by R.J. Reynolds Tobacco Company in 1982 to study the activity and effects of nicotine, a compound that interacts non-selectively with all nicotinic receptors. Since that time, we have developed a deep understanding of the biological characteristics and functions of NNRs and have learned that compounds that interact with NNRs have the potential to achieve positive medical effects by modulating their activity. We have built an extensive patent estate covering the structure or therapeutic use of small molecules designed to regulate the central nervous system by selectively affecting specific NNR subtypes.

We are developing our most advanced product candidates as treatments for target indications in three therapeutic areas: cognitive impairment, depression and anxiety, and pain. Within these areas, we have three product candidates in clinical development and two preclinical product candidates.

Cognitive Impairment

TC-1734. Our lead product candidate is a novel small molecule that we refer to as TC-1734. In December 2005, we entered into a collaborative research and license agreement with AstraZeneca AB for the development and worldwide commercialization of TC-1734 as a treatment for Alzheimer's disease, cognitive deficits in schizophrenia and potentially other conditions marked by cognitive impairment such as attention deficit hyperactivity disorder, commonly referred to as ADHD, age associated memory impairment, commonly referred to as AAMI, and mild cognitive impairment, commonly referred to as MCI. In March 2006, we completed a Phase II clinical trial of TC-1734 in AAMI designed to further assess the effects of TC-1734 on cognition in a cognitively impaired older adult population. We previously completed two other clinical trials of TC-1734, one in AAMI and one in MCI. We expect AstraZeneca to initiate two Phase II clinical trials of TC-1734 in the first half of 2007, one in mild to moderate Alzheimer's disease and one in cognitive deficits in schizophrenia.

Our agreement with AstraZeneca relating to TC-1734 became effective in January 2006. AstraZeneca paid us an initial fee of $10 million in February 2006. AstraZeneca has agreed to make an additional payment to us of $20 million if it decides to conduct a Phase II clinical trial of TC-1734 following the completion of additional safety and product characterization studies that AstraZeneca is conducting at its expense to generate further data with respect to TC-1734. We expect AstraZeneca to complete these safety and product characterization studies within approximately 12 to 15 months from January 2006. Under the agreement, we are eligible to receive other payments of up to $249 million, contingent upon the achievement of development, regulatory and first commercial sale milestones for TC-1734 for Alzheimer's disease, cognitive deficits in schizophrenia and ADHD, and royalties on future product sales. If TC-1734 is developed under the agreement for indications other than Alzheimer's disease, cognitive deficits in schizophrenia and ADHD, we would also be eligible to receive payments contingent upon the achievement of development, regulatory and first commercial sale milestones for TC-1734 for those indications. AstraZeneca is responsible for the commercialization of TC-1734 and any compounds that arise out of the a4ß2 research collaboration described below that it

elects to advance. We have the option to co-promote TC-1734 and any other compounds that are selected for advancement arising out of the research collaboration in the United States to specified classes of specialist physicians.

Depression/Anxiety

Mecamylamine hydrochloride and TC-5214. Mecamylamine hydrochloride is the active ingredient in Inversine, which is our only product approved by the U.S. Food and Drug Administration, or FDA, for marketing. Inversine is approved for the management of moderately severe to severe essential hypertension, a high blood pressure disorder. However, we believe that Inversine is prescribed predominantly for the treatment of neuropsychiatric disorders, including Tourette's syndrome, autism and bipolar disorder. We are currently conducting a Phase II clinical trial of mecamylamine hydrochloride for depression as an add-on therapy to citalopram hydrobromide, a commonly prescribed anti-depressant. We expect the results of this trial to be available in the fourth quarter of 2006.

TC-5214, one of the molecular components of mecamylamine hydrochloride, is a separate preclinical product candidate. If the results of our ongoing Phase II clinical trial of mecamylamine hydrochloride are favorable, we may accelerate the development of TC-5214 as an add-on therapy for depression in lieu of further advancement of mecamylamine hydrochloride. We do not expect to pursue the clinical development of both mecamylamine hydrochloride and TC-5214 for depression.

TC-2216. TC-2216 is a novel small molecule that we are developing as an oral treatment for depression and anxiety disorders. TC-2216 is currently a preclinical product candidate. We are currently conducting additional preclinical safety studies necessary to support the filing of an investigational new drug application, or IND, for clinical trials of TC-2216. We plan to file an IND for TC-2216 in the second half of 2006. We are also evaluating TC-2216 as a potential product candidate for smoking cessation or obesity instead of or in addition to depression and anxiety disorders.

Pain

TC-2696. TC-2696 is a novel small molecule that we are developing as a treatment for acute post-operative pain. Depending on clinical trial results, available resources and other considerations, we may pursue development of TC-2696 for other classes of pain in addition to or instead of acute post-operative pain. In 2004, we completed a Phase I single rising dose clinical trial of TC-2696 that we conducted in France. We are currently conducting a Phase I multiple rising dose clinical trial in France to further assess the safety and tolerability profile of TC-2696. We expect the full results of this trial to be available in the third quarter of 2006. We have not submitted an IND for clinical trials of TC-2696 in the United States.

In a single rising dose clinical trial, each subject in a dose group receives a dosage of the drug being evaluated only one time, with subjects in each subsequent dose group receiving a pre-determined higher dosage than subjects in the preceding dose group. In a multiple rising dose clinical trial, each subject in a dose group receives a dosage of the drug being evaluated multiple times, with subjects in each subsequent dose group receiving a pre-determined higher dosage than subjects in the preceding dose group.

Under our agreement with AstraZeneca relating to TC-1734, we and AstraZeneca have initiated a preclinical research collaboration designed to discover and develop additional compounds that, like TC-1734, act on the a4ß2 NNR. AstraZeneca is responsible for funding the research collaboration, which has an initial term of four years and can be extended by mutual

agreement. In addition to our a4ß2 research collaboration with AstraZeneca, we have a preclinical program focused on identifying and developing compounds that selectively target the a7 NNR, which we believe may have application in the treatment of conditions such as schizophrenia, cognitive impairment and inflammation. We have selected a lead compound that we refer to as TC-5619 that acts selectively on the a7 NNR. We are currently conducting additional preclinical studies necessary to support the planned filing in 2007 of an IND for clinical trials of TC-5619. We have additional preclinical programs in areas in which we believe drugs that target specific NNR subtypes can be exploited for medical benefit, such as smoking cessation and obesity.

We develop product candidates using our proprietary databases and computer-based molecular design technologies, which we refer to collectively as Pentad. Pentad relies on extensive biological data for a library of diverse compounds that we have developed and gathered over more than 20 years. Pentad enables us to efficiently identify, prioritize, characterize and optimize novel compounds designed to selectively target specific NNR subtypes in an effort to achieve desired medical results and limit adverse side effects. We used Pentad to design or optimize TC-1734, TC-2696, TC-2216 and TC-5619.

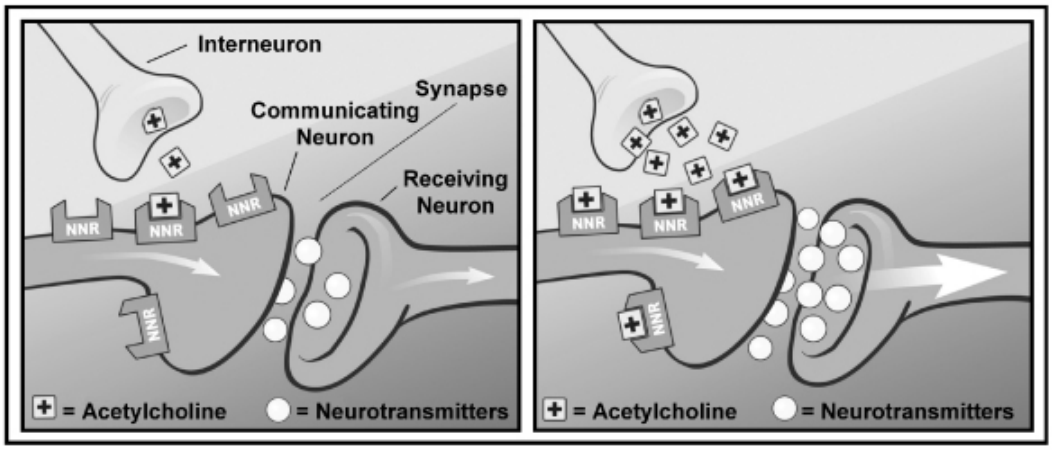
Role of NNRs in the Nervous System

The human nervous system is a massive communications network that sends and receives information throughout the body via billions of specialized nerve cells known as neurons. Neurons continually gather information about the body's internal and external environment and send signals to the brain. These signals pass from one neuron to another across a gap between a communicating neuron and a receiving neuron known as a synapse. Electrical impulses of a communicating neuron are converted into chemicals called neurotransmitters that are released by the communicating neuron and bind to specialized proteins known as receptors located across the synapse on the receiving neuron to enable the signal to continue. The major neurotransmitters in the brain are dopamine, serotonin, norepinephrine, glutamate, gamma-aminobutyric acid, or GABA, and acetylcholine.

NNRs are a class of receptors found in the nervous system that play a critical role in modulating the release of neurotransmitters to regulate nervous system activity. When the neurotransmitter acetylcholine is released from a nearby neuron, called an interneuron, and binds to an NNR on a communicating neuron, the flow of neurotransmitters from the communicating neuron to a receiving neuron is adjusted by the NNR. This action, known as neuromodulation, results in a greater release of neurotransmitters across the synapse when the nervous system is understimulated and a lesser release of neurotransmitters across the synapse when the nervous system is overstimulated. As neuromodulators, NNRs serve as the nervous system's self-adjusting "volume knob."

The nervous system will not operate properly if the relative levels of key neurotransmitters in the brain are not maintained in a normal balance. A disruption in this balance can cause many common nervous system diseases and disorders. We believe that compounds that target NNRs to trigger their activity can be used to treat these diseases and disorders.

The following diagrams illustrate the role of NNRs in neuromodulation. In the illustration on the left, the release of a limited amount of acetylcholine from the interneuron causes the NNRs to release a limited amount of neurotransmitters across the synapse. In the illustration on the right, the release of more acetylcholine from the interneuron causes the NNRs to release a greater amount of neurotransmitters.



NNRs are comprised of five protein subunits that are arranged like staves of a barrel around a central pore. Each different combination of five subunits represents an NNR subtype. There are several subtypes, each of which is identified by Greek letters. Scientific evidence has established that individual NNR subtypes have particular functions in the body that are relevant to a number of debilitating diseases and disorders, as set forth below.

NNR Subtype	Primary Functions Impacted	Diseases or Disorders Potentially Implicated
a4ß2	cognition; pain perception	Alzheimer's disease; cognitive deficits in schizophrenia; AAMI; MCI; ADHD acute, chronic and neuropathic pain
a7	sensory gating; cognition; inflammation	schizophrenia; cognitive impairment
a6ß3	motor control	Parkinson's disease

Our scientists and their former colleagues at R.J. Reynolds Tobacco Company have played a prominent role in the growth of knowledge about NNRs, as well as the effects of compounds that mimic the action of acetylcholine and interact with different NNR subtypes. For example, we believe that nicotine's well-documented abilities to enhance attention, learning and memory result primarily from its interaction with the a4ß2 NNR and the a7 NNR in the brain. Many published studies evaluating the effects of nicotine in humans and animals, as well as published studies showing the prevalence of diseases such as Alzheimer's disease and Parkinson's disease in non-smokers as compared to smokers, suggest the therapeutic effects of compounds such as nicotine that interact with NNRs. However, despite their positive effects, these

compounds have historically not been desirable as therapies because they have not been sufficiently selective. This means that these compounds interact not only with NNRs, but also with nicotinic receptors in the muscles and in groups of nerve cells known as ganglia that are associated with adverse effects such as increased heart rate, high blood pressure, irregular heartbeat, nausea, vomiting and a dangerous slowing of breathing known as respiratory depression.

Based on our years of focus on NNRs and the expertise we have built over that time, we are developing product candidates that are designed to interact selectively with specific NNR subtypes to promote positive medical effects and limit adverse side effects.

Our Business Strategy

Our goal is to become a leader in the discovery, development and commercialization of novel drugs that selectively target NNRs in order to treat diseases and disorders where there is significant medical need and commercial potential. To achieve this goal, we are pursuing the following strategies:

- *Develop and commercialize drugs that selectively target specific NNR subtypes.* Based on our understanding of the role of NNRs in the nervous system, we believe that drugs designed to selectively target specific NNR subtypes can have positive medical effects with limited or no adverse side effects. We use our scientific expertise and Pentad to identify compounds that selectively target specific NNR subtypes as potential treatments for diseases and disorders of the central nervous system.
- *Collaborate selectively to develop and commercialize product candidates.* In December 2005, we entered into a collaborative research and license agreement with AstraZeneca for the development and worldwide commercialization of TC-1734 as a treatment for Alzheimer's disease, cognitive deficits in schizophrenia and potentially other conditions marked by cognitive impairment. Under the agreement, we and AstraZeneca have initiated a preclinical research collaboration designed to discover and develop additional compounds that, like TC-1734, act on the a4ß2 NNR. We intend to selectively enter into additional collaboration agreements with leading pharmaceutical and biotechnology companies to assist us in furthering the development of our product candidates. In particular, we intend to enter into these third-party arrangements for target indications in which our potential collaborator has particular expertise or that involve a large, primary care market that must be served by large sales and marketing organizations. In entering into these collaboration agreements, our goal will be to maintain co-promotion or co-commercialization rights in the United States and, in some cases, other markets. Under our collaboration agreement with AstraZeneca, we have the option to co-promote TC-1734 and any compounds that are selected for advancement arising out of the research collaboration under the agreement in the United States to specified classes of specialist physicians.
- *Remain at the forefront of the commercialization of NNR research*. We have established ourselves as a leader in NNR research over the last 20 years. Our scientists and their former colleagues at RJR have published more than 150 NNR-related articles in leading scientific journals and more than 200 abstracts. Our leadership position in this area is also reflected in our extensive patent estate that includes 82 issued or pending United States patents and patent applications and numerous foreign counterparts. We intend to continue to invest significant resources to build upon our NNR expertise and to expand our intellectual property portfolio. We augment our own research by collaborating with commercial and academic institutions that seek access to our proprietary knowledge and compounds.

- *Identify and prioritize indications in which drugs that selectively target specific NNR subtypes can be exploited for medical benefit*. We have identified numerous indications in which NNRs have been implicated and for which we believe that drugs that selectively target specific NNR subtypes can provide a medical benefit. We prioritize our product development opportunities in an effort to sustain our product pipeline for indications in which there is a significant medical need and commercial potential.
- *Build a specialized sales and marketing organization.* We intend to build an internal sales and marketing organization for target indications in which specialists heavily influence the market, particularly neurology and psychiatry. We believe that we can effectively serve these markets with a specialized sales force, enabling us to retain greater value from our product candidates that receive marketing approval than if we relied on a third party's sales force.

Opportunities in Our Target Indications

Because NNRs are so widespread in the body, we believe that there are a number of areas in which compounds that target NNRs could provide a therapeutic benefit, including:

- diseases and disorders of the central nervous system, commonly referred to as the CNS;
- smoking cessation;
- obesity; and
- inflammation.

Our primary product development focus is on diseases and disorders of the CNS, which represent a major segment of the global healthcare environment. Espicom Business Intelligence, a provider of business information for the pharmaceutical and other industries, estimates the total worldwide CNS pharmaceutical market was $65 billion in 2004. Three of the top ten selling drugs in the world in 2004, Eli Lilly's Zyprexa, Pfizer's Zoloft and Wyeth's Effexor, treat diseases and disorders of the CNS. However, despite their commercial success, many current CNS drugs are only moderately effective or are accompanied by significant side effects or other drawbacks. Accordingly, we believe that substantial opportunities exist for new therapies that address CNS diseases and disorders. We are currently conducting a Phase II clinical trial of mecamylamine hydrochloride for depression as an add-on therapy to citalopram hydrobromide. We are also currently conducting a Phase I multiple rising dose clinical trial of TC-2696, our product candidate for pain. We expect AstraZeneca to initiate Phase II clinical trials of TC-1734 in Alzheimer's disease and cognitive deficits in schizophrenia in the first half of 2007.

Alzheimer's Disease

Alzheimer's disease, the most common form of dementia, is a debilitating brain disorder for which there is no cure. The disease progresses in stages from mild to moderate to severe and gradually destroys a person's memory and ability to learn, reason, make judgments, communicate and carry out daily activities. Mild Alzheimer's disease is characterized by mild forgetfulness and difficulty acquiring basic information and communicating. Patients generally exhibit the symptoms of mild Alzheimer's disease for two to four years before progressing to the moderate stage. Moderate Alzheimer's disease is characterized by forgetfulness, failure to recognize friends and family, disorientation regarding time and place and personality changes. Patients generally exhibit the symptoms of moderate Alzheimer's disease for up to ten years

before progressing to the severe stage. Severe Alzheimer's disease is characterized by difficulty performing simple tasks and activities associated with daily living. Patients with severe Alzheimer's disease require continuous care and generally do not survive for more than three years.

The Business Insights Healthcare Report titled *The CNS Market Outlook to 2010* estimates that Alzheimer's disease affects approximately 13.7 million people in the world's seven major pharmaceutical markets, which are the United States, France, Germany, Italy, Spain, the United Kingdom and Japan, including approximately 4.5 million people in the United States. That report notes that studies of the causes, distribution and control of disease indicate that an estimated 5% of persons over age 65 and an estimated 24% of persons over age 85 suffer from the disease. Espicom Business Intelligence estimates that the worldwide market for Alzheimer's disease therapies was approximately $3.0 billion in 2004.

The treatment of Alzheimer's disease is currently dominated by a class of drugs called acetylcholinesterase inhibitors, which includes Aricept, Reminyl and Exelon. The treatment most recently approved by the FDA is Namenda, which has a different mechanism of action than acetylcholinesterase inhibitors and is the only product approved for the treatment of moderate to severe Alzheimer's disease. We believe that acetylcholinesterase inhibitors have limitations in that only about 25% of Alzheimer's disease patients who take them show symptomatic improvement and that they have not been demonstrated to substantially delay the progressive deterioration and death of cells in the brain that can lead to more severe impairment and debilitation.

Cognitive Deficits in Schizophrenia

Schizophrenia is a chronic, severe and disabling form of psychosis. The disease is characterized by symptoms such as delusions, hallucinations, the inability to disregard familiar stimuli, sometimes referred to as sensory gating, disorganized speech, grossly disorganized or catatonic behavior and prolonged loss of emotion, feeling, volition or drive. In addition, schizophrenia is often marked by impairment in cognitive functions, such as attention, vigilance, memory, and reasoning, that plays a primary role in the inability of schizophrenic patients to function normally.

The Business Insights Healthcare Report estimates that schizophrenia affects approximately 8.3 million people in the world's seven major pharmaceutical markets, including approximately 3.7 million people in the United States. Scientists have estimated that up to 75% of schizophrenic patients are cognitively impaired.

Traditional treatments for schizophrenia are not effective to treat cognitive deficits in schizophrenia. While it has been reported that more recently developed treatments for schizophrenia, known as atypical anti-psychotics, may have some effect on cognitive impairment, it has also been reported that there is little evidence that the effect is lasting and leads to an improvement in daily functioning. Also, atypical anti-psychotics may cause agranulocytosis, an acute disease characterized by significant loss of white blood cells that prevent infection, as well as agitation, anxiety, muscle tremor, drowsiness, dizziness, headache, insomnia, weight gain and diabetes. There are currently no products approved for the treatment of cognitive deficits in schizophrenia.

AAMI

The term age associated memory impairment, or AAMI, describes a common condition characterized by gradual memory loss or other cognitive impairment that generally occurs with normal aging. A person who is at least 50 years of age and scores at least one standard deviation below the mean established for young adults on a standardized memory test without evidence of dementia, neurological illness or other medical cause may be classified with AAMI. AAMI is not currently listed in *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, or DSM-IV, the manual published by the American Psychiatric Association to establish diagnostic criteria. However, DSM-IV does list the term "age related cognitive decline," which is often used by the medical community interchangeably with AAMI, as an "objectively identified decline in cognitive functioning consequent to the aging process that is within normal limits given the person's age." Although estimates of the prevalence of AAMI in the elderly vary greatly because of varying methodologies and definitions of AAMI, one published study indicates that AAMI may affect as many as 38% of people over age 65. Based on a 2000 report of the Federal Interagency Forum on Aging-Related Statistics, this represents over 13 million people in the United States alone. The Federal Interagency Forum report projects that the number of people in the United States age 65 or older will double by 2030. There are currently no products approved for the treatment of AAMI.

Depression/Anxiety

Depression is a severe psychiatric mood disorder. It is characterized by a wide range of symptoms that cause significant impairment in daily functioning, such as persistent despondence, loss of interest in normal activities, changes in appetite, difficulty in sleeping, agitation, apathy or feelings of guilt. The most common forms of depression are major depressive disorder and dysthymia, which is less severe.

Anxiety disorders are generally characterized by symptoms of unfounded chronic, exaggerated worry and tension. There are several different types of anxiety disorders, including panic disorder, obsessive-compulsive disorder, post-traumatic stress disorder, social phobia and generalized anxiety disorder. People diagnosed with depression are also often diagnosed with an anxiety disorder.

The Business Insights Healthcare Report estimates that depression affects approximately 80 million people in the seven major pharmaceutical markets, including approximately 44 million people in the United States. According to the National Institute of Mental Health, anxiety disorders affect approximately 19 million people in the United States. Wood Mackenzie estimates that the worldwide market for anti-depressants was approximately $16.9 billion in 2004.

Depression is thought to be associated with the disruption and imbalance in the brain of the neurotransmitters dopamine, norepinephrine and serotonin. Anxiety disorders are similarly thought to be associated with the disruption and imbalance in the brain of these same neurotransmitters, as well as acetylcholine. Medications currently used to treat depression, such as selective serotonin reuptake inhibitors, or SSRIs, dual uptake inhibitors, and tricyclics, are designed to increase the levels of one or more of those neurotransmitters. However, these drugs may take two to four weeks to be effective, if at all, and may cause side effects like nausea, increased sweating, fatigue and sexual dysfunction that are experienced before any benefit. Moreover, experts have estimated that approximately 70% of patients with depression do not achieve remission with SSRIs. Medications other than anti-depressants often used to treat anxiety disorders include benzodiazepines and azapirones. Azapirones may not be

immediately effective. Prolonged use of a benzodiazepine can result in a tolerance to the drug, ultimately making it ineffective. Benzodiazepines may also increase falls, and cause confusion and memory problems in the elderly.

Pain

Pain occurs when base nerve endings known as pain receptors are activated and a pain signal is transmitted through the nervous system to the brain. There are two general categories of pain, nociceptive and neuropathic. With nociceptive pain, the pain signal starts with damage to tissue and is typically accompanied by inflammation. With neuropathic pain, the pain signal results from inflammation of the peripheral nerves or other injury to the nervous system itself. A common form of neuropathic pain is sciatica, which is characterized by compression of the sciatic nerve resulting in leg and back pain. Neuropathic pain also arises from diabetes, cancer and exposure to chemotherapy or radiation. Both nociceptive and neuropathic pain can be either acute or chronic.

According to the Business Insights Healthcare Report, the worldwide market for pain therapies was approximately $13.9 billion in 2004. That report estimates that approximately 115 million people in the world's seven major pharmaceutical markets suffer annually from acute nociceptive pain following a surgical procedure. That report also estimates that 43 million people in the world's seven major pharmaceutical markets suffer annually from some form of neuropathic pain.

There is no single product available to treat all types of pain, and we believe that there are limitations to the existing treatments for each individual type of pain. Acute pain is typically treated with a class of drugs known as opioids. Prolonged use of opioids, however, may result in a tolerance to the drug, ultimately making it ineffective. In addition, the use of opioids may result in addiction and abuse. As a result, physicians are often reluctant to prescribe opioids for an extended period of time or at all. Chronic pain is most often treated with a class of drugs known as non-steroidal anti-inflammatory drugs. These drugs are often not sufficiently effective. In a nationwide survey of over 1,000 adults conducted in the United States in August 2003, only 58% of chronic pain sufferers rated their prescription medications as very or somewhat effective. No class of drugs, including opioids and non-steroidal anti-inflammatory drugs, has demonstrated consistent effectiveness in treating neuropathic pain.

Our Product Development Pipeline

We are developing our most advanced product candidates as treatments for target indications in three therapeutic areas: cognitive impairment, depression and anxiety, and pain. Within these areas, we have three product candidates in clinical development and two preclinical product candidates. In addition to these product candidates, we have preclinical programs in areas in which we believe that NNRs can be exploited for medical benefit. Mecamylamine hydrochloride, our product candidate currently in a Phase II clinical trial as an add-on therapy for depression, is approved in the United States as Inversine for the management of moderately severe to severe essential hypertension. Except for Inversine for the management of hypertension, neither the FDA nor any foreign regulatory authority has approved any of our product candidates for marketing.

The following table summarizes our product development pipeline.

Area of Therapeutic Focus	Product Candidate	Target Indication	Status of Development	Commercial Rights
Cognitive Impairment	TC-1734	Alzheimer's disease	Phase II trial in MCI complete; initiation of Phase II trial in mild to moderate Alzheimer's disease expected in the first half of 2007	AstraZeneca
		Cognitive deficits in schizophrenia	Initiation of Phase II trial in cognitive deficits in schizophrenia expected in the first half of 2007	AstraZeneca
		AAMI	Two Phase II trials complete	AstraZeneca
Depression/Anxiety	Mecamylamine hydrochloride	Depression	Phase II trial ongoing; results expected in the fourth quarter of 2006	Targacept
	TC-5214	Depression	Preclinical	Targacept
	TC-2216	Depression and anxiety disorders	Preclinical	Targacept
Pain	TC-2696	Acute post-operative pain	Initial Phase I trial complete; separate Phase I trial ongoing; full results expected in the third quarter of 2006	Targacept

We conducted our Phase II clinical trial of TC-1734 that we completed in March 2006 in the United States. We previously conducted two other Phase II clinical trials of TC-1734 in the United Kingdom. We are currently conducting our Phase I clinical trial of TC-2696 in France. We also conducted our previous Phase I clinical trial of TC-2696 in France and have not submitted an IND for clinical trials of TC-2696 in the United States. We are currently conducting our Phase II clinical trial of mecamylamine hydrochloride in the United States and India.

Under our collaboration agreement with AstraZeneca, AstraZeneca is conducting additional safety and product characterization studies to generate further data with respect to TC-1734 before deciding whether to proceed with the planned Phase II clinical trials of TC-1734 in Alzheimer's disease and cognitive deficits in schizophrenia. We expect AstraZeneca to complete these safety and product characterization studies within approximately 12 to 15 months from January 2006.

In addition to our product candidates described above, we have a preclinical product candidate that we refer to as TC-5619 that acts selectively on the α7 NNR. We may offer to AstraZeneca the right to develop and commercialize TC-5619 as a treatment for any or all of schizophrenia and various conditions marked by cognitive impairment under the terms of our collaboration agreement. If we do not offer this right to AstraZeneca, we may pursue the development and commercialization of TC-5619 for other indications, such as inflammation.

Cognitive Impairment

We are developing TC-1734 in collaboration with AstraZeneca as an oral treatment for Alzheimer's disease, cognitive deficits in schizophrenia and potentially other conditions marked by cognitive impairment, such as ADHD, AAMI and MCI.

TC-1734

TC-1734 is a novel small molecule. In March 2006, we completed a Phase II clinical trial of TC-1734 in 168 persons with AAMI. In 2004, we completed a Phase II clinical trial of TC-1734 in 70 persons with AAMI and a Phase II clinical trial of TC-1734 in 36 persons with MCI, a condition marked by cognitive impairment that is more severe than AAMI but less severe than Alzheimer's disease. We had previously evaluated TC-1734 in 84 healthy volunteers in four Phase I clinical trials.

While the exact causes of Alzheimer's disease, AAMI and MCI are unknown, the aging process is generally accompanied by a decline of cognitive function linked to a progressive deterioration and death of cells in the brain. This is known as neurodegeneration. If neurodegeneration reaches a more advanced stage, such as in Alzheimer's disease, a person becomes debilitated and unable to care for himself or herself. In addition, published third-party studies have shown that patients with Alzheimer's disease have deficient levels of acetylcholine and other key neurotransmitters in the brain. We believe that these neurotransmitter levels are also deficient, perhaps to a lesser degree, in persons with schizophrenia, AAMI and MCI.

Published third-party studies have shown a reduced number of a4ß2 NNRs in persons with dementia, suggesting the involvement of a4ß2 in cognition. In our preclinical animal studies, TC-1734 triggered activity of a4ß2, enhanced the release of acetylcholine, enhanced memory and showed meaningful separation between the doses at which positive effects on memory and side effects were first seen. In two preclinical in vitro studies that we conducted, TC-1734 protected neuronal cells from deterioration and death, a process known as neuroprotection. Based on these results and published studies that link neuroprotection to exposure to nicotine, a non-selective activator of all NNRs with particularly strong activity at a4ß2, we believe that TC-1734 has the potential to prevent or delay neurodegeneration.

In other published third-party studies, nicotine administered by injection or by patch improved attention and learning in Alzheimer's disease patients. In addition, studies have shown that Alzheimer's disease is more prevalent in non-smokers than in smokers. We believe that these studies suggest the potential of drugs that target NNRs to treat Alzheimer's disease.

In addition to Alzheimer's disease and cognitive deficits in schizophrenia, we and AstraZeneca plan to evaluate potential additional clinical development of TC-1734 for other indications such as ADHD, AAMI and MCI.

Clinical Development of TC-1734

Phase II Clinical Trial Completed in 2006. In March 2006, we completed a double blind, placebo controlled Phase II clinical trial of TC-1734 in AAMI. The trial was designed to provide additional evidence as to whether TC-1734 improves cognitive performance in cognitively impaired older adults. We conducted the trial at 16 sites in the United States. We recruited 193 subjects between the ages of 50 and 80, who were classified with AAMI, to participate in the trial.

The trial design provided for three dose groups, 25mg of TC-1734, 50mg of TC-1734 and placebo. Each group was dosed once daily for 16 weeks. Subjects in the 50mg dose group received 25mg for the first two weeks of dosing, 37.5mg for the next two weeks of dosing and 50mg for the remaining 12 weeks of dosing. Of the 193 subjects enrolled in the trial, 59 were randomly assigned to the 25mg dose group, 68 were randomly assigned to the 50mg dose group and 66 were randomly assigned to the placebo group. Of these, 53 subjects in the 25mg dose group, 57 subjects in the 50mg dose group and 58 subjects in the placebo group completed the trial.

Each subject was assessed using a computer-based test battery developed by CDR Ltd. to test cognitive function. We tested each subject at various time points prior to the first day of the 16-week dosing period to establish baseline. We tested subjects again at eight weeks and on the last day of the 16-week dosing period. The CDR test battery includes measures of attention, speed of cognitive processes and memory that assess the ability to react to stimuli, recognize words and pictures and recall words. These measures are then used to make composite assessments on the following five factors:

- power of attention, which assesses the intensity of concentration;
- continuity of attention, which assesses the ability to sustain concentration;
- working memory, or short-term memory, which assesses the ability to retain for a short period of time information that has not been previously learned;
- episodic memory, or long-term memory, which assesses the ability to store, hold for an extended period of time and retrieve information of an episodic nature, such as an event, name, object, scene or appointment; and
- speed of memory, which assesses the time it takes to recall an item from memory.

We also used the CDR test battery in the Phase II clinical trials of TC-1734 in AAMI and MCI that we completed in 2004 and in our Phase I clinical trials of TC-1734. We selected the CDR test battery because of its comprehensive measures and because CDR's extensive database of test results in unimpaired persons enables assessment of clinical relevance. CDR has indicated that its battery has been used to assess cognitive performance in over 500 clinical trials worldwide.

Primary Endpoints

The primary endpoints of a clinical trial are the one or more outcome variables specified in advance in the protocol for the trial that are determined to be the most important in assessing whether the primary objective of the trial has been achieved. There were three co-primary efficacy endpoints for this trial:

- *power of attention* – change from baseline on the power of attention factor of the CDR test battery at the end of the 16-week dosing period, as compared to placebo;
- *episodic memory* – change from baseline on the episodic memory factor of the CDR test battery at the end of the 16-week dosing period, as compared to placebo; and
- *subject global impression* – composite score on an overall cognitive improvement scale comprised of three seven-point measures in which each subject rates himself or herself on attention, memory and speed of thinking at the end of the 16-week dosing period, as compared to placebo.

We used the power of attention factor because it appeared to be the most sensitive CDR test factor in measuring improvement in cognitive performance in our previously completed Phase II clinical trial in AAMI. We used the episodic memory factor because we believe it is particularly applicable to Alzheimer's disease. Scientists have suggested that episodic memory is the earliest deficit that an Alzheimer's disease patient suffers. We used the subject global

impression scale as a measure of overall cognitive improvement to assess whether the effects of TC-1734 on aspects of cognition in a cognitively impaired older adult population are clinically meaningful.

The CDR test data are presented in this prospectus on a per protocol basis. This means that, for each trial, only data from subjects who complied with at least 80% of the dosing schedule and who completed the cognitive test battery assessments on the first and last day of the dosing period are included in the efficacy analysis. The data are presented on this basis because we believe that including partial data from subjects who did not satisfy the compliance criteria would require the interpolation of a substantial amount of unavailable data and prevent an appropriate statistical analysis of the results of the trial as designed.

Subjects receiving TC-1734 in the 50mg dose group showed improvement as compared to subjects dosed with placebo on all three co-primary efficacy endpoints. These results were statistically significant. Subjects receiving TC-1734 in the 25mg dose group showed improvement as compared to subjects dosed with placebo on the power of attention endpoint. This result was statistically significant.

A clinical trial result is statistically significant if it is unlikely to have occurred by chance. The statistical significance of clinical trial results is determined by a widely used statistical method that establishes the p-value of the results. Under this method, a p-value of 0.05 or less represents statistical significance. If a p-value is above 0.05, the result is not statistically significant, or NS. The p-values for the primary endpoints for the TC-1734 dose groups are set forth below.

Primary Endpoint	25mg TC-1734	50mg TC-1734
CDR – Power of Attention	0.023	0.010
CDR – Episodic Memory	NS	0.030
Subject Global Impression	NS	0.008

We believe that the achievement of statistically significant results in favor of TC-1734 on all three co-primary endpoints in the 50mg dose group of this trial suggests that TC-1734 enhances cognitive function in a cognitively impaired older adult population and supports further clinical development of TC-1734. In particular, we believe that the achievement of a statistically significant result in favor of TC-1734 on the subject global impression endpoint in the 50mg dose group suggests that the effects on cognition are clinically meaningful. However, the results that we observed in this Phase II trial in AAMI may not be replicated in any future clinical trials of TC-1734 that we or AstraZeneca conduct in Alzheimer's disease, cognitive deficits in schizophrenia, AAMI or any other indication.

Secondary Endpoints

Secondary endpoints of a clinical trial are measures specified in advance in the protocol for the trial that are either related to the primary objective of the trial or are outcome variables to be used in assessing whether secondary objectives of the trial have been achieved. We used a number of secondary endpoints for this trial, including improvement as compared to placebo at the end of the 16-week dosing period on the following factors:

- each of the three individual measures comprising the subject global impression scale, which we refer to as SGI subscores – memory, attention and speed of thinking; and
- each of the remaining three factors of the CDR test battery – continuity of attention, working memory and speed of memory.

Subjects receiving 25mg or 50mg doses of TC-1734 showed improvement as compared to subjects dosed with placebo in several of these measures. In particular, subjects in the 50mg dose group showed improvement on all three components of the subject global impression scale, and each of these results was statistically significant. The p-values for these secondary endpoints for the TC-1734 dose groups are set forth below.

Secondary Endpoint	25mg TC-1734	50mg TC-1734
SGI Subscore – Attention	NS	0.010
SGI Subscore – Memory	NS	0.022
SGI Subscore – Speed of Thinking	NS	0.020
CDR – Continuity of Attention	0.012	NS
CDR – Working Memory	NS	0.003
CDR – Speed of Memory	0.001	0.003

We are currently analyzing data from the trial with respect to additional secondary endpoints that we used in the trial. However, we do not expect the results of the trial on the co-primary endpoints and the six secondary endpoints described in this prospectus to change as a result of our analysis of the additional secondary endpoints.

Tolerability

TC-1734 was generally well tolerated in this trial as compared to placebo. We reported two serious adverse events experienced by subjects dosed with TC-1734. One of these subjects was diagnosed with lung cancer after being assigned to a dose group. The principal investigator for the trial site for this subject described the event as not related to TC-1734. The other subject was diagnosed with a myocardial infarction, commonly known as a heart attack, after being dosed for approximately 12 weeks. The principal investigator for the trial site for this subject described the event as possibly related to TC-1734. Because of the age range of the subject population for this trial, the types of the two serious adverse events that we observed were not unexpected.

There were no clinically significant differences among the two TC-1734 dose groups and the placebo group in the incidence of adverse events. The adverse events that we observed included dizziness, headaches, diarrhea, back pain, head colds, upper respiratory tract infections, nausea and joint pain. The most frequently observed adverse event was dizziness. However, the number of subjects in the placebo group who experienced dizziness was substantially the same as the number of subjects who experienced dizziness in the group dosed with 50mg of TC-1734 and greater than the number of subjects who experienced dizziness in the group dosed with 25mg of TC-1734.

Previous Phase II Clinical Trials. In 2004, we completed two double blind, placebo controlled Phase II clinical trials of TC-1734. One trial evaluated 70 persons at least 60 years of age classified with AAMI and the other trial evaluated 36 persons at least 60 years of age classified with MCI. We conducted the trials at multiple sites in the United Kingdom under clinical trial exemptions, the United Kingdom equivalent to an IND. The primary objective of each trial was to assess the safety and tolerability of TC-1734 in elderly subjects compared to placebo. Secondary objectives of each trial were to assess the efficacy of TC-1734 in improving cognitive function and changes in mood state. We did not observe any clinically significant effect on mood state in either trial.

In the AAMI trial, the subjects were divided into four dose groups, 50mg, 100mg, 125mg and 150mg. In the MCI trial, the subjects were divided into two dose groups, 50mg and 100mg. In both trials, each subject was initially dosed either with the applicable dose of TC-1734 or a placebo daily over a three-week period. Then, after a two-week period without being dosed, each

subject was changed to be dosed with either a placebo or TC-1734, as the case may be, daily for another three-week period. We anticipated that the two-week period without dosing would allow each subject to return to a pre-treatment state prior to the beginning of the second three-week dosing period and eliminate any carryover effect of the treatment in the first dosing period on a subject's performance in the second dosing period. Each subject took TC-1734 or a placebo before eating on the day of dosing. During the trials, routine safety measures were recorded and pharmacokinetic assessments were made for each subject. In addition, subjects were assessed for changes in cognitive function before dosing and at one, two and four hours after dosing on the first day of the three-week dosing period and then again on the last day of the dosing period. Subjects were also assessed for mood state on the first and last day of the three-week dosing period. The trials were double blind, meaning that neither the subjects nor the clinical investigators knew during the trials which subjects were receiving TC-1734 and which were receiving the placebo.

In the 50mg, 100mg and 125mg arms of the AAMI trial, TC-1734 was well tolerated, with no serious adverse events reported. In the 150mg dose group, three out of eight subjects treated with TC-1734 experienced side effects such as headache, lightheadedness, dizziness and vomiting and dropped out of the trial. Because of these side effects, we ceased dosing new subjects at 150mg.

We used the CDR test battery in both the AAMI and MCI trials to test for changes in cognitive function. The CDR test data from both trials are presented in this prospectus on a per protocol basis. The data are presented on this basis because we believe that including partial data from subjects who did not satisfy the compliance criteria would require the interpolation of a substantial amount of unavailable data and prevent an appropriate statistical analysis of the results of the trial as designed. On this basis, the AAMI data includes 20 subjects in the 50mg dose group, 20 subjects in the 100mg dose group, 19 subjects in the 125mg dose group and five subjects in the 150mg dose group. In some cases, dosing in the first three-week dosing period may have had an effect on performance on one or more factors in the cognitive test battery in the second three-week dosing period. This is referred to as treatment-by-period interaction and is identified by a statistical analysis of a dose group's performance on a particular test factor in the first dosing period versus the dose group's performance on that test factor in the second dosing period. In instances in which our statistical analysis indicated that a treatment-by-period interaction might have occurred for a particular dose group and a particular test factor, we have included in the results described in this prospectus only the first dosing period for that dose group for that test factor. The effect of including only the first dosing period in the results described in this prospectus for a particular dose group and a particular test factor is to reduce, by 50%, both the number of evaluated subjects in that dose group for that test factor that were dosed with TC-1734 and the number of subjects in that dose group for that test factor that were dosed with placebo. Where this occurred, because the number of evaluated subjects was substantially smaller, the improvement in the performance of subjects dosed with TC-1734 as compared to the performance of subjects dosed with placebo required to achieve statistical significance in favor of TC-1734 was greater than it would have been if there had been no treatment-by-period interaction and data from both dosing periods for that dose group and that test factor had been included in the results.

Compared to subjects who received placebo, subjects who received TC-1734 in the 50mg dose group showed improvements on four of the five factors: power of attention; continuity of attention; episodic memory; and speed of memory. These results were statistically significant. In the 50mg dose group, the result on the power of attention factor had a p-value of 0.001. In addition, the result on the continuity of attention factor had a p-value of 0.001, the result on the episodic memory factor had a p-value of 0.019, and the result on the speed of memory factor had a p-value of 0.010, in each case including only the first dosing period due to treatment-by-period

interaction. Subjects in the 50mg dose group who received placebo performed better than subjects who received TC-1734 on the working memory factor. This result was not statistically significant.

The positive effects that we observed in the 50mg dose group were less pronounced in the other dose groups. In the 100mg dose group, we observed improvement in subjects who received TC-1734 only on the episodic memory factor. The result was statistically significant with a p-value of 0.022. Subjects in the 100mg dose group who received placebo performed better than subjects who received TC-1734 on the speed of memory factor at one of the time points evaluated and the result was statistically significant. In the 125mg dose group, we observed improvements in subjects who received TC-1734 on two of the factors at one of the time points evaluated, in each case including only the first dosing period due to treatment-by-period interaction. The result on the working memory factor, with a p-value of 0.034, was statistically significant. We observed a strong trend in favor of TC-1734, but not statistical significance, on the episodic memory factor, with a p-value of 0.080. The result on the speed of memory factor includes only the first dosing period due to treatment-by-period interaction. Subjects in the 125mg dose group who received placebo performed better than subjects who received TC-1734 on the speed of memory factor and the result was statistically significant. In the 150mg dose group, we observed improvement on four of the factors for the five subjects who completed the trial and received TC-1734. The results on the continuity of attention factor, with a p-value of 0.049, and the speed of memory factor, with a p-value of 0.018, were statistically significant. We observed a strong trend in favor of TC-1734, but not statistical significance, on the power of attention factor at one of the time points evaluated, with a p-value of 0.081, and on the working memory factor, with a p-value of 0.094. The results of the AAMI trial suggest that TC-1734 is well tolerated at a dose range of up to 125mg, that 150mg is the maximum tolerated dose of TC-1734 for this trial design and that the compound had positive effects on at least one aspect of cognition assessed by the CDR test battery at each tolerated dose tested.

To generate additional data related to the tolerability of TC-1734, we also tested eight elderly persons classified with AAMI at a dose of 150mg, after having eaten, using the same trial design. This enabled us to assess the impact of food on the tolerability of TC-1734 by comparing it in subjects dosed at 150mg who had eaten and in subjects dosed at 150mg who had not eaten. On a per protocol basis, we evaluated six subjects dosed at 150mg who had eaten. As we expected, the results indicated that the 150mg dose of TC-1734 was better tolerated in subjects who had eaten than in subjects who had not eaten. We observed no serious adverse events. In this dose group, we observed improvement in subjects who received TC-1734 on the continuity of attention factor at one of the time points evaluated, and the result was statistically significant with a p-value of 0.028. We also observed improvement in subjects who received TC-1734 on the speed of memory factor, including only the first dosing period due to treatment-by-period interaction. The result on the speed of memory factor was statistically significant, with a p-value of 0.0460. In addition, we observed a strong trend in favor of TC-1734, but not statistical significance, in this dose group on the episodic memory factor, with a p-value of 0.100.

As in the AAMI trial, TC-1734 was well tolerated in the MCI trial, with only one serious adverse event reported. A subject who had a history of an abnormally slow heart rate lost consciousness and was hospitalized approximately one-and-one-half weeks following the end of the dosing phase of the trial. We do not believe that this adverse event was related to TC-1734. In the 100mg dose group of the trial, subjects who received TC-1734 showed improvement on the episodic memory factor, and the result was statistically significant with a p-value of 0.044. We also observed a strong trend in favor of TC-1734, but not statistical significance, in this dose group on the working memory factor, with a p-value of 0.070, and on the speed of memory factor at one of the time points evaluated, with a p-value of 0.100. The result on the speed of

memory factor includes only the first dosing period due to treatment-by-period interaction. Subjects in the 50mg dose group of the trial who received TC-1734 did not show improvement. Subjects who received placebo performed better than subjects who received TC-1734 on the working memory and speed of memory factors and those results were statistically significant. The result on the speed of memory factor includes only the first dosing period due to treatment-by-period interaction.

Phase I Clinical Trials. We have completed four Phase I clinical trials of TC-1734 in 84 healthy volunteers in which the compound was well tolerated. The results of these trials are summarized below.

- In a single rising dose trial with eight dose groups each comprised of six volunteers between the ages of 21 and 45, the compound was well tolerated in doses of up to 320mg. We also observed an acceleration in brainwaves thought to be associated with positive effects on attention, suggesting that the compound had reached the brain.
- In a multiple rising dose trial with four dose groups each comprised of six volunteers between the ages of 18 and 43, 50mg, 100mg and 200mg doses of TC-1734 or placebo were administered over a 10-day period. We observed a dose-dependent positive effect on attention at the end of the trial measured by the ability of the volunteers to focus on a particular task to the exclusion of other tasks.
- In another trial, six volunteers between the ages of 64 and 73 were given a single 80mg dose to assess the compound's pharmacokinetics, which refers to a drug's absorption, distribution and metabolism in, and excretion from, the body. We observed positive effects on memory and learning, including improved episodic memory based on word recall and picture recognition assessments. These effects lasted up to 48 hours after a single oral dose.
- In a food interaction trial, six volunteers between the ages of 22 and 45 were administered an 80mg dose with or without having eaten and the compound was well tolerated.

Plans for Future Development in Alzheimer's Disease. We believe that the effects that we observed in our completed Phase II clinical trials of TC-1734 indicate that TC-1734 has the potential to be an effective treatment for Alzheimer's disease. Our belief is based in part on the results of our Phase II clinical trial of TC-1734 in persons with MCI and the suspected relationship between MCI and Alzheimer's disease. Researchers have estimated that between 10% and 15% of persons with MCI are diagnosed with Alzheimer's disease each year. In addition, 80% of persons with MCI who participated in a third-party study were diagnosed with Alzheimer's disease within six years of being diagnosed with MCI. These data suggest that there may be a disease progression from MCI to Alzheimer's disease. Moreover, scientists have suggested that episodic memory is the earliest deficit that an Alzheimer's disease patient suffers. Published third-party studies have shown that tests that assess episodic memory best distinguish persons with Alzheimer's disease from unimpaired elderly persons. As described above, we observed positive effects on the episodic memory factor in some of the dose groups in our previous Phase II clinical trials of TC-1734 in AAMI and MCI.

We expect AstraZeneca to initiate a double blind, placebo controlled Phase II clinical trial of TC-1734 for the treatment of mild to moderate Alzheimer's disease in the first half of 2007. The planned trial design includes several TC-1734 dose groups and a group to be dosed with a marketed treatment for Alzheimer's disease, with a number of patients that AstraZeneca expects to be adequate to detect a statistically significant response on the trial's outcome measures. The existing development plan for TC-1734 specifies that the trial will include approximately 790 patients with mild to moderate Alzheimer's disease. We expect that patients will be randomly assigned to a dose group of 25mg, 50mg or 100mg of TC-1734, to a dose group of donepezil, a

commonly prescribed treatment for mild to moderate Alzheimer's disease, or to placebo. The planned co-primary outcome measures of the trial are the Alzheimer's Disease Assessment Scale-cognitive subscale, or ADAS-Cog, the measure most often used to assess the efficacy of drugs for Alzheimer's disease, and a clinician interview-based impression of change, or CIBIC, scale. We anticipate that a cognitive test battery would also be included in the trial as a secondary measure. The planned trial design for the Phase II clinical trial of TC-1734 in mild to moderate Alzheimer's disease may change based on the results of the safety and product characterization studies of TC-1734 that AstraZeneca is conducting prior to deciding to initiate a Phase II clinical trial of TC-1734 or other factors. Changes to the trial design could relate to the number of subjects, dose groups, endpoints or any other details of the planned trial. AstraZeneca has significant control over trial design, as well as the conduct and timing of development efforts with respect to TC-1734.

Plans for Future Development in Cognitive Deficits in Schizophrenia. We believe that TC-1734 also has the potential to be an effective treatment for cognitive deficits in schizophrenia. In a 2004 survey of 46 neuroscientists and neuropharmacologists conducted in connection with a National Institute of Mental Health initiative known as Measurement and Treatment Research to Improve Cognition in Schizophrenia, or MATRICS, designed to support the development of pharmacological agents for improving the cognitive deficits in schizophrenia, deficits in attention and vigilance were identified most often as the most important cognitive deficit in schizophrenia. As described above, we observed positive effects on attention in two of the dose groups in our completed Phase II clinical trial of TC-1734 in AAMI.

We expect AstraZeneca to initiate a double blind, placebo controlled Phase II clinical trial of TC-1734 as a therapy for the treatment of cognitive deficits in schizophrenia together with an approved therapy for the psychosis symptoms of schizophrenia in the first half of 2007. The planned trial design includes several TC-1734 dose groups, with a number of patients that AstraZeneca expects to be adequate to detect a statistically significant response on the trial's outcome measures. In particular, we expect that TC-1734 will be administered together with one or more representative marketed drugs from the drug class known as atypical anti-psychotics. We expect the trial to include between 400 and 600 patients with schizophrenia and that patients will be randomly assigned to a dose group of 25mg, 50mg or 100mg of TC-1734, or placebo. The planned primary outcome measure of the trial is a cognitive test battery that we expect MATRICS to identify. We anticipate that a number of other cognitive scales would be included in the trial as secondary measures. The planned trial design for the Phase II clinical trial of TC-1734 in cognitive deficits in schizophrenia may change based on the results of the safety and product characterization studies of TC-1734 that AstraZeneca is conducting prior to deciding to initiate a Phase II clinical trial of TC-1734 or other factors. Changes to the trial design could relate to the number of subjects, dose groups, endpoints or any other details of the planned trial. AstraZeneca has significant control over trial design, as well as the conduct and timing of development efforts with respect to TC-1734.

Plans for Future Development in AAMI. We do not have, and we do not believe that AstraZeneca has, any current plan to pursue development of TC-1734 for the treatment of AAMI beyond the Phase II clinical trial that we completed in March 2006. However, AstraZeneca has agreed that it may pursue additional development and commercialization of TC-1734 for the treatment of AAMI at such time it determines in the future that a favorable regulatory environment exists for the introduction of products for the treatment of AAMI to the market. We believe that the results of our completed Phase II clinical trials of TC-1734 in AAMI and MCI and the neuroprotective effect that we observed in preclinical in vitro studies of TC-1734 suggest the potential of TC-1734 as an early treatment for progressive cognitive impairment.

In three letters that we have received from the FDA in connection with the protocol for the Phase II trial of TC-1734 for the treatment of AAMI that we completed in March 2006 and subsequent protocol amendment submissions, the FDA informed us that it believes it is questionable whether AAMI satisfies the criteria necessary for AAMI to be recognized as a distinct clinical condition. The FDA also informed us that it is not clear that our Phase II clinical trial design and efficacy endpoints are appropriate for measuring the clinical effect of TC-1734 in AAMI. In particular, the FDA characterized it as unclear whether the power of attention factor of the CDR test battery is an appropriate outcome measure to use for assessing the effect of a drug on AAMI, in which the only claimed deficit is an impairment of memory. We have not had any discussions with the FDA regarding whether AAMI is a clinical entity for which approval of a drug is possible. Even if the FDA were ultimately to be unwilling to recognize AAMI as a distinct clinical condition, we believe that our recently completed Phase II AAMI trial could benefit us and AstraZeneca in our efforts to gain marketing approval of TC-1734 for Alzheimer's disease because it further established the safety profile of TC-1734 and further demonstrated its cognitive effects in an expanded number of cognitively impaired older adults.

Other TC-1734 Development Studies. In our completed clinical trials of TC-1734, we used a particular salt form of TC-1734 that we refer to as the 112 salt. We have developed an alternate salt form of TC-1734 that we refer to as the 226 salt that we and AstraZeneca may use in future clinical trials of TC-1734 and as the commercial form. We believe that the 226 salt will cost less to make than the 112 salt. We also believe that the 226 salt will be more soluble than the 112 salt. In the fourth quarter of 2005, we completed a bioavailability study in which a single dose of the 112 salt and a single dose of the 226 salt were administered to 12 healthy volunteers. Bioavailability studies are typically designed to assess the extent to which a drug is absorbed into the blood. In this study, we determined that levels of TC-1734 observed in the blood following administration of the two salts were substantially equivalent.

In addition, our agreement with AstraZeneca provides for AstraZeneca to conduct safety and product characterization studies at its expense to generate further data with respect to TC-1734 before deciding whether to proceed with the planned Phase II clinical trials of TC-1734 in mild to moderate Alzheimer's disease and cognitive deficits in schizophrenia. These studies consist of:

- in vitro studies to assess whether TC-1734, when administered at a therapeutically-relevant dose, activates a particular protein that can activate an enzyme known as CYP1A1 that is considered by some scientists to increase susceptibility to cancer;
- a clinical trial to characterize the cardiovascular effects of various doses of TC-1734 in persons who break down and eliminate, or metabolize, TC-1734 at varying rates;
- a single-dose study in dogs to further assess TC-1734's cardiovascular effects; and
- small clinical trials to evaluate the interaction and combined effects of TC-1734 with paroxetine, a known inhibitor of a key enzyme involved in TC-1734's primary metabolic pathway, and with multiple commonly prescribed treatments for schizophrenia.

The drug interaction trials are designed to determine whether the metabolism or safety of TC-1734 or any of these commonly prescribed treatments is adversely affected when administered with the other drug. A drug that is generally safe when taken alone may be not be safe or may not be as safe when taken together with other drugs.

Depression/Anxiety

We are currently conducting a clinical trial of mecamylamine hydrochloride for depression as an add-on therapy to citalopram hydrobromide. In addition, we have two preclinical product candidates for depression, TC-5214, which is one of the molecular components of mecamylamine hydrochloride, and TC-2216, which we are developing for either or both of depression and anxiety disorders. We are also evaluating TC-2216 as a potential product candidate for smoking cessation or obesity instead of or in addition to depression and anxiety disorders.

Mecamylamine hydrochloride and TC-5214

Mecamylamine hydrochloride is the active ingredient in Inversine, which is currently our only approved product. Inversine is approved in the United States for the management of moderately severe to severe essential hypertension. We believe that Inversine is prescribed predominantly for the treatment of neuropsychiatric disorders, including Tourette's syndrome, autism and bipolar disorder, in children and adolescents at a lower dose than is used for hypertension. Inversine has been approved for marketing since the 1950s. We acquired marketing rights to the product in August 2002 from Layton Bioscience, Inc., which had previously acquired the rights from Merck & Co., Inc. In connection with our acquisition, we assumed Layton's obligations under the agreement pursuant to which Layton acquired the rights from Merck. Pursuant to that agreement, we pay Merck an amount each year based on annual sales of Inversine, subject to a specified annual maximum. Our annual payment obligation to Merck expires in 2008.

Preliminary results of a clinical trial conducted by researchers at Yale University and reported in 2004 showed that mecamylamine hydrochloride had anti-depressant effects in patients who were not fully responding to various commonly prescribed anti-depressants when used as an add-on therapy to the anti-depressant as compared to when patients were treated with the anti-depressant and a placebo. In addition, in a third-party preclinical study published in 2004, rats lacking the ß2 NNR subunit did not respond to a known anti-depressant. We believe that this study suggests a correlation between abnormal ß2 activity and depression. We also believe that mecamylamine hydrochloride may act to normalize the activity of ß2.

Based in part on these results, we are currently conducting a clinical trial of mecamylamine hydrochloride for depression as an add-on therapy to citalopram hydrobromide, a commonly prescribed anti-depressant marketed as Celexa. We are conducting the trial at one site in the United States and nine sites in India. The trial design provides for two phases. In the first phase, patients with a diagnosis of depression are administered 20mg to 40mg doses of citalopram hydrobromide over six weeks and evaluated based on improvement on the Hamilton Rating Scale, an accepted rating scale for depression, to determine whether they are responding favorably. We enrolled 349 patients into the first phase of the trial. Patients who do not respond favorably or do not respond in full are enrolled into the second phase of the trial. The second phase is double blind and placebo controlled and is designed to include approximately 160 evaluable patients. As of March 24, 2006, we have enrolled 172 patients into the second phase of the trial. In the second phase, patients are randomly assigned into dose groups of mecamylamine hydrochloride or placebo, in each case together with the established dose of citalopram hydrobromide, over eight weeks. Each patient that is assigned to receive mecamylamine hydrochloride is administered a 5mg dose daily for the first two weeks of the trial. Based on the investigating physician's assessment of tolerability and therapeutic response, the physician can elect to increase the dose to 7.5mg for the next two weeks or to maintain the dose at 5mg. Following the second two-week period, the investigating physician can again elect

to increase the dose to 10mg for the remaining four weeks or to maintain the existing dose. The primary efficacy endpoint of the trial is improvement on the Hamilton Rating Scale as compared to placebo. We are also using several other rating scales as secondary measures.

As of March 24, 2006, two serious adverse events were reported in connection with the second phase of this trial. Because the trial is double blind, we do not yet know whether the patients who experienced these events were dosed with mecamylamine hydrochloride and citalopram or with placebo and citalopram. One of these patients was hospitalized due to nausea, weakness and vertigo, or dizziness and disorientation, after being dosed for approximately six weeks. While hospitalized, the patient experienced low blood pressure, abnormal heart contractions and a slow heart rate. The other patient experienced increased blood pressure, dizziness and lightheadedness after being dosed for approximately three weeks. This patient's blood pressure returned to normal levels after being administered blood pressure medication. The principal investigators for the trial sites for the subjects who experienced these events described the events as possibly related to mecamylamine hydrochloride. We believe that the two reported serious adverse events are independent and unrelated to each other.

The design for this trial is adaptive, which means that interim analyses are permitted to be undertaken at prescribed intervals, and with limited effect on the statistical power of the trial, to assess whether the number of patients included in the trial is adequate to achieve statistical significance in the trial's outcome measures. We engaged an independent statistician to conduct an interim analysis and to make a recommendation as to whether it would be advisable to increase the number of patients in the trial. The independent statistician reviewed available data from the first 105 patients who completed the trial. In March 2006, the independent statistician recommended that we increase the number of patients by 607 patients per dose group based on his interim analysis of data relating to the primary efficacy endpoint of the trial. This recommendation is consistent with a prior recommendation from the same independent statistician based on available data from the first 50 patients who had completed the trial. We do not expect to implement the independent statistician's recommendation to increase the number of patients and plan to complete the trial as designed.

We believe that the recommendation from the independent statistician suggests a modest trend in favor of mecamylamine hydrochloride on the primary efficacy endpoint for the trial. However, we also believe that the recommendation from the independent statistician suggests that, when data from all subjects who complete the trial become available, the result on the primary efficacy endpoint for the trial may not be statistically significant. We expect the results of the trial to be available in the fourth quarter of 2006.

TC-5214 is one of the enantiomers of mecamylamine hydrochloride. Enantiomers are chemical substances that are mirror images of each other and have the same chemical but potentially different biological properties. TC-5214 is a preclinical product candidate. We have licensed from the University of South Florida Research Foundation rights under an allowed patent application that, if issued, would provide us with coverage for the composition of TC-5214 for use as a pharmaceutical. TC-5214 has shown anti-depressant effects in several preclinical rodent models.

If the results of our ongoing Phase II trial of mecamylamine hydrochloride are favorable, we may accelerate the development of TC-5214 as an add-on therapy for depression in lieu of further development of mecamylamine hydrochloride. We do not expect to pursue the clinical development of both mecamylamine hydrochloride and TC-5214 for depression.

TC-2216

TC-2216 is a novel small molecule that we are developing as an oral treatment for depression and anxiety disorders. Depression and anxiety disorders often occur together, and anti-depressants are often also used to treat anxiety disorders. TC-2216 showed greater potency in our preclinical studies than, and anti-depressant effects comparable to, selective serotonin reuptake inhibitors and tricyclics, which are commonly used treatments for depression. In other preclinical studies that we conducted, TC-2216 showed anxiety-relieving effects. In addition, in our preclinical in vitro studies, we found TC-2216 to act on the a4ß2 NNR to modulate the release of neurotransmitters that are involved in mood and to avoid interaction with nicotinic receptors in the muscles and ganglia that are associated with side effects. We are currently conducting additional preclinical safety studies necessary to support the filing of an IND for clinical trials of TC-2216. We plan to file an IND for TC-2216 in the second half of 2006. Based on our preclinical findings that TC-2216 modulates the release of dopamine and reduces weight gain and published animal studies that have linked nicotine's addictive effects to the release of dopamine, we are also evaluating TC-2216 as a potential product candidate for smoking cessation or obesity instead of or in addition to depression and anxiety disorders.

A number of reported studies in humans and animals have linked nicotine to improvements in symptoms of depression. In one of these studies, nicotine administered via patch produced short-term improvements in symptoms in patients with depression based on a significant reduction in scores on the Hamilton Rating Scale after the second day. Because many current anti-depressants do not take effect for two to four weeks, the rapid onset of action of nicotine suggests a potentially significant advantage for drugs that target NNRs to treat depression.

Pain

We are developing TC-2696 for acute post-operative pain. Depending on clinical trial results, available resources and other considerations, we may pursue development of TC-2696 for other classes of pain in addition to or instead of acute post-operative pain.

TC-2696

TC-2696 is a novel small molecule that we are developing as a treatment for acute post-operative pain. We have completed a Phase I clinical trial of TC-2696. TC-2696 demonstrated pain-relieving effects in models of acute, chronic and inflammatory nociceptive pain and of neuropathic pain with comparable or higher potency in preclinical animal models than morphine or indomethacin, the generally accepted standards of comparison. In these studies, the compound was rapidly absorbed and demonstrated an acceptable toxicology profile.

In our preclinical in vitro studies of TC-2696, we found the compound to be a potent activator of the a4ß2 NNR and to avoid interaction with nicotinic receptors in the muscles and ganglia that are associated with side effects. Published studies conducted by third parties have shown that compounds that activate a4ß2 have pain-relieving effects in animals. We believe these effects are caused in part by the activation of NNRs that are abundant in CNS pathways to block the transmission of pain signals to the brain. In contrast, opioids act through a different mechanism of action. In our preclinical animal studies, TC-2696 did not result in tolerance following repeated administration. This suggests a potential advantage of TC-2696 compared to existing treatments for acute post-operative pain.

Clinical Development of TC-2696

Completed Phase I Clinical Trial. In 2004, we completed a placebo controlled Phase I single rising dose clinical trial of TC-2696 conducted to determine its safety and tolerability profile in healthy volunteers. The trial was conducted in France with 44 healthy volunteers divided into dose groups of 2mg, 5mg, 10mg, 20mg, 50mg, 100mg, 150mg and 200mg. In the trial, TC-2696 was well tolerated at doses of up to 150mg. At 150mg, we observed mild to moderate dizziness and lightheadedness. At 200mg, we observed nausea, vomiting and elevated blood pressure and heart rate.

We included a surrogate measure in our Phase I clinical trial of TC-2696 to provide an indication of the potential efficacy of this product candidate as a treatment for pain. The surrogate measure involved the use of a metal probe, which emitted increasing amounts of heat. We used the surrogate measure to assess pain threshold, which was indicated by the temperature of the metal probe at which subjects first reported feeling pain, and pain tolerance, which was indicated by subjects reporting the temperatures of the metal probe as bearable or not bearable. We also assessed pain relief, which was indicated by subjects making subjective estimations of the degree of pain on the day of assessment as compared to the first day of the trial. Using this surrogate measure, we observed a drug effect on at least one of the assessments at one or more time intervals in each of the 5mg, 10mg, 50mg and 150mg dose groups.

Ongoing Phase I Clinical Trial. We are currently conducting a Phase I multiple rising dose clinical trial to further assess the safety and tolerability profile of TC-2696. The trial design provides for 24 healthy volunteers to be randomized into three dose groups, 25mg, 50mg and 100mg. In each dose group, six subjects receive TC-2696 and two subjects receive placebo twice per day for ten days. We have completed the dosing phase of the trial for both the 25mg and 50mg dose groups. TC-2696 was generally well tolerated in both of these dose groups. All of the volunteers in the 25mg dose group and all but two of the volunteers in the 50mg dose group completed the trial. Of the two volunteers in the 50mg dose group who did not complete the trial, one discontinued participation due to elevated heart rate and dizziness and the other discontinued participation due to anguish and malaise. Because we replaced one of these two discontinued volunteers, seven total subjects in the 50mg dose group completed the trial. In the 100mg dose group, we suspended further dosing after two of three volunteers discontinued participation in the trial due to dizziness, nausea and, in one case, vomiting. Both of these volunteers had received a single dose of TC-2696 prior to discontinuing participation in the trial. We did not see comparable effects at 100mg in our completed single rising dose trial of TC-2696. Based on in vitro metabolism studies of TC-2696 that we subsequently conducted, we currently believe that the different effects of 100mg in our single rising dose trial and our multiple rising dose trial may be due to the primary metabolic pathway of TC-2696 and genetic differences with respect to that pathway. We are currently exploring potential causes of the different effects and plan to evaluate whether to continue dosing at 100mg following the completion of our analysis. If we complete the 100mg dose group of the trial, we plan to consider expanding the trial to include a 150mg dose group. We expect that, if we complete the 100mg dose group or add a 150mg dose group for this trial, we will include only subjects who are efficient metabolizers through the primary metabolic pathway of TC-2696.

In addition to assessing safety and tolerability, we are also using the same surrogate measure that we used in our completed Phase I single rising dose trial of TC-2696 in this Phase I multiple rising dose trial to provide an indication of the potential efficacy of this product candidate as a treatment for pain. We have received results on the surrogate measure from the 25mg and 50mg dose groups. In both dose groups, we observed a strong trend in favor of

TC-2696, but not statistical significance, in pain relief on all days assessed. Subjects dosed with TC-2696 consistently reported a greater reduction in the degree of pain felt on the day of assessment versus the first day of the trial, as compared to subjects dosed with placebo. We did not observe a drug effect in our assessments of pain threshold and pain tolerance.

We expect the full results of this trial to be available in the third quarter of 2006. If the results are favorable, we plan to initiate a Phase II clinical trial of TC-2696 in molar extraction patients in the fourth quarter of 2006.

Discontinued Clinical Development

In December 2004, we discontinued clinical development of two compounds that were not designed using our Pentad drug discovery technology. We elected to discontinue development of our compound TC-5231, which we had been developing as a treatment for attention deficit hyperactivity disorder, after we determined that, while well tolerated in the trial population of children and adolescents between the ages of 6 and 17, it failed to meet defined efficacy endpoints in a Phase II clinical trial. TC-5231 is a low-dose reformulation of mecamylamine hydrochloride, the active ingredient in our product Inversine.

We and Dr. Falk Pharma elected to discontinue development of our compound TC-2403, which we had been developing in collaboration with Dr. Falk Pharma in an enema formulation as a treatment for ulcerative colitis, after we determined that it failed to meet defined efficacy endpoints in a Phase II clinical trial. Pursuant to the terms of a collaboration agreement that we entered into with Dr. Falk Pharma, we shared the development costs of TC-2403 evenly with Dr. Falk Pharma.

Our Preclinical Research Programs

We focus our preclinical research efforts in areas in which we believe NNRs can be exploited for medical benefit and on indications for which we believe we can efficiently develop marketable product candidates. In selecting our target indications, we have considered a number of factors, including:

- the availability of preclinical or clinical data that suggest the relevance of NNRs to the indication;
- the size of the potential market opportunity for the indication;
- the projected development time required for a product candidate for the indication to reach the market;
- input received from scientific and medical experts in the indication at meetings that we convene; and
- the existence of well-defined clinical endpoints to assess the efficacy of a product candidate in the treatment of the indication.

Based on our consideration of these factors, we currently have a preclinical research collaboration under our agreement with AstraZeneca to discover and develop additional compounds that act on the a4ß2 NNR. We also have a preclinical research program focused on identifying and developing compounds that selectively target the a7 NNR and other preclinical research programs in smoking cessation and obesity, in addition to our preclinical product candidates for depression. Our current research objective is to file at least one IND or foreign equivalent each year beginning in 2006.

a7

A number of published studies have indicated an association between the a7 NNR and schizophrenia. Schizophrenia is a chronic, severe and disabling form of psychosis. In a 2004 survey of 46 cognitive neuroscientists and neuropharmacologists conducted in connection with the MATRICS initiative, a7 was selected more often than any other target as the target of most interest in the development of treatments for cognitive deficits in schizophrenia. Other published studies have suggested an association between the a7 NNR and cognitive function. Accordingly, we believe that the compounds that act selectively on the a7 NNR, or that act selectively on both the a7 and a4ß2 NNRs, may be useful in treating either or both of schizophrenia and cognitive impairment. We also believe that compounds that act on the a7 NNR may be exploited to treat inflammation.

We have selected a lead compound that we refer to as TC-5619 that acts selectively on the a7 NNR. We are currently conducting additional preclinical studies necessary to support the planned filing in 2007 of an IND for clinical trials of TC-5619. If we seek to exploit TC-5619 as a treatment for Alzheimer's disease, cognitive deficits in schizophrenia, other conditions marked by cognitive impairment or schizophrenia, we have the right prior to filing an IND to offer to AstraZeneca the right to develop and commercialize TC-5619 under the terms of the agreement. If we do not offer TC-5619 to AstraZeneca, we are generally not permitted to develop or commercialize TC-5619 for any of these indications. However, we would be permitted to pursue the development and commercialization of TC-5619 for other indications.

Smoking Cessation

Due primarily to nicotine's addictive effects, it is very difficult to quit smoking. Published animal studies have linked nicotine's addictive effects to the release of dopamine in regions in the brain involved in feelings of reward and pleasure. Although the specific NNR implicated in the regulation of dopamine is not fully characterized, several reported studies suggest that the a6, a4 and ß4 NNRs may be involved. These studies have shown that selectively blocking a6, a4 or ß4 reduced the rewarding effects of nicotine in mice. Other studies have shown that mice deficient in the ß2 NNR failed to respond to nicotine and had reduced activity in the brain regions associated with reward and pleasure. We are evaluating a number of compounds, including TC-2216, in a variety of animal models of smoking cessation and nicotine dependence for advancement in our smoking cessation program.

Obesity

A number of published studies have demonstrated that non-smokers generally weigh significantly more than smokers, and nicotine is believed to be responsible. These studies have also shown that smokers gain weight when they stop smoking. Moreover, reported studies with animals have shown that food intake and body weight gain are reduced following repeated administration of nicotine and that the effects are reversed when the nicotine administration is stopped.

As part of our evaluation of our compounds for other indications, we also assess each compound for a preliminary signal of its ability to induce weight loss. We are collecting this data and plan to conduct additional preclinical evaluation of the most promising compounds for obesity.

Our Drug Discovery Technologies—Pentad

We use proprietary databases and computer-based molecular design technologies to identify promising product candidates. We refer to these technologies collectively as Pentad.

We designed Pentad to predict the likelihood that novel compounds will interact with various NNRs, the degree of the interaction and the potential of these compounds to be developed as drugs based on projected pharmacokinetic profiles. Pentad consists of sophisticated computer-based simulation methodologies and extensive biological data from a library of diverse compounds that we have developed and gathered over more than 20 years. To date, we have applied Pentad specifically in the discovery and optimization of NNR-targeted therapeutics, but we believe it has application to a wide range of targets.

Pentad's virtual screening enables us to more rapidly identify clinically-viable compounds than we believe could be achieved using traditional laboratory synthesis and screening methods. This allows us to reduce drug development time by focusing our resources on compounds that we believe have a greater likelihood of clinical success. We used Pentad to design or optimize TC-1734, TC-2696, TC-2216 and TC-5619.

Our use of Pentad to design new classes of compounds selective for the a7 NNR is an example of its capabilities. We conducted virtual screening of nearly 11,000 compounds and, based on the results, synthesized 115 of them. In preclinical tests, 43 of the synthesized compounds were highly selective to the a7 NNR, showed a low degree of binding to NNRs involved in side effects, were bioavailable and passed the blood-brain barrier. We identified the 43 compounds in only six months and are currently evaluating many of these compounds, including TC-5619.

Strategic Collaborations

AstraZeneca AB

In December 2005, we entered into a collaborative research and license agreement with AstraZeneca AB under which we granted AstraZeneca exclusive development and worldwide commercialization rights to TC-1734 as a treatment for specified indications. The agreement became effective in January 2006. Under the agreement, AstraZeneca has agreed to pursue development and commercialization of TC-1734 as a treatment for Alzheimer's disease and cognitive deficits in schizophrenia. AstraZeneca has also agreed to pursue development and commercialization of TC-1734 as a treatment for ADHD if TC-1734 achieves the primary efficacy endpoints in a Phase II clinical trial for Alzheimer's disease or cognitive deficits in schizophrenia or a Phase III clinical trial of TC-1734 is otherwise initiated for Alzheimer's disease or cognitive deficits in schizophrenia. In addition, AstraZeneca can develop and commercialize TC-1734 for AAMI, MCI, any other indication that is deemed a cognitive disorder under the agreement and schizophrenia. We and AstraZeneca have also initiated a preclinical research collaboration under the agreement.

Payment Terms. AstraZeneca paid us an initial fee of $10 million in February 2006. AstraZeneca has agreed to make an additional payment of $20 million to us if it decides to conduct a Phase II clinical trial of TC-1734 following the completion of additional safety and product characterization studies that AstraZeneca is conducting at its expense to generate further data with respect to TC-1734. These studies are described in greater detail under "—Cognitive Impairment—Clinical Development of TC-1734—Other TC-1734 Development Studies." We are eligible to receive other payments of up to $249 million, contingent upon the

achievement of development, regulatory and first commercial sale milestones for TC-1734 for Alzheimer's disease, cognitive deficits in schizophrenia and ADHD, and stepped double-digit royalties on future TC-1734 product sales. If TC-1734 is developed under the agreement for an indication in addition to Alzheimer's disease, cognitive deficits in schizophrenia and ADHD, we would also be eligible to receive payments of up to $52 million, contingent upon the achievement of development, regulatory and first commercial sale milestones for TC-1734, for each such indication. Under the terms of a sponsored research agreement and subsequent license agreement, we are required to pay the University of Kentucky Research Foundation a low single digit percentage of any of these payments, including royalties, that we receive from AstraZeneca relating to TC-1734.

AstraZeneca's obligation to pay royalties to us for each compound subject to the collaboration expires on a country-by-country basis on the later of expiration of our patent rights that provide exclusivity for that compound in that country or twelve years after the first commercial sale in that country of either that compound or any related compound that meets specified criteria. If AstraZeneca obtains a patent covering the composition of a compound that is derived within a specified period from a compound that is subject to the collaboration, the term of AstraZeneca's patent would also be taken into account in determining the term of AstraZeneca's obligation to pay royalties to us for that derived compound. The U.S. patent rights to TC-1734 expire between 2016 and 2018. We also have a pending U.S. patent application that, if issued, would expire in 2025. The corresponding foreign patent rights expire between 2017 and 2019. We also have foreign patent applications that, if issued, would expire between 2017 and 2025. Royalty rates are subject to reduction under the agreement in specified circumstances, including in any country if the licensed compound is no longer subject to adequate patent protection in that country or if AstraZeneca licenses patent rights from any third party under circumstances in which the product that we license to AstraZeneca might infringe the third party's patent rights.

Research Collaboration. The agreement provides for a research collaboration under which we and AstraZeneca are conducting research designed to discover and develop additional compounds that, like TC-1734, act on the a4ß2 NNR. AstraZeneca has the right to exclusively license a specified number of these compounds, together with metabolites of these compounds and derivatives and other compounds related to these compounds that meet specified criteria for the same indications for which AstraZeneca has development and commercialization rights for TC-1734. Under the agreement, we are eligible to receive additional payments of up to $145 million, contingent upon the achievement of development, regulatory and first commercial sale milestones for each compound discovered and developed as part of the research collaboration, and stepped royalties on future product sales. The initial term of the research collaboration is four years and can be extended by mutual agreement. AstraZeneca can terminate the research collaboration upon at least six months notice effective three years after the research term begins.

Research Fees. While AstraZeneca is conducting the additional safety and product characterization studies on TC-1734, AstraZeneca has agreed to pay us research fees equal to 50% of our research expenses in the collaboration, subject to a specified limit. If our agreement with AstraZeneca continues in effect following the completion of the safety and product characterization studies, AstraZeneca has agreed to pay us additional research fees equal to the remaining 50% of our research expenses incurred while those studies were conducted and thereafter additional research fees equal to 100% of our research expenses in the collaboration, subject to specified limits. In that event, we would be entitled to receive a minimum of

$23.7 million in aggregate research fees over the four-year term of the research collaboration. Based on the current budget for the research collaboration, we expect to receive approximately $26.4 million in aggregate research fees under the agreement.

Development and Commercialization Costs. AstraZeneca is responsible for the clinical development and commercialization of TC-1734 and any compounds that arise out of the research collaboration that it elects to advance and has agreed to assume substantially all development costs, except for costs that we incurred to complete the Phase II clinical trial of TC-1734 in AAMI that we completed in March 2006. We have the option to co-promote TC-1734 and any compounds that are selected for advancement arising out of the research collaboration in the United States to specified classes of specialist physicians. If we exercise our co-promotion option, AstraZeneca is required to provide training to our sales force and compensate us for our detailing efforts following regulatory approval.

Exclusivity Rights and Restrictions. Neither we nor AstraZeneca are permitted outside of the collaboration to develop or commercialize compounds that act on the a4ß2 NNR and meet pre-defined criteria for Alzheimer's disease, cognitive deficits in schizophrenia, other conditions marked by cognitive impairment, schizophrenia or any indication for which AstraZeneca has development and commercialization rights under the agreement. This restriction on AstraZeneca lapses 30 months after the end of the research term. This restriction on us will lapse if AstraZeneca commences clinical development outside of the collaboration for a compound that acts on the a4ß2 NNR and meets pre-defined criteria.

We are entitled to offer to AstraZeneca the right to develop and commercialize any compound that acts on any NNR other than a4ß2 for any indication for which AstraZeneca has development and commercialization rights under the agreement. If we do not offer this right to AstraZeneca for a compound that acts on any NNR other than the a4ß2 NNR, we are generally not permitted to develop or commercialize the compound for any indication for which AstraZeneca has development and commercialization rights under the agreement. If we offer a compound to AstraZeneca, AstraZeneca could license the compound from us, together with metabolites of the compound and derivatives and other compounds related to the compound that meet specified criteria, under terms specified in the agreement. Alternatively, AstraZeneca could negotiate a development plan with us pursuant to which we would conduct development intended to provide a pre-defined indication of efficacy. AstraZeneca could license the compound from us after we complete the additional development. For each compound licensed by AstraZeneca through this process, we are eligible to receive payments of up to $266 million, contingent upon the achievement of development, regulatory and first commercial sale milestones, as well as stepped royalties on future product sales. If AstraZeneca elects not to license the compound, we are permitted to develop and commercialize the compound for any indication, except that, if we had offered the compound to AstraZeneca for schizophrenia, we will not be able to develop or commercialize the compound for any cognitive disorder. The agreement limits the number of compounds that we are permitted to offer to AstraZeneca through this process. We are generally not permitted to develop or commercialize compounds that act on any NNR for any indication for which AstraZeneca has development and commercialization rights under the agreement except through this process.

We are also entitled to offer to AstraZeneca the right to develop and commercialize (1) any compound for which AstraZeneca has development and commercialization rights for specified indications under the agreement or (2) any other compound that meets pre-defined criteria for cognitive activity, is in the same chemical family and acts on the same NNR or NNRs as any compound for which AstraZeneca has development and commercialization rights for specified

indications under the agreement for any indication for which AstraZeneca does not have development and commercialization rights under the agreement. If we do not offer this right to AstraZeneca, we are not permitted to develop or commercialize the compound.

If AstraZeneca commences clinical development outside of the collaboration of a compound that acts on any NNR other than the a7 NNR and meets other pre-defined criteria, the restriction on our right to develop and commercialize compounds that act on any NNR, other than the a4ß2 NNR, for any indication for which AstraZeneca has development and commercialization rights under the agreement will lapse.

If, in the future, we seek a strategic collaborator to develop or commercialize compounds for depression, anxiety or bipolar disorder, AstraZeneca has a right of first negotiation with us. If we and AstraZeneca do not agree on terms on which we would collaborate for these indications, for the following three years we would only be permitted to enter into a collaboration for those indications on more favorable terms than the terms offered by AstraZeneca.

Termination. AstraZeneca can terminate the agreement if it determines in its sole discretion on or before April 20, 2007 not to proceed with the further development of TC-1734 based on the results of the additional safety and product characterization studies that it conducts and all other factors relevant to TC-1734. In that event, we will be required to reimburse AstraZeneca for the amount of all research fees that it paid to us under the a4ß2 research collaboration while it conducted those studies. We would also be required to pay AstraZeneca an additional $5 million as compensation for assigning to us the data and any intellectual property generated in the studies, but we would not be required to refund the $10 million initial fee that AstraZeneca has paid us. AstraZeneca can also terminate the agreement without cause upon 90 days notice given any time after the earlier of the end of the research term and four years after the research term begins. We can terminate the agreement within 30 days after the end of the period in which AstraZeneca can terminate the agreement based on its determination not to proceed with the further development of TC-1734 if AstraZeneca has not notified us that it has decided to conduct a Phase II clinical trial of TC-1734. Either we or AstraZeneca can terminate the agreement in the event of the bankruptcy or uncured material breach of the other party. However, if a breach by AstraZeneca is limited to any specific compound or specified key market, we can terminate the agreement only with respect to that compound or key market. If a competitor of AstraZeneca acquires control of us, AstraZeneca can terminate the agreement or specified provisions of the agreement, including our right to participate on the committee overseeing development under the agreement and our co-promotion rights.

Aventis Pharma SA

In January 2002, we entered into a collaborative research, development and commercialization agreement with Aventis relating to the development and commercialization of Aventis compounds for Alzheimer's disease and other CNS disorders. The research term of the agreement expired in December 2004. No Aventis compounds were advanced into clinical development during the research term or within six months after expiration of the research term. As a result, we are not eligible to receive any further payments under the agreement.

There are two series of compounds that Aventis initially selected for advancement under the agreement, but ultimately elected not to develop under the agreement. Under the terms of the agreement, these Aventis compounds are available to us for in-licensing for use in

indications other than the treatment or prevention of CNS disorders or for use in specified CNS indications if Aventis is not developing its own product for those indications, subject to our making milestone and royalty payments to Aventis. Our right to in-license these compounds expires on June 30, 2007. We do not currently expect to exercise our in-licensing rights.

In addition, in January 2002, we had also entered into an amended and restated collaborative research and license agreement with Aventis for the development and commercialization of specified Targacept compounds, including TC-1734, for the treatment or prevention of Alzheimer's disease. This agreement terminated effective January 2, 2005. While the agreement was in effect, both we and Aventis were restricted from developing or commercializing compounds with specified activity at the a4ß2 or a7 NNRs for Alzheimer's disease, except under either the agreement or our other collaboration agreement with Aventis described above.

The Stanley Medical Research Institute

On December 15, 2004, we entered into a development agreement for one of our compounds with The Stanley Medical Research Institute, or SMRI, a nonprofit organization that supports research and development of treatments for schizophrenia. We and The Stanley Medical Research Institute terminated the development agreement in December 2005 in anticipation of our collaboration agreement with AstraZeneca.

Patents and Proprietary Rights

We actively seek to protect the proprietary technology that we consider important to our business, including chemical species, compositions and forms, their methods of use and processes for their manufacture, as well as modified forms of naturally-expressed receptors, in the United States and other key pharmaceutical markets. We also rely upon trade secrets and contracts to protect our proprietary information.

As of March 24, 2006, our patent estate includes 58 patents issued in the United States and 18 patent applications pending in the United States, including six U.S. patent applications that have been allowed but have not yet issued, and numerous issued patents and pending patent applications in countries other than the United States. Our issued patents and pending patent applications in the United States include composition of matter coverage on a number of different structural families of compounds. The actual protection afforded by a patent varies from country to country and depends upon many factors, including the type of patent, the scope of its coverage and the availability of legal remedies in a particular country.

Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. In the United States, The United States Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act, permits a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years. The patent term restoration period is generally one-half the time between the effective date of an IND and the submission date of an NDA, plus the time between the submission date of an NDA and the approval of that application. Only one patent applicable to an approved drug is eligible for the extension, and the extension must be applied for prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves applications for patent term extension. We expect to consider applying for patent

term extensions for some of our current patents, to add patent life beyond the expiration date, depending on the expected length of clinical trials and other factors involved in the filing of a new drug application.

We consider the following United States patents that we own or license to be most important to the protection of our most advanced product candidates.

Area of Therapeutic Focus	Product Candidate	Patent Scope	Patent Expiration
Cognitive Impairment	TC-1734	Composition of matter for TC-1734	June 2018
		Composition of matter for a family of compounds that includes TC-1734	April 2016
		Methods of use of a family of compounds that includes TC-1734 for treatment and prevention of CNS disorders	February 2017
Depression/Anxiety	Mecamylamine hydrochloride	Methods of use of mecamylamine for nicotine-responsive psychiatric disorders, including depression	September 2017
	TC-5214	Methods of use of S-mecamylamine for neuropsychiatric disorders, including depression	December 2019
		Pharmaceutical composition of S-mecamylamine (allowed)	December 2019
	TC-2216	Composition of matter for a family of compounds that includes TC-2216	June 2023
Pain	TC-2696	Composition of matter for TC-2696 (allowed)	June 2018
		Composition of matter for a family of compounds that includes TC-2696	April 2016
		Method of use of a family of compounds that includes TC-2696 for eliciting an analgesic effect	August 2017

We also have an issued patent in the United States covering composition of matter for a family of compounds that includes TC-5619, our preclinical product candidate that acts selectively on the α7 NNR. This patent expires in August 2019.

In addition to these patents and patent applications, we have later-expiring patents relating to some of these product candidates that cover a particular form or composition, use as part of combination therapy or method of preparation or use. These patents could provide additional or a longer period of protection. We also have patent applications pending that seek equivalent or substantially comparable protection for our product candidates in key international markets.

License Agreements

We are parties to four license agreements that are important to our business.

University of South Florida Research Foundation

Pursuant to a license agreement with the University of South Florida Research Foundation, or USFRF, we hold an exclusive worldwide license to patents and patent applications owned by USFRF for use in the development and commercialization of mecamylamine hydrochloride and other specified compounds. The licensed patents and patent applications include an issued patent covering methods of use for the treatment of depression, ADHD, Tourette's syndrome and nicotine-responsive neuropsychiatric disorders and pending patent applications covering the pharmaceutical composition of the molecular components of mecamylamine hydrochloride. Under the agreement, we are obligated to pay to USFRF:

- an annual license fee until a new drug application or its equivalent is filed to cover the use of a product subject to the license to treat a neuropsychiatric disorder;

- an annual fee to maintain our rights of first refusal to acquire rights to the licensed patents and patent applications beyond the scope of our current license;
- royalties on net sales of products subject to the license or a percentage of royalties received from a sublicensee;
- aggregate payments of up to $200,000 based on the achievement of specified regulatory milestones; and
- a percentage of other amounts that we receive from a sublicensee.

The aggregate annual license fees are creditable, up to a specified amount per year, against future royalties.

We are required to use commercially reasonable efforts to develop or to market and sell a product covered by the agreement. In particular, we are required to spend a specified minimum amount on research and development of products covered by the agreement each year until we receive marketing approval for a covered product. If USFRF believes that we are not meeting our diligence obligation, it is entitled to terminate the agreement following a cure period. If we do not agree with USFRF's determination, we can submit the matter to binding arbitration. In addition, if we have not received marketing approval of a product covered by the agreement on or before December 31, 2012, USFRF can make our license nonexclusive.

We may terminate the agreement at any time. If not earlier terminated, the agreement will terminate upon expiration of the last to expire of the licensed patent rights.

Virginia Commonwealth University Intellectual Property Foundation

Pursuant to a license agreement with Virginia Commonwealth University Intellectual Property Foundation, or VCUIPF, we hold a non-exclusive worldwide license to patents covering a method of use of a family of compounds that includes TC-2696 for eliciting an analgesic effect. Under the agreement, we are obligated to pay to VCUIPF:

- an annual license fee and an additional annual fee to maintain the right at any time to convert the license into an exclusive license for an additional fee;
- royalties on net sales of products subject to the license or a percentage of amounts received from a sublicensee; and
- aggregate payments of up to $900,000 based on the achievement of specified development and regulatory milestones.

We are required to use reasonable efforts to bring one or more products covered by the agreement to market. We may terminate the agreement at any time with 90 days notice. If the agreement is not earlier terminated, our obligation to pay royalties under the agreement will terminate upon expiration of the licensed patent rights.

Wake Forest University Health Sciences

Pursuant to a license agreement with Wake Forest University Health Sciences, or WFUHS, we hold an exclusive worldwide license to patents covering a method of use of a family of compounds that includes TC- 2696 for the treatment of chronic or female-specific pain. Under the agreement, we paid WFUHS a non-refundable upfront license fee of $25,000 and are obligated to pay to WFUHS:

- royalties on net sales of products subject to the license or, if less, a percentage of amounts received from a sublicensee;

- aggregate payments of up to $878,000 per product subject to the license based on the achievement of specified development and regulatory milestones; and
- a percentage of other amounts that we receive from a sublicensee.
- a percentage of other amounts that we receive from a sublicensee.

We are required to use commercially reasonable efforts to pursue the development of at least one product covered by the agreement and to bring at least one such product to market. We may terminate the agreement at any time with 60 days notice. If not earlier terminated, the agreement will terminate upon expiration of the last to expire of the licensed patent rights.

University of Kentucky Research Foundation

Pursuant to a sponsored research agreement, the University of Kentucky Research Foundation, or UKRF, agreed to assign to R.J. Reynolds Tobacco Company UKRF's rights to inventions that resulted in patents related to TC-1734, TC-2696 and other earlier-stage compounds in our portfolio. These patents were subsequently assigned by RJR to us in August 2000. Under the sponsored research agreement and a subsequent license agreement with UKRF, we are obligated to pay royalties to UKRF based on amounts received from any licensee of these patents, including AstraZeneca. In addition, under the license agreement, RJR paid UKRF an upfront license fee of $20,000.

Trade Secrets

In addition to patents, we rely upon unpatented trade secrets and know-how and continuing technological innovation to develop and maintain our competitive position. For example, we maintain Pentad as an unpatented trade secret. We seek to protect our proprietary information, in part, using confidentiality agreements with our commercial partners, collaborators, employees and consultants and invention assignment agreements with our employees. We also have confidentiality agreements or invention assignment agreements with some of our commercial partners and consultants. These agreements are designed to protect our proprietary information and, in the case of the invention assignment agreements, to grant us ownership of technologies that are developed through a relationship with a third party. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our trade secrets may otherwise become known or be independently discovered by competitors. To the extent that our commercial partners, collaborators, employees and consultants use intellectual property owned by others in their work for us, disputes may arise as to the rights in related or resulting know-how and inventions.

Sales and Marketing

We currently have limited sales and distribution capabilities and limited experience in marketing and selling pharmaceutical products. Our current strategy is to selectively enter into collaboration agreements with third parties for target indications in which our potential collaborator has particular expertise or that involve a large, primary care market that must be served by large sales and marketing organizations. In entering into these collaboration agreements, our goal will be to maintain co-promotion or co-commercialization rights in the United States and, in some cases, other markets. In order to implement our strategy successfully, we must develop a specialized sales and marketing organization with sufficient technical expertise. Our product currently available in the market, Inversine, is distributed by Cord Logistics, Inc., a Cardinal Health company, pursuant to an exclusive distribution

agreement. Our agreement with Cord Logistics is terminable by either party at the end of each contract year upon 90 days prior notice or at any time upon 180 days notice. We paid Cord Logistics approximately $150,000 in each of 2004 and 2005.

Manufacturing

All of our product candidates are compounds of low molecular weight, commonly referred to as small molecules. We have selected these compounds in part for their ease of synthesis and the low cost of their starting materials. All of our current product candidates are manufactured in a simple synthetic process from readily available starting materials. We expect to continue to develop drug candidates that can be produced cost-effectively by third-party contract manufacturers.

We are able to manufacture the quantities of our product candidates necessary for relatively short preclinical toxicology studies ourselves. We believe that this allows us to accelerate the drug development process by not having to rely on a third party for all of our manufacturing needs. However, we do rely and expect to continue to rely on a number of contract manufacturers to produce enough of our product candidates for use in more lengthy preclinical research. We also depend on these contract manufacturers to manufacture our product candidates in accordance with current good manufacturing practices, or cGMP, for use in clinical trials. We will ultimately depend on contract manufacturers for the manufacture of our products for commercial sale, as well as for process development. Contract manufacturers are subject to extensive governmental regulation.

Third parties currently manufacture Inversine and its active ingredient for us. Also, we have entered into a development and production agreement with Siegfried Ltd. Under this agreement, Siegfried has agreed to provide us with process development services and clinical trial material at specified rates for product candidates that we elect to introduce into the agreement. We have also agreed, following marketing approval or anticipated marketing approval of any product candidate for which Siegfried performs services under the agreement, to negotiate for a separate multi-year commercial supply agreement with Siegfried for a substantial percentage of our contracted supply needs for that product candidate, except in limited circumstances. Either we or Siegfried can terminate the agreement at any time on 12 months notice or immediately in the event of an uncured material breach by the other party.

Competition

Our industry is subject to rapid and intense technological change. We face, and will continue to face, worldwide competition from biotechnology, biopharmaceutical and pharmaceutical companies, research institutions, government agencies and academic institutions. Many of these competitors are established in the CNS field and are developing and commercializing pharmaceutical products that would compete with our product candidates that are approved for marketing. Many of our competitors and potential competitors have more resources than we do and have already successfully developed and marketed drugs. Mergers and acquisitions in the pharmaceutical industry may result in even greater resources being concentrated in our competitors.

We also face substantial competition from therapies designed to target NNRs. We are aware of several prominent pharmaceutical companies with product candidates designed to target NNRs in development, including Pfizer, with an NNR-targeted compound for which it has filed an NDA for smoking cessation, Sanofi-Aventis, with an NNR-targeted compound that has completed a Phase II clinical trial for smoking cessation, and Abbott Laboratories, with an

NNR-targeted compound in Phase II for Alzheimer's disease, ADHD and schizophrenia and a second NNR-targeted compound in Phase I for pain. In addition, we believe that other companies have active NNR-based research programs, including, Merck & Co., AstraZeneca, Eli Lilly, Memory Pharmaceuticals, Critical Therapeutics and NeuroSearch A/S. We expect to face increased competition in the future if NNR-targeted therapeutics are further validated and if companies initiate or grow NNR-based programs or otherwise enter the CNS market.

In addition, there are several pharmaceutical companies in the United States and globally that currently market and sell drugs for indications that we are targeting. There is currently no approved product either for cognitive deficits in schizophrenia or AAMI. We believe that the primary competitive products for use in indications that we are currently targeting include:

- for mild to moderate Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer/Eisai, Reminyl from Johnson & Johnson and Exelon from Novartis and for moderate to severe Alzheimer's disease, Namenda from Forest Laboratories, which acts by regulating the neurotransmitter glutamate;
- for pain, non-steroidal anti-inflammatory drugs such as Celebrex from Pfizer and opioids such as OxyContin from Purdue Pharma;
- for depression, selective serotonin reuptake inhibitors such as Prozac from Eli Lilly, Paxil/Seroxar from GlaxoSmithKline, Zoloft from Pfizer, Celexa from Forest Laboratories and Lexapro from Forest Laboratories and the dual uptake inhibitor Effexor from Wyeth;
- for schizophrenia, anti-psychotics such as Seroquel from AstraZeneca, Zyprexa from Eli Lilly, Risperdal from Johnson & Johnson, Geodon from Pfizer and Abilify from Bristol-Myers Squibb; and
- for smoking cessation, Zyban from GlaxoSmithKline.

Many of these products have well-known brand names, are distributed by large pharmaceutical companies with substantial resources and have achieved widespread acceptance among physicians and patients. Furthermore, pharmaceutical and biotechnology companies are currently developing additional treatments for the indications that we are targeting that may be approved for marketing and sale prior to any approval of our product candidates.

We expect to compete based upon, among other things, the efficacy of our products and favorable side effect profiles. Our ability to compete successfully will depend on our continued ability to attract and retain skilled and experienced scientific, clinical development and executive personnel, to identify and develop viable product candidates and to exploit these products and compounds commercially before others are able to develop competitive products. In addition, our ability to compete may be affected by insurers and other third-party payors encouraging the use of generic products. This may have the effect of making branded products less attractive from a cost perspective to buyers.

Government Regulation

Drug Regulation in the United States

The research, preclinical and clinical testing, manufacture and marketing of drug products are extensively regulated by the FDA and other governmental authorities in the United States. The Federal Food, Drug and Cosmetic Act and other federal and state statutes and regulations regulate the research, development, testing, manufacture, storage, record keeping, labeling, promotion and marketing and distribution of drug products.

The steps ordinarily required before a new drug may be marketed in the United States include:

- preclinical laboratory tests, preclinical studies in animals and formulation studies;
- the submission of an IND to the FDA, or comparable documents to regulatory bodies in foreign countries in which clinical trials are to be held, which must become effective before clinical trials may begin;
- adequate and well-controlled clinical trials to establish the safety and efficacy in humans of the drug for each indication;
- the submission of a new drug application, or NDA, to the FDA using the Common Technical Document, a format for non-clinical, clinical and quality data acceptable to regulatory authorities in the United States, European Union and Japan; and
- FDA review and approval of the NDA before any commercial sale or shipment of the drug.

Preclinical tests typically include laboratory evaluation of product chemistry, formulation and stability, as well as animal studies to evaluate toxicity and metabolism. Preclinical tests are regulated by the FDA under its good laboratory practice regulations. The results of preclinical tests are submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of an IND before clinical testing in humans may begin. If the FDA has not advised otherwise within this 30-day period, the proposed trial may begin. If the FDA has comments or questions, they must be resolved to the satisfaction of the FDA before the trial can begin. In addition, the FDA may halt proposed or ongoing clinical trials at any time, in which event the trial cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. The IND application process may be extremely costly and substantially delay development of product candidates. Moreover, positive results in preclinical tests do not ensure positive results in clinical trials.

Clinical trials involve the administration of the drug to healthy volunteers or patients under the supervision of a qualified principal investigator. Clinical trials must be conducted in compliance with federal regulations and requirements and under established protocols. These protocols detail the objectives of the clinical trial, the parameters to be used in monitoring safety, the efficacy criteria to be evaluated and the analyses to be relied on. The study protocol and informed consent information for patients in clinical trials must also be approved by an institutional review board at each institution where the clinical trials are conducted.

Clinical evaluation involves a time-consuming and costly process, ordinarily involving the following three phases:

- Phase I clinical trials are typically conducted with a small number of healthy human volunteers as subjects to determine an early safety and tolerability profile, including side effects associated with increasing doses, a maximum tolerated dose and pharmacokinetics.
- Phase II clinical trials are typically well-controlled and conducted with groups of patients afflicted with the disease or condition for which the investigational drug is being tested in order to determine, among other things, potential efficacy preliminarily, and an expanded safety profile that identifies short term side effects and risks.
- Phase III clinical trials are typically large-scale, geographically diverse, adequate and well-controlled and conducted with patients afflicted with a target disease or condition after obtaining preliminary evidence suggesting effectiveness. Phase III clinical trials are intended to collect additional data on effectiveness and safety necessary to evaluate the overall risk-benefit profile of the drug and provide an adequate basis for labeling.

The FDA, the study sponsor and the institutional review boards reviewing each clinical trial site closely monitor the progress of each of the three phases of clinical trials that are conducted in the United States. They may change or terminate the testing based upon the data accumulated to that point and their assessment of the relative risks and benefits to the patient.

Upon successful completion of Phase III trials, a company may submit an NDA including the results of preclinical studies and clinical trials and data relating to the product candidate's chemistry, pharmacology, manufacture, safety and effectiveness to the FDA in order to obtain approval to market the product in the United States. This submission is expensive, both in terms of studies and analyses required to generate and compile the requisite data and the significant user fees required for NDA submission.

The FDA has 60 days from its receipt of an NDA to determine if it will accept the filing for a substantive review. The FDA may refuse the filing, which would result in the loss of 25% of the application user fee. If the FDA accepts the filing, it begins an in-depth review. Under current performance goals, the FDA has either six or ten months to review and act on the NDA, depending upon whether the review is classified by the FDA as priority or standard. The FDA often extends the review timeline by requesting additional information or clarification. The FDA may refer issues to an advisory committee for review, evaluation and recommendation as to whether the application should be approved, but the FDA is not bound by any recommendation of an advisory committee.

If the FDA's evaluation of the NDA and the manufacturing facilities are favorable, the FDA may issue an approval letter, or, in many cases, an approvable letter followed by an approval letter. An approvable letter usually contains a number of conditions that must be met in order to secure final approval. If the FDA decides that the conditions have been met, it will issue an approval letter. An approval letter makes a drug available for physicians to prescribe in the United States, but authorizes commercial marketing of the drug only for specific indications. After a drug has been approved for a particular indication, other trials and studies may be conducted to explore its use for treatment of new indications. The drug may not be labeled or promoted for a new indication without a supplemental NDA approval by the FDA.

The FDA may also refuse to approve an NDA, or may issue a not approvable letter. A not approvable letter outlines the deficiencies in the submission and often requires additional testing or information. Even if the applicant completes the additional testing and submits additional information, the FDA may ultimately decide that the application does not satisfy the regulatory criteria for approval.

Satisfaction of FDA pre-market approval requirements for new drugs typically takes several years. The actual time required may vary substantially based upon the type, complexity and novelty of the product or target disease. Government regulation may delay or prevent marketing of potential products for a considerable period of time and require costly procedures. Success in early stage clinical trials does not assure success in later stage clinical trials. Data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations that could delay, limit or prevent regulatory approval.

Even if a drug receives regulatory approval, the FDA may require post-marketing studies, sometimes referred to as Phase IV studies, to monitor the effects of approved drugs and may limit further marketing based on the results of these post-marketing studies. Moreover, the FDA may impose restrictions on the drug or withdraw its approval if a company does not stay in compliance with pre- and post-market regulatory standards or if problems relating to safety or

effectiveness of the drug occur after it reaches the marketplace. The FDA has broad post-market regulatory and enforcement powers, including the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products and withdraw approvals.

Once an NDA is approved, the product it covers becomes a listed drug that can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that is therapeutically equivalent to a marketed drug. This means, among other things, that it has the same active ingredients in the same strengths and dosage form as the listed drug, is labeled for the same conditions of use and has been demonstrated to be bioequivalent to the listed drug, unless specified differences are approved pursuant to a suitability petition. There is generally no requirement, other than the requirement for evidence of bioequivalence, for an ANDA applicant to conduct or submit results of preclinical tests or clinical trials to establish the safety or efficacy of its drug product. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, are listed as such by the FDA and can typically be substituted by pharmacists under prescriptions written for the original listed drug.

Federal law provides for a period of three years of exclusivity following approval of a drug that contains previously approved active ingredients but is approved in a new dosage, dosage form or route of administration, or for a new use if new clinical trials were required to support the approval. During this three-year exclusivity period, the FDA cannot grant approval of an ANDA for a generic version of the listed drug. However, the FDA can approve generic equivalents of that listed drug based on other listed drugs with the same active ingredient, such as a generic that is the same in every way but its indication for use, and thus the value of this exclusivity may be limited. Federal law also provides a period of five years of exclusivity following approval of a drug that does not contain any previously approved active ingredients. During the five-year exclusivity period, no ANDA for a generic version of the listed drug can be submitted unless the submission accompanies a challenge to a listed patent, in which case the submission may be made four years following the original product approval.

In addition, applicants submitting an ANDA for a drug that has listed patents are required to make one of four certifications regarding each listed patent, which may include certifying that one or more listed patents are invalid or not infringed. If an applicant certifies invalidity or non-infringement, it is required to provide notice of its filing to the new drug application sponsor and the patent holder. If the patent holder then initiates a suit for patent infringement against the ANDA applicant within 45 days of receipt of the notice, the FDA cannot grant effective approval of the ANDA until either 30 months has passed or there has been a court decision holding that the patents in question are invalid or not infringed. The first of the ANDA applicants submitting substantially complete applications certifying that listed patents for a particular product are invalid or not infringed may qualify for an exclusivity period of 180 days, which runs from the date the generic product is first marketed. Until any effective 180-day exclusivity expires, the FDA cannot grant effective approval of subsequently submitted ANDAs.

The manufacturers of approved drugs and their manufacturing facilities are subject to continuous review and periodic inspections by the FDA and must comply with the FDA's current good manufacturing process, or cGMP, regulations. A manufacturer will be subject to possible legal or regulatory action, such as suspension of manufacturing, seizure of product or recall of a product, if it does not comply with the FDA's rules. We intend to contract with third parties to manufacture our products, and our ability to control their compliance with FDA requirements will be limited.

We must also notify the FDA of any change in an approved product beyond variations already allowed in the approval. Changes to the product, its labeling or its manufacturing could

require prior FDA approval and may require further clinical investigations to support the change. Such approvals may be expensive and time-consuming, and if not approved, the product will not be allowed to be marketed as modified.

The FDA also administers a number of complex regulations and policies regarding advertising, promotion and labeling of marketed pharmaceuticals. These regulations and policies include requirements that affect direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. Failure to abide by the FDA's regulations can result in penalties, including the issuance of a warning letter mandating the correction of deviations from FDA standards or the publication of corrective advertising, as well as civil and criminal investigations and prosecutions.

From time to time, legislation is drafted and introduced in the U.S. Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of drug products. In addition, the FDA regulations and guidance are often revised or reinterpreted in ways that may significantly affect our business and our products. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed, or what the impact of these changes, if any, may be.

Fast Track Designation

Congress enacted the Food and Drug Administration Modernization Act of 1997, or FDAMA, in part, to ensure the timely availability of safe and effective drugs, biologics and medical devices by expediting the FDA review process for some new products. FDAMA establishes a statutory program for the approval of a so-called fast track product, defined as a new drug or biologic intended for the treatment of a serious or life-threatening condition that demonstrates the potential to address unmet medical needs for that condition. Under the fast track program, the sponsor of a new drug or biologic may request the FDA to designate the drug or biologic as a fast track product at any time during clinical development of the product. Fast track designation provides for an expedited review of a product, which is intended to accelerate FDA approval. Although we have not yet requested fast track designation for any of our product candidates, we may seek fast track designation in the future. We will never be sure that we will obtain fast track designation. We cannot predict the ultimate impact, if any, of the fast track process on the timing or likelihood of FDA approval of any of our potential products.

Drug Regulation Outside the United States

In addition to U.S. regulations, we are subject to a variety of foreign regulations governing clinical trials and potential commercial sales and distribution of our products and product candidates. Even if we obtain FDA approval for a product, we must obtain approval of a product by the regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, we may submit marketing authorizations either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this latter procedure, the holder of a national marketing authorization may submit an application

to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

Third-Party Reimbursement

In the United States, European Union and elsewhere, sales of pharmaceutical products depend in part on the availability of reimbursement to the patient from third-party payors, such as government health administrative authorities, managed care providers and private insurance plans. Third-party payors are increasingly challenging the prices charged for medical products and services and examining their cost-effectiveness. For example, the European Union generally provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement. It is possible that none of our product candidates that receive marketing approval will be considered cost-effective or that reimbursement to patients will not be sufficient to allow us to maintain price levels that enable us to realize a satisfactory return on our investment in product development.

Price Controls

In the United States there have been, and we expect that there will continue to be, a number of federal and state proposals to implement governmental pricing control on pharmaceutical products. In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union generally provides options for its member states to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. We do not know whether any country that has price controls will allow favorable pricing arrangements for any of our product candidates.

Employees

As of March 24, 2006, we had 74 full-time employees, 33 of whom are Ph.D.s, M.D.s or both, and four part-time employees. Our management believes that relations with our employees are good. None of our employees is represented under a collective bargaining agreement.

Property and Facilities

We lease approximately 40,000 square feet of laboratory and office space located in the Piedmont Triad Research Park in Winston-Salem, North Carolina. We have rights exercisable until March 31, 2006 to lease additional space in this facility. The term of our lease expires August 1, 2007, and we have a renewal option for an additional five-year term. If we elect to renew the lease, we will have rights to lease additional space in this facility during the renewal term. The current monthly payment under our lease is approximately $123,000. We believe that our leased facilities, together with our rights to lease additional space, are adequate to satisfy our current needs.

Legal Proceedings

We are not currently a party to any material legal proceedings.

MANAGEMENT

Executive Officers and Directors

The name, age and position of our executive officers and directors as of February 28, 2006 are as follows:

Name	Age	Position
Mark Skaletsky (1) (2)	57	Chairman of the Board of Directors
J. Donald deBethizy, Ph.D.	55	Chief Executive Officer, President and Director
Merouane Bencherif, M.D., Ph.D.	51	Vice President, Preclinical Research
Jeffrey P. Brennan	48	Vice President, Business and Commercial Development
William S. Caldwell, Ph.D.	52	Vice President, Drug Discovery and Development
Geoffrey C. Dunbar, M.D.	58	Vice President, Clinical Development and Regulatory Affairs
Alan A. Musso	44	Vice President, Chief Financial Officer, Treasurer and Secretary
Peter A. Zorn	35	Vice President, Legal Affairs, General Counsel and Assistant Secretary
M. James Barrett, Ph.D. (1)	63	Director
Charles A. Blixt (2) (3)	54	Director
Errol B. De Souza, Ph.D. (2) (3)	52	Director
Ann F. Hanham, Ph.D.	53	Director
Elaine V. Jones, Ph.D. (1) (2)	51	Director
John P. Richard (3)	48	Director

(1) Member of the Compensation Committee.
(2) Member of the Governance and Nominating Committee.
(3) Member of the Audit Committee.

Mark Skaletsky has been a member of our board of directors since February 2001 and has been our Chairman since January 2002. Since March 2001, he has been the chairman and chief executive officer of Trine Pharmaceuticals, Inc., formerly Essential Therapeutics, Inc., a privately held drug discovery and development company. From May 1993 to January 2001, Mr. Skaletsky was the president and chief executive officer of GelTex Pharmaceuticals, Inc., a publicly traded pharmaceutical company. Mr. Skaletsky is a member of the boards of directors of Alkermes, Inc., ImmunoGen, Inc. and Advanced Magnetics, Inc., each of which is a publicly traded company. Essential Therapeutics and its wholly owned subsidiaries filed for protection under Chapter 11 of the United States Bankruptcy Code in May 2003. The plan of reorganization for Essential Therapeutics became effective in October 2003 by order of the United States Bankruptcy Court for the District of Delaware, and Essential Therapeutics was renamed Trine Pharmaceuticals, Inc. in November 2003.

J. Donald deBethizy, Ph.D. has been our Chief Executive Officer and a member of our board of directors since August 2000. Dr. deBethizy has been our President since March 1997. From March 1985 to March 1997, Dr. deBethizy worked for R.J. Reynolds Tobacco Company in various capacities, most recently as vice president of product evaluation, research and development. Dr. deBethizy has been an adjunct professor in the Department of Physiology and Pharmacology at Wake Forest University School of Medicine since October 1991 and has been an adjunct professor of toxicology in the Integrated Toxicology Program at Duke University since May 1988.

Merouane Bencherif, M.D., Ph.D. has been our Vice President, Preclinical Research since August 2002. He was our Vice President, Biological Sciences from August 2000 to August 2002 and our Senior Manager and Director of Pharmacology and Clinical Sciences from February 1999 to August 2000. From July 1993 to February 1999, Dr. Bencherif worked for R.J. Reynolds Tobacco Company's Research and Development (Pharmacology) Department in various capacities as a scientist, most recently as a master scientist from March 1998 to February 1999. Dr. Bencherif was an adjunct assistant professor from March 1996 to March 2002 and, since March 2002, has been an associate professor in the Department of Physiology and Pharmacology at Wake Forest University School of Medicine.

Jeffrey P. Brennan has been our Vice President, Business and Commercial Development since September 2003. From September 2000 to May 2003, Mr. Brennan was vice president, commercial development at Sanofi-Synthélabo Inc., a publicly traded global pharmaceutical company based in Paris, France. From November 1996 to September 2000, Mr. Brennan served as vice president, business development at Sanofi-Synthélabo.

William S. Caldwell, Ph.D. has been our Vice President, Drug Discovery and Development since August 2000. From January 1999 to August 2000, Dr. Caldwell was our Director, Chemistry and Operations.

Geoffrey C. Dunbar, M.D. has been our Vice President, Clinical Development and Regulatory Affairs since June 2001. From January 1997 to June 2001, Dr. Dunbar was vice president, clinical development—neurosciences at Bristol-Myers Squibb Company, a publicly traded global pharmaceutical company.

Alan A. Musso has been our Vice President, Chief Financial Officer, Treasurer and Secretary since February 2002. From February 2001 to February 2002, Mr. Musso was vice president and chief financial officer of Osiris Therapeutics, Inc., a privately held biotechnology company. From April 1997 to February 2001, Mr. Musso was the chief financial officer for Cato Research & Cato Holding Company, a privately held global contract research organization. Mr. Musso also was the chief financial officer of Vascular Genetics, Inc., a privately held gene therapy company, from October 1997 to February 2000. In addition, Mr. Musso was employed by Pfizer Inc., a publicly traded global pharmaceutical company, from April 1989 to December 1994, first as a senior auditor and then as a general accounting manager for one of Pfizer's manufacturing facilities. Mr. Musso is a certified public accountant and a certified management accountant.

Peter A. Zorn has been our Vice President, Legal Affairs, General Counsel and Assistant Secretary since January 2006. He was our Corporate Counsel and Assistant Secretary from May 2003 to January 2006. From January 1998 to May 2003, Mr. Zorn practiced with the law firm Womble Carlyle Sandridge & Rice, PLLC.

M. James Barrett, Ph.D. has been a member of our board of directors since December 2002. Since September 2001, Dr. Barrett has been a general partner of New Enterprise Associates, a venture capital firm that focuses on the medical and life sciences and information technology industries. From 1997 to 2001, he was chairman and chief executive officer of Sensors for Medicine and Science, Inc., a privately held company that he founded and which develops optical chemical sensing technologies. He continues to serve as its chairman and is a member of the boards of directors of the publicly traded companies MedImmune, Inc., Pharmion Corporation and Inhibitex, Inc.

Charles A. Blixt has been a member of our board of directors since August 2000. Since January 1998, he has been executive vice president and general counsel of R.J. Reynolds

Tobacco Company. Since June 1999, he has held positions of increasing responsibility with R.J. Reynolds Tobacco Holdings, Inc. and is currently president and a director. R.J. Reynolds Tobacco Holdings, Inc. is the parent company of R.J. Reynolds Tobacco Company. Since August 2004, he has been executive vice president, general counsel and assistant secretary of Reynolds American Inc.

Errol B. De Souza, Ph.D. has been a member of our board of directors since January 2004. Since March 2003, he has been president, chief executive officer and a director of Archemix Corporation, a privately held biotechnology company. From September 2002 to March 2003, he was president, chief executive officer and a director of Synaptic Pharmaceutical Corporation, a publicly traded biopharmaceutical company that was acquired by H. Lundbeck A/S in March 2003. From December 1999 to September 2002, he was senior vice president and site head of U.S. drug innovation & approval (research and development) of Aventis Pharma SA, a pharmaceutical company formed by the merger of Hoechst Marion Roussel and Rhone-Poulenc Rorer Inc. From September 1998 until December 1999, Dr. De Souza was senior vice president and global head, lead generation of Hoechst Marion Roussel. In 1992, Dr. De Souza co-founded Neurocrine Biosciences, Inc., a publicly traded biopharmaceutical company. Dr. De Souza is a member of the boards of directors of IDEXX Laboratories, Inc. and Palatin Technologies, Inc., each of which is a publicly traded company.

Ann F. Hanham, Ph.D. has been a member of our board of directors since September 2005. Ms. Hanham has been with Burrill & Company LLC, a merchant bank, since February 2000. Since January 2004, she has been a managing director, from January 2001 to January 2004, she was a director and from February 2000 to January 2001, she was an associate at Burrill & Company LLC.

Elaine V. Jones, Ph.D. has been a member of our board of directors since August 2000. Since August 2003, she has been a general partner of EuclidSR Associates, L.P., which is the general partner of EuclidSR Partners, L.P., a venture capital fund that focuses on life sciences and information technology companies. Dr. Jones was an investment manager from June 1999 to September 2001, and was a vice president from September 2001 to August 2003, for S.R. One, Limited, a venture capital subsidiary of SmithKline Beecham.

John P. Richard has been a member of our board of directors since November 2002. In June 2005, he became a partner of Georgia Venture Partners, a biotechnology venture capital firm. In addition, since April 1999, he has been an independent biotechnology consultant. He also has been Senior Business Advisor to GPC Biotech AG, a drug discovery and development company based in Munich, Germany and traded on the Frankfurt Stock Exchange, since April 1999. Prior to April 1999, Mr. Richard served as executive vice president, business development of SEQUUS Pharmaceuticals, Inc., a publicly traded biotechnology company that became a wholly owned subsidiary of ALZA Corporation in March 1999. Mr. Richard is a member of the board of directors of Altus Pharmaceuticals Inc., a publicly traded company.

Board Composition

Our board of directors consists of eight members, each of whom was elected in accordance with the terms of a stockholders agreement that will terminate upon the completion of this offering. With the exception of Dr. deBethizy, all of our directors are “independent directors” within the meaning of NASDAQ regulations. There are no family relationships among any of our directors or executive officers.

Following the completion of this offering, our board of directors will consist of eight members divided into three classes:

- Class I, for a term expiring at the first annual meeting of stockholders following the completion of this offering;
- Class II, for a term expiring at the second annual meeting of stockholders following the completion of this offering; and
- Class III, for a term expiring at the third annual meeting of stockholders following the completion of this offering.

At each annual meeting of stockholders after the initial classification, or at a special meeting in lieu of an annual meeting, a class of directors will be elected to serve for a three-year term to succeed the directors of the same class whose terms are then expiring. Our Class I directors will be Elaine V. Jones and Charles A. Blixt. Our Class II directors will be M. James Barrett, John P. Richard and J. Donald deBethizy. Our Class III directors will be Ann F. Hanham, Errol B. De Souza and Mark Skaletsky.

Board Committees

Audit Committee

The members of our audit committee are Messrs. Blixt, De Souza and Richard. Mr. Blixt chairs the committee. The audit committee assists the board of directors in its oversight of our accounting, financial reporting and internal control functions. Specific responsibilities of our audit committee include:

- oversight of the audits of our financial statements and our internal control over financial reporting;
- monitoring the performance of our independent auditors, including determining whether to engage or dismiss the independent auditors and to assess the independent auditors’ qualifications and independence;
- oversight of our compliance with legal and regulatory requirements, including approval of related party transactions and establishment of procedures for the receipt, retention and treatment of complaints regarding accounting, internal accounting controls and auditing matters; and
- preparing the report required to be included in our annual proxy statement in accordance with Securities and Exchange Commission rules and regulations.

Compensation Committee

The members of our compensation committee are Mr. Skaletsky and Drs. Barrett and Jones. Mr. Skaletsky chairs the committee. The purpose of our compensation committee is to discharge the responsibilities of our board of directors relating to compensation of our executive officers. Specific responsibilities of our compensation committee include:

- establishing and periodically reviewing our compensation philosophy and the adequacy of compensation plans and programs for our executive officers and other employees;
- establishing compensation arrangements and incentive goals for our executive officers and administering compensation plans;
- reviewing the performance of our executive officers and awarding incentive compensation and adjusting compensation arrangements as appropriate based upon performance; and
- preparing the report on executive compensation for inclusion in our annual proxy statement in accordance with Securities and Exchange Commission rules and regulations.

Governance and Nominating Committee

The members of our governance and nominating committee are Messrs. Skaletsky and Blixt and Drs. De Souza and Jones. Mr. Skaletsky chairs the committee. Specific responsibilities of our governance and nominating committee include:

- identifying individuals qualified to serve as directors, recommending to our board of directors nominees for election at our annual meetings of stockholders and recommending to our board of directors individuals to fill vacancies on the board;
- making recommendations to the board of directors concerning the criteria for board membership and the size, composition and compensation of the board of directors and its committees;
- assisting the board of directors in establishing and maintaining effective corporate governance practices and procedures; and
- conducting an annual review of the effectiveness of the board of directors and its committees.

Compensation Committee Interlocks and Insider Participation

None of our executive officers serve as a member of the board of directors or compensation committee, or other committee serving an equivalent function, of any other entity that has one or more of its executive officers serving as a member of our board of directors or our compensation committee. None of the members of our compensation committee has ever been our employee.

Director Compensation

In the past, each of our directors who is not our employee, or his or her designee, has received a nonqualified stock option to purchase 3,333 shares of our common stock upon his or her initial election to our board of directors. Additionally, upon each non-employee director's annual reelection, he or she, or his or her designee, has been granted a nonqualified stock option to purchase 1,000 shares of common stock. However, our chairman received a nonqualified stock option to purchase 4,666 shares upon his or her initial election and a nonqualified stock option to purchase 1,666 shares upon his or her annual reelection. Each of these options:

- has a ten-year term;
- has an exercise price of $0.08 per share; and
- vests one year after the date of grant if the director attended at least 75% of the regular board meetings held during that year.

In lieu of any such nonqualified stock option, each non-employee director could elect to receive a restricted stock award for the same number of shares of stock at a purchase price of $0.08 per share. Each non-employee director who is not affiliated with one of our investors or a group of our investors has received, in addition to the equity compensation described above, cash compensation in the amount of $15,000 per year as an annual retainer, except that the chairman of the board has received an annual cash retainer of $25,000. Each director is reimbursed for expenses incurred in connection with his or her attendance at meetings of the board of directors and its committees. We have not historically paid any additional compensation for service on any committees of the board of directors.

In December 2005, we amended stock options to purchase 6,000 shares of our common stock that had been granted to our directors who are not our employees, or their designees, in order to address taxation issues that arise due to recently enacted Internal Revenue Code Section 409A and related guidance. As amended, the affected stock options are not exercisable after March 15, 2007.

We have adopted a new director compensation program that will become effective concurrently with the completion of this offering. Each non-employee director will receive an annual cash retainer of $20,000 payable in quarterly installments. Each member of a committee of the board will receive an additional annual cash retainer of $2,500, the chairman of our audit committee will receive an additional annual cash retainer of $7,500 and the chairman of each of our compensation and governance and nominating committees will each receive an additional annual cash retainer of $2,500. Each non-employee director also will receive a nonqualified stock option to purchase 25,000 shares of common stock upon initial election as a director and a nonqualified stock option to purchase 7,500 shares of common stock upon annual reelection. The chairman of the board will receive a nonqualified stock option to purchase 10,000 shares of common stock upon initial election as chairman, in addition to the option to purchase 25,000 shares of common stock upon initial election as a director, and a nonqualified stock option to purchase 12,500 shares of common stock upon annual reelection. For more information, please see "Management—Stock Option and Other Compensation Plans—2006 Stock Incentive Plan."

Executive Compensation

The following table sets forth information for the periods indicated regarding compensation awarded to, earned by or paid to our chief executive officer and our five other most highly compensated executive officers who were serving as executive officers as of December 31, 2005. We refer to these officers in this prospectus as our named executive officers.

Summary Compensation Table

Name and Principal Position	Year	Annual Compensation		Long-Term Compensation	All Other Compensation
		Salary	Bonus	Shares Underlying Options (#)	
J. Donald deBethizy, Ph.D.	2005	$310,000	$105,400	174,000	$ 14,000(1)
President and Chief Executive Officer	2004	283,250	90,640	—	13,000(1)
	2003	275,000	66,000	262,578(2)	12,000(1)
Merouane Bencherif, M.D., Ph.D.	2005	200,000	51,000	50,000	12,092(1)
Vice President, Preclinical Research	2004	170,000	40,800	—	12,518(1)
	2003	161,000	38,640	78,083(2)	11,485(1)
Jeffrey P. Brennan (3)	2005	234,000	59,670	40,000	14,000(1)
Vice President, Business and Commercial Development	2004	225,000	54,000	—	111,748(4)
	2003	75,000	13,500	22,533(2)	4,500(1)
William S. Caldwell, Ph.D.	2005	193,752	49,407	42,000	12,073(1)
Vice President, Drug Discovery and Development	2004	170,000	40,800	—	11,947(1)
	2003	161,750	29,115	71,251(2)	11,314(1)
Geoffrey C. Dunbar, M.D.	2005	264,316	67,401	54,000	14,000(1)
Vice President, Clinical Development and Regulatory Affairs	2004	254,150	60,996	—	13,000(1)
	2003	246,750	44,415	89,119(2)	12,000(1)
Alan A. Musso	2005	205,000	52,275	48,000	14,000(1)
Vice President, Chief Financial Officer, Treasurer and Secretary	2004	190,000	45,600	—	13,000(1)
	2003	181,731(5)	32,400	71,156(2)	12,000(1)

(1) Consists of our contributions under the Targacept Retirement Savings Plan, our 401(k) plan.
(2) A portion of these options reflects grants made on January 26, 2004 under our 2000 equity incentive plan in lieu of a cash bonus for fiscal year 2003.
(3) Mr. Brennan joined us in September 2003.
(4) Consists of $12,190 of contributions under our 401(k) plan and reimbursement of $99,558 in relocation expenses.
(5) Salary amount includes compensation of $1,731 in lieu of accrued vacation.

Stock Options

The following table sets forth information regarding grants of stock options to purchase shares of our common stock to our named executive officers during the year ended December 31, 2005.

The potential realizable values set forth in the following table are calculated based on the term of the option at the time of grant and reflect gains that could be achieved for the options if exercised at the end of the option term. The 5% and 10% assumed annual rates of compounded stock price appreciation are required by the Securities and Exchange Commission and do not represent our estimate or projection of our future stock price performance. Actual gains, if any, on stock option exercises depend on the future performance of the common stock and the date on which the options are exercised.

Option Grants in Last Fiscal Year

Name	Number of Securities Underlying Options Granted	Percentage of Total Options Granted to Employees in Fiscal Year	Exercise Price Per Share	Expiration Date	Potential Realizable Value at Assumed Annual Rates of Stock Price Appreciation for Option Terms (1)	
					5%	10%
J. Donald deBethizy, Ph.D.	174,000	26.9%	$ 1.75	3/29/2015	$ 3,097,200	$ 5,110,380
Merouane Bencherif, M.D., Ph.D.	50,000	7.7	1.75	3/29/2015	890,000	1,468,500
Jeffrey P. Brennan	40,000	6.2	1.75	3/29/2015	712,000	1,174,800
William S. Caldwell, Ph.D.	42,000	6.5	1.75	3/29/2015	747,600	1,233,540
Geoffrey C. Dunbar, M.D.	54,000	8.4	1.75	3/29/2015	961,200	1,585,980
Alan A. Musso	48,000	7.4	1.75	3/29/2015	854,400	1,409,760

(1) The dollar amounts under these columns are the result of rates set by the Securities and Exchange Commission and, therefore, are not intended to forecast possible future appreciation, if any, in the price of the underlying common stock. The potential realizable values at 5% and 10% appreciation are calculated using an assumed initial public offering price of $12.00 per share and assuming that the market price appreciates from this price at the indicated rate for the entire term of each option and that each option is exercised at the exercise price and sold on the last day of its term at the assumed appreciated price.

Option Exercises and Year-End Option Values

The following table sets forth information regarding the number of shares of our common stock issued upon option exercises by our named executive officers during the year ended December 31, 2005 and the value realized by our named executive officers. The table also sets forth information regarding the number and value of unexercised stock options held by our named executive officers as of December 31, 2005. There was no public trading market for our common stock as of December 31, 2005. Accordingly, as permitted by the rules of the Securities and Exchange Commission, we have calculated the value of the unexercised in-the-money options at fiscal year end by determining the difference between the exercise price per share and an assumed fair market value of our common stock as of December 31, 2005 equal to an assumed initial offering price of $12.00 per share.

Aggregated Option Exercises in Last Fiscal Year and Fiscal Year-End Option Values

Name	Number of Shares Acquired on Exercise	Value Realized	Number of Securities Underlying Unexercised Options Held at December 31, 2005		Value of Unexercised In-the-Money Options at December 31, 2005	
			Exercisable	Unexercisable	Exercisable	Unexercisable
J. Donald deBethizy, Ph.D.	—	—	242,293	183,698	$ 2,033,149	$ 1,882,905
Merouane Bencherif, M.D., Ph.D.	—	—	102,772	52,470	848,166	537,818
Jeffrey P. Brennan	—	—	32,755	29,778	292,380	305,225
William S. Caldwell, Ph.D.	—	—	96,063	44,363	785,048	454,721
Geoffrey C. Dunbar, M.D.	—	—	89,599	56,147	730,100	575,507
Alan A. Musso	399	$ 1,728	88,777	49,579	720,407	508,185

Employment Agreements

We have entered into employment agreements with each of our named executive officers. Each employment agreement continues until terminated by either party to the agreement, with the exception of Mr. Brennan's employment agreement, which is set to expire on December 31, 2007.

Under the terms of these employment agreements, Dr. deBethizy is employed as our Chief Executive Officer and President at a minimum annual base salary of $225,000; Dr. Dunbar is employed as our Vice President, Clinical Development and Regulatory Affairs at a minimum annual base salary of $246,750; Mr. Brennan is employed as our Vice President, Business and Commercial Development at a minimum annual base salary of $225,000; Mr. Musso is employed as our Vice President and Chief Financial Officer at a minimum annual base salary of $180,000; Dr. Bencherif is employed as our Vice President, Preclinical Research at a minimum annual base salary of $135,000; and Dr. Caldwell is employed as our Vice President, Drug Discovery and Development at a minimum annual base salary of $135,000. For 2006, the base salary of Dr. deBethizy is $335,000; the base salary of Dr. Dunbar is $269,602; the base salary of Mr. Brennan is $245,700; the base salary of Mr. Musso is $220,375; the base salary of Dr. Bencherif is $208,000; and the base salary of Dr. Caldwell is $208,000.

The employment agreements provide that the annual base salaries of each of the named executive officers will be reviewed and are subject to increase in accordance with our policies and procedures, and in addition, will be increased annually as necessary to be consistent with the median base salaries of employees in similar positions at comparable companies as described in the then current Radford Biotechnology Compensation Report.

In addition to annual base salary, each named executive officer is eligible to receive awards under our 2000 equity incentive plan and earn an annual bonus equal to a percentage of his annual base salary. The employment agreements provide that Dr. deBethizy is eligible to earn an annual bonus of up to 35% of his annual base salary; each of Dr. Dunbar and Mr. Brennan is eligible to earn an annual bonus of up to 30% of his annual base salary; and each of Mr. Musso and Drs. Bencherif and Caldwell is eligible to earn an annual bonus of up to 25% of his annual base salary. In 2001, our board of directors increased the annual bonus for Dr. deBethizy to up to 40% of his annual base salary. In 2002, our board of directors increased the annual bonus for each of Drs. Bencherif and Caldwell to up to 30% of his annual base salary and in 2003 increased the annual bonus for Mr. Musso to up to 30% of his annual base salary. For 2006, Dr. deBethizy is also eligible to earn up to an additional 30% of his base salary, and each of Drs. Bencherif, Caldwell and Dunbar and Messrs. Musso and Brennan is also eligible to earn up to an additional 22.5% of his base salary, if in 2006 AstraZeneca elects to conduct a Phase II trial of TC-1734 following completion of additional safety and product characterization studies that AstraZeneca is conducting. Our board of directors or compensation committee, in their discretion, may increase the annual bonus for each named executive officer beyond these percentages.

Under the terms of the employment agreements, the named executive officers cannot disclose any of our proprietary information during the periods of their employment. In addition, the employment agreements prohibit the named executive officers from soliciting, on behalf of themselves or any entity other than us, any of our customers or clients for the period of employment and nine months following termination of employment, and in the case of Dr. deBethizy, one year following termination. Furthermore, any inventions, discoveries, improvements and developments made by the named executive officers during their employment with us become and remain our property.

If a named executive officer's employment terminates for any reason, the named executive officer is entitled to receive a lump sum equal to any base salary, bonus and other compensation earned and due but not paid through the effective date of termination. In addition, if we terminate a named executive officer's employment other than for just cause or a named executive officer terminates his employment for good reason, in each case as that term is defined in his agreement, he is entitled to receive:

- severance, payable monthly, equal to his then current base salary for twelve months in the case of Dr. deBethizy and nine months for all other named executive officers, following termination or, if shorter, until he secures other employment;
- acceleration of unvested options to purchase capital stock or restricted stock—Dr. deBethizy is entitled to twelve months acceleration, Mr. Brennan is entitled to nine months acceleration and all other named executive officers are entitled to six months acceleration;
- continuation of the health and life insurance benefits coverage provided to him as of the date of termination for the period during which he receives severance; and
- up to $10,000 in outplacement counseling services.

Stock Option and Other Compensation Plans

2000 Equity Incentive Plan

We maintain a 2000 equity incentive plan, which we refer to as our 2000 plan, that our board of directors and stockholders have approved. As of February 28, 2006, an aggregate of 1,878,888 shares of common stock had been authorized for issuance under our 2000 plan, of which options to purchase an aggregate of 1,631,110 shares of common stock were outstanding at a weighted average exercise price of $2.91 per share, 14,665 shares of common stock were issued and outstanding in the form of restricted stock and 30,968 shares of common stock were available for future grant. Upon completion of this offering, 35,143 shares of common stock subject to unvested options outstanding as of February 28, 2006 will immediately vest.

Our 2000 plan provides for the grant of a variety of stock-based awards, including incentive stock options, nonqualified stock options, stock appreciation rights, performance awards, bonus stock and restricted stock, to our employees, directors, independent contractors, consultants and advisors.

Administration of the Plan. Our 2000 plan is administered by the compensation committee of our board of directors, which, among other things, determines the terms and recipients of grants under the 2000 plan.

Options. Recipients of stock options under our 2000 plan have the right to purchase a stated number of shares of common stock at a stated exercise price, subject to any other terms and conditions that may be stated in connection with the option grant. We may grant options at an exercise price equal to, less than or greater than the fair market value of our common stock on the date of grant, except that we may not grant incentive stock options at an option price less than 100% of the fair market value of our common stock on the date of grant (or 110% of the fair market value for incentive stock options granted to optionees holding more than 10% of the voting power of all shares of our capital stock). Grant recipients may pay the exercise price of stock options by various methods permitted under our 2000 plan. Unless modified with respect to any particular grant:

- an employee who is terminated for any reason other than death, disability or cause will have 90 days to exercise options vested as of the termination date;
- an employee who terminates due to death or disability will have one year, or until the end of the respective option periods, if sooner, to exercise options that are vested as of the termination date;
- an employee who is terminated for cause will forfeit all options immediately upon termination; and
- non-employee optionees who are terminated will have 90 days, or until the end of the respective option periods, if sooner, to exercise options that are vested as of the termination date unless service terminates for cause, in which case the options terminate immediately.

Stock Awards. We may grant stock awards to participants subject to certain restrictions or no restrictions. Until they are vested and earned, unless an individual award agreement provides otherwise, grantees will not have the right to vote shares of restricted stock or the right to receive dividends or other distributions paid on such shares. If a grantee's employment or other service terminates during the restriction period or if any other conditions are not met, the restricted stock still subject to restrictions will terminate, unless an individual award agreement provides otherwise, and the shares must be immediately returned to us.

Significant Transactions. If:

- any entity or person acquires 50% or more of our outstanding common stock or, if such person owned shares as of August 22, 2000, 67% of our outstanding common stock; or
- our stockholders approve a sale or disposition of all or substantially all of our assets or a merger or consolidation in which we would not be the surviving or continuing corporation or which would result in the conversion of our common stock into cash, securities or other property (other than a merger or consolidation in which holders of common stock immediately prior to the merger or consolidation have the same proportionate ownership of common stock of the surviving corporation immediately after the merger as immediately before),

all awards outstanding under our 2000 plan would become immediately vested and exercisable unless, in the case of a merger, consolidation, share exchange or asset sale or disposition, the board of directors or compensation committee determines that outstanding awards will not become immediately vested and exercisable because steps have been taken, such as the assumption of the awards or substitution of substantially equivalent awards by the other party, as it deems equitable to protect the rights of participants in our 2000 plan. Upon completion of this offering, all awards outstanding under our 2000 plan granted prior to August 20, 2003 will become immediately vested and exercisable.

Termination and Amendment. We may grant awards under our 2000 plan until August 21, 2010, unless our 2000 plan is terminated prior to that date. The board of directors may amend or terminate our 2000 plan at any time, subject to the rights of holders of outstanding awards and subject to any requirements under Section 409A of the Internal Revenue Code. Our 2006 stock incentive plan, which we refer to as our 2006 plan, is intended to serve as the successor equity incentive program to our 2000 plan. However, our board of directors may not amend our 2000 plan without stockholder approval if stockholder approval is required under applicable law, rule or regulation.

Certain Tax Matters. Upon completion of this offering, we expect that the 2000 plan will be amended and restated to address the effect of recently-enacted Section 409A of the Internal Revenue Code. For a discussion of the general scope of these amendments, see “2006 Stock Incentive Plan—Internal Revenue Code Section 409A Requirements,” below. For a discussion of the general tax consequences of awards granted under the 2000 plan, see the comparable discussion of similar awards granted under the 2006 plan under “2006 Stock Incentive Plan—General Federal Income Tax Consequences,” below.

Option Repricing. On April 7, 2005, in order to promote a closer identification of the interests of our employees with those of us and our stockholders, our board of directors authorized the amendment of each existing employee stock option agreement in order to reduce the exercise price per share with respect to all employee stock options that were outstanding but not yet exercisable as of March 31, 2005. The exercise price per share with respect to each such portion that was not yet exercisable as of March 31, 2005, constituting in the aggregate 354,672 underlying shares of our common stock, was repriced to $1.75 per share. Prior to the repricing, the weighted average exercise price per share with respect to the portions that were not yet exercisable as of March 31, 2005 was $5.13. Prior to the repricing, no outstanding option held by our employees had an exercise price of less than $1.75 per share. All other terms and conditions governing the portions that were not yet exercisable as of March 31, 2005, including the vesting schedules, remain unchanged from the terms and conditions set forth in the original agreements. The affected options are required to be accounted for as a modification of an award under SFAS 123R. The fair market value was calculated immediately

prior to the modification and immediately after the modification to determine the incremental fair market value. This incremental value and the fair market value of unvested options that were modified will be expensed as compensation on a quarterly basis, until the date that the option is exercised or forfeited or expires unexercised.

2006 Stock Incentive Plan

Introduction. Our 2006 plan is intended to serve as the successor equity incentive program to our 2000 plan. Our 2006 plan will become effective on the day prior to the date that the underwriting agreement for this offering is signed. At that time, all of the shares reserved for grant under our 2000 plan will instead become reserved for grant under our 2006 plan.

Subject to adjustments as provided in our 2006 plan, the maximum number of shares that we may issue pursuant to awards granted under our 2006 plan may not exceed the sum of (i) 2,700,000 shares, plus (ii) up to 30,968 shares of common stock remaining available for issuance as of the effective date under our 2000 plan, plus (iii) up to 1,631,110 shares subject to any award granted under our 2000 plan that is forfeited, cancelled, terminated, expires or lapses for any reason without the issuance of shares pursuant to the award. The maximum number of shares of common stock that we may issue under our 2006 plan pursuant to the grant of incentive stock options is 4,362,078 or, if less, the maximum number of shares issuable under the 2006 plan. In addition, (i) we may not grant to any participant options and stock appreciation rights, or SARs, that are not related to an option for more than 500,000 shares of common stock in any calendar year; (ii) we may not grant to any participant awards for more than 500,000 shares of common stock in any calendar year; and (iii) participants may not be paid more than $1,000,000 with respect to any cash-settled award granted in any calendar year, subject to adjustments as provided in our 2006 plan. For purposes of these restrictions, we will treat an option and related SAR as a single award. The following will not be included in calculating the share limitations set forth above: (i) dividends, including dividends paid in shares of common stock, or dividend equivalents paid in cash in connection with outstanding awards; (ii) awards which by their terms are settled in cash rather than the issuance of shares; (iii) any shares subject to an award under our 2006 plan that is forfeited, cancelled, terminated, expires or lapses for any reason and shares subject to an award that are repurchased or reacquired by us; and (iv) any shares a participant surrenders or we withhold to pay the option or purchase price for an award or use to satisfy any tax withholding requirement in connection with the exercise, vesting or earning of an award if, in accordance with the terms of our 2006 plan, a participant pays such option or purchase price or satisfies such tax withholding by either tendering previously owned shares or having us withhold shares.

We may adjust the number of shares reserved for issuance under our 2006 plan and the terms of awards in the event of an adjustment in our capital stock structure or one of our affiliates due to a merger, stock split, stock dividend or similar event.

Purpose and Eligibility. The purpose of our 2006 plan is to encourage and enable selected employees and our directors and independent contractors to acquire or increase their holdings of common stock and other proprietary interests in us in order to promote a closer identification of their interests with those of us and our stockholders, thereby further stimulating their efforts to enhance our efficiency, soundness, profitability, growth and stockholder value. The purpose will be carried out by the granting of awards to selected participants. We may grant awards under our 2006 plan which include incentive stock options and nonqualified stock options; SARs; restricted awards in the form of restricted stock awards and restricted stock units; performance awards in the form of performance shares and performance units; phantom stock

awards; director options in the form of initial options and annual options; and dividend equivalent awards. We discuss the material terms of each type of award below.

Administration; Amendment and Termination. Our board of directors, or upon its delegation, the compensation committee of our board of directors, will administer our 2006 plan. In this discussion, we refer to our board of directors and the compensation committee collectively as the administrator. Under the terms of our 2006 plan, the administrator has full and final authority to take any action with respect to our 2006 plan, including, without limitation, the authority to: (i) determine all matters relating to awards, including selection of individuals to be granted awards, the types of awards, the number of shares, if any, of common stock subject to an award, and the terms, conditions, restrictions and limitations of an award; (ii) prescribe the form or forms of agreements evidencing awards granted under our 2006 plan; (iii) establish, amend and rescind rules and regulations for the administration of our 2006 plan; and (iv) construe and interpret our 2006 plan, awards and award agreements made under the 2006 plan, interpret rules and regulations for administering the 2006 plan and make all other determinations deemed necessary or advisable for administering the 2006 plan.

In certain circumstances and subject to certain terms and conditions, the administrator may delegate to one or more of our officers the authority to grant awards, and to make any or all of the determinations reserved for the administrator in our 2006 plan with respect to such awards.

Our board of directors may amend, alter or terminate our 2006 plan at any time, subject to the following: (i) stockholder approval is required of any amendment if such approval is required by applicable law, rule or regulation; and (ii) except for anti-dilution adjustments made under our 2006 plan, the option price for any outstanding option or base price of any outstanding SAR may not be decreased after the date of grant, nor may any participant surrender any outstanding option or SAR to us as consideration for the grant of a new option or SAR with a lower option or base price than the original option or SAR, as the case may be, without stockholder approval of any such action. Our board of directors may also amend, alter or terminate any award, although participant consent is generally required if such action would materially and adversely affect the participant's rights with respect to the award.

The administrator has the authority to amend the 2006 plan and any award, without participant consent and, except where required by applicable law, rule or regulation, without stockholder approval, in order to comply with applicable laws, rules or regulations or changes to such laws, rules or regulations. In addition, the administrator has the authority to make adjustments to awards upon the occurrence of certain unusual or nonrecurring events, if the administrator determines that such adjustments are appropriate in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under our 2006 plan or necessary or appropriate to comply with applicable laws, rules or regulations. The administrator may (subject to any requirements imposed by Section 409A of the Internal Revenue Code) cause any award or any portion of an award granted under our 2006 plan to be cancelled in consideration of an alternative award or cash payment of an equivalent cash value, as determined by the administrator, made to the holder of the cancelled award. The administrator also may determine, in its discretion, that a participant's rights, payments and/or benefits with respect to an award, including but not limited to any shares issued or issuable and/or cash paid or payable with respect to an award, will be subject to reduction, cancellation, forfeiture or recoupment upon the occurrence of certain specified events, in addition to any otherwise applicable vesting or performance conditions of an award. Subject to the requirements of Internal Revenue Code Section 409A, the administrator also may, in its sole discretion, modify or extend the terms and conditions for exercise, vesting or earning of an award and/or accelerate the date that any award which was not otherwise exercisable, vested or

earned may become exercisable, vested or earned, in whole or in part, without any obligation to accelerate such date with respect to any other award. In addition, the administrator may terminate any award and distribute benefits to participants subject to the requirements of the 2006 plan and Internal Revenue Code Section 409A.

Options. Our 2006 plan authorizes the grant of both incentive stock options and nonqualified stock options, both of which are exercisable for shares of common stock, although incentive stock options may only be granted to our employees. The administrator will determine the option price at which a participant may exercise an option, and the option price must be:

- with respect to incentive stock options, no less than 100% of the fair market value per share of our common stock on the date of grant, or 110% of the fair market value with respect to incentive stock options granted to an employee who owns stock representing more than 10% of the total voting power of all classes of our stock or stock of our parent or subsidiary corporation, if any;
- with respect to nonqualified stock options, no less than 85% of the fair market value per share of our common stock on the date of grant; and
- not less than the par value per share of our common stock.

The administrator may authorize the grant of substitute or assumed options of an acquired entity with an option price of less than the fair market value on the grant date if the options are assumed or substituted in accordance with Section 424(a) of the Internal Revenue Code and if the assumed or substituted options were granted with an option price at least equal to fair market value on the original grant date or otherwise comply with Internal Revenue Code Section 409A.

Unless an individual award agreement provides otherwise, a participant may pay the option price in the form of cash or cash equivalent; in addition, where the administrator and applicable laws, rules and regulations permit, a participant may also make payment:

- by delivery of shares of common stock the participant has owned for such time period, if any, that the administrator determines, if otherwise acceptable to the administrator;
- by shares of common stock withheld upon exercise;
- with respect only to purchase upon exercise of an option after a public market for the common stock exists, by delivery of written notice of exercise to us and delivery to a broker of written notice of exercise and irrevocable instructions to promptly deliver to us the amount of sale or loan proceeds to pay the option price;
- by such other payment methods as the administrator may approve and which are acceptable under applicable law; or
- by any combination of these methods.

At the time of option grant, the administrator will determine the term and conditions of an option and the period or periods during which a participant may exercise an option and the option term for each option (which, in the case of incentive stock options, may not exceed 10 years, or five years with respect to an employee who owns stock and who possesses more than 10% of the total combined voting power of all classes of our stock or stock of our parent or subsidiary corporation, if any). Options are also subject to certain restrictions on exercise if the participant terminates employment or service. The administrator has authority to establish other terms and conditions related to options.

Director Options. Each non-employee director who is first elected or appointed to our board of directors after the public offering date will receive an initial option to purchase 25,000 shares of common stock on the fifth business day after such director is first elected or appointed to our board of directors. A non-employee director who is first elected or appointed as chairman of the board also will receive an initial option for 10,000 shares. In addition, we will grant to each non-employee director, on an annual basis commencing with the 2006 annual meeting of stockholders, a director option to purchase 7,500 shares of common stock or, in the case of the chairman of the board, a director option to purchase 12,500 shares. This annual option will be granted to a director upon his or her reelection to the board on the fifth business day after the applicable annual or other stockholders meeting, provided that such director continues to serve as a member of our board of directors as of such grant date. Director options will be designated as nonqualified options. The option price at which a director may exercise a director option will be 100% of the fair market value per share of the common stock on the date the option is granted. Each initial option will vest and become exercisable on the first anniversary of the date of grant with respect to one-third of the shares subject to the option. Each initial option will vest with respect to the remaining two-thirds of the shares subject to the option on a pro rata quarterly basis over the next two years, so that the option will be vested in full as of the third anniversary of the date of grant, if the director continues in service during such period. Each annual option will vest in full on the first anniversary of the date of grant if the director is in service on that date. The option period of a director option is 10 years. Director options are also subject to certain restrictions on exercise if the director's service on our board of directors terminates. The administrator also has authority to establish other terms and conditions related to director options.

Stock Appreciation Rights. Under the terms of our 2006 plan, we may grant SARs to the holder of an option with respect to all or a portion of the shares of common stock subject to the option or we may grant SARs separately. The holder of an SAR may receive consideration paid either (i) in cash; (ii) shares of common stock valued at fair market value on the date of the SAR exercise; or (iii) a combination of cash and shares of common stock, as the administrator determines. Upon exercise of an SAR, a participant is entitled to receive from us consideration in an amount determined by multiplying:

- the difference between the fair market value of a share of common stock on the date of exercise of the SAR over the base price of the SAR by
- the number of shares of common stock with respect to which the SAR is being exercised.

Notwithstanding the foregoing, the administrator may limit the amount payable in its discretion. The base price may be no less than 100% of the fair market value per share of the common stock on the date the SAR is granted. To the extent required by Internal Revenue Code Section 409A, SARs will be structured in a manner designed to be exempt from, or to comply with, the requirements of Internal Revenue Code Section 409A.

SARs are exercisable according to the terms established by the administrator and stated in the applicable award agreement. Upon the exercise of an SAR granted to the holder of an option, the related option is deemed to be cancelled to the extent of the number of shares as to which the holder of an option exercises the SAR. No participant may exercise an SAR more than 10 years after it was granted, or such shorter period as may apply to related options. Each award agreement will set forth the extent to which the holder of an SAR will have the right to exercise an SAR following termination of the holder's employment or service with us.

Restricted Awards. Subject to the limitations of our 2006 plan, the administrator may in its sole discretion grant restricted awards to such individuals in such numbers, upon such terms

and at such times as the administrator shall determine. Restricted awards may be in the form of restricted stock awards and/or restricted stock units that are subject to certain conditions, which conditions must be met in order for the restricted award to vest and be earned, in whole or in part, and no longer subject to forfeiture. Restricted stock awards may be payable in shares of common stock. Restricted stock units may be payable in cash or shares of common stock, or partly in cash and partly in shares of common stock, in accordance with the terms of our 2006 plan and the discretion of the administrator.

The administrator has authority to determine the nature, length and starting date of the period during which a participant may earn a restricted award and will determine the conditions that must be met in order for a restricted award to be granted or to vest or be earned. These conditions may include:

- payment of a stipulated purchase price;
- attainment of performance objectives;
- continued service or employment for a certain period of time or a combination of attainment of performance objectives and continued service;
- retirement;
- displacement;
- disability;
- death; or
- any combination of such conditions.

However, restricted awards that vest based solely on continued service or the passage of time will be subject to a minimum restriction period of one year, except in the case of restricted awards assumed or substituted in connection with mergers or other business transactions, restricted awards granted in connection with recruitment or hiring of a participant and/or restricted awards granted under an incentive compensation or bonus program.

In the case of restricted awards based upon performance criteria, or a combination of performance criteria and continued service, the administrator will determine the performance measures applicable to such restricted awards, which performance measures may be based upon such corporate, business unit or division and/or individual performance factors and criteria as the administrator in its discretion may deem appropriate; provided, however, that such performance factors will be limited to the specific performance measures listed below.

Subject to the terms of the 2006 plan and the requirements of Internal Revenue Code Section 409A, the administrator has authority to determine whether and to what degree restricted awards have vested and been earned and are payable. The administrator also may, subject to Internal Revenue Code Section 409A, accelerate the date that any restricted award will be deemed vested or earned, without any obligation to accelerate such date with respect to other restricted awards. If a participant's employment or service is terminated for any reason and all or any part of a restricted award has not vested or been earned pursuant to the terms of our 2006 plan and the individual award, the participant will forfeit the award unless the administrator determines otherwise.

Performance Awards. Subject to the limitations of our 2006 plan, the administrator may in its discretion grant performance awards to such eligible individuals upon such terms and conditions and at such times as the administrator shall determine. Performance awards may be

in the form of performance shares and/or performance units. An award of a performance share is a grant of a right to receive shares of our common stock, the cash value thereof or a combination thereof in the administrator's discretion, which is contingent upon the achievement of performance or other objectives during a specified period and which has a value on the date of grant equal to the fair market value of a share of our common stock. An award of a performance unit is a grant of a right to receive shares of our common stock or a designated dollar value amount of common stock that is contingent upon the achievement of performance or other objectives during a specified period, and that has an initial value determined in a dollar amount established by the administrator at the time of grant.

Subject to the terms of the 2006 plan and the requirements of Internal Revenue Code Section 409A, the administrator has the authority to determine the nature, length and starting date of the period during which a participant may earn a performance award and will determine the conditions that must be met in order for a performance award to be granted or to vest or be earned. These conditions may include specific performance objectives, continued service or employment for a certain period of time, or a combination of such conditions. In the case of performance awards based on performance criteria, the administrator will determine the performance measures applicable to such awards, which performance measures may be based upon such corporate, business unit or division and/or individual performance factors and criteria as the administrator in its discretion may deem appropriate; provided, however, that such performance factors will be limited to the specific performance measures listed below.

The administrator has authority to determine whether and to what degree performance awards have been earned and are payable. The administrator also may, subject to Internal Revenue Code Section 409A, accelerate the date that any performance award will be deemed to be earned in whole or in part, without any obligation to accelerate such date with respect to other performance awards. If a participant's employment or service is terminated for any reason and all or part of a performance award has not been earned pursuant to the terms of our 2006 plan and the individual award agreement, the participant will forfeit the award unless the administrator determines otherwise.

Phantom Stock Awards. Subject to the limitations of our 2006 plan, the administrator may in its discretion grant phantom stock awards to such eligible individuals in such numbers, upon such terms and at such times as the administrator shall determine. An award of phantom stock is an award of a number of hypothetical share units with respect to shares of our common stock, with a value per unit based on the fair market value of a share of common stock.

Subject to the terms of the 2006 plan and the requirements of Internal Revenue Code Section 409A, the administrator has the authority to determine whether and to what degree phantom stock awards have vested and are payable. Upon vesting of all or part of a phantom stock award and satisfaction of other terms and conditions that the administrator determines, the holder of a phantom stock award will be entitled to a payment of an amount equal to the fair market value of one share of our common stock with respect to each such phantom stock unit that has vested and is payable. We may make payment in cash, shares of common stock, or a combination of cash and stock, as determined by the administrator. The administrator may determine the forms and terms of payment of phantom stock awards in accordance with our 2006 plan. If a participant's employment or service is terminated for any reason and all or any part of a phantom stock award has not vested and become payable pursuant to the terms of our 2006 plan and the individual award, the participant will forfeit the award unless the administrator determines otherwise.

Dividend and Dividend Equivalents. The administrator may provide that awards granted under our 2006 plan earn dividends or dividend equivalents. We may pay such dividends or dividend equivalents currently or credit such dividends or dividend equivalents to a participant's account, subject to any requirements under Internal Revenue Code Section 409A and such restrictions and conditions as the administrator may establish with respect to the crediting of an account, including reinvestment in additional shares of common stock or share equivalents.

Change in Control. Upon a change in control as defined in our 2006 plan, and unless Internal Revenue Code Section 409A requires otherwise, our 2006 plan provides that the administrator shall have the sole discretion to determine the effect, if any, on awards granted under the 2006 plan, including the vesting, earning and/or exercisability of the award. The administrator's discretion includes the discretion to determine that an award shall vest, be earned or become exercisable in whole or in part, shall be assumed or substituted for another award, shall be cancelled without the payment of consideration, shall be cancelled in exchange for a cash payment or other consideration, or that other actions or no actions shall be taken with respect to the award. The administrator also has discretion to determine that acceleration shall be subject to both a change of control and termination of employment or service.

Transferability. Incentive stock options are not transferable other than by will or the laws of intestate succession or, in the administrator's discretion, as may otherwise be permitted in accordance with Treasury Regulation Section 1.421-1(b)(2) or successor provisions. Nonqualified stock options, director options and SARs are not transferable other than by will or the laws of intestate succession, except as permitted by the administrator in a manner consistent with the registration provisions of the Securities Act. Restricted awards, performance awards and phantom stock awards are not generally transferable, including by sale, assignment, pledge or hypothecation, other than by will or the laws of intestate succession, and participants may not sell, transfer, assign, pledge or otherwise encumber shares subject to such awards until the restriction period and/or performance period has expired and until all conditions to vesting and/or earning the award have been met.

General Federal Income Tax Consequences. Under current federal laws, in general, recipients of awards and grants of nonqualified stock options, SARs, restricted stock, dividend equivalents, performance awards and stock payments under our 2006 plan are taxable under the Internal Revenue Code upon their actual or constructive receipt of common stock or cash with respect to such awards or grants and, subject to Section 162(m) of the Internal Revenue Code and certain reporting requirements, we will be entitled to an income tax deduction with respect to the amounts taxable as ordinary income to such recipients. Under Sections 421 and 422 of the Internal Revenue Code, recipients of incentive stock options are generally not taxed on their receipt of common stock upon their exercises of incentive stock options if the option stock is held for specified minimum holding periods and, in such event, we would not be entitled to income tax deductions with respect to such exercises. If Internal Revenue Code Section 409A is deemed to apply to the 2006 plan or any award, and the 2006 plan and award do not, when considered together, satisfy the requirements of Section 409A during a taxable year, the participant will have ordinary income on the amount of all deferrals subject to Section 409A in the year of non-compliance to the extent that the award is not subject to a substantial risk of forfeiture. The participant will be subject to an additional tax of 20 percent on all amounts includible in income and may also be subject to interest charges under Section 409A. Subject to Section 162(m) of the Internal Revenue Code and certain reporting requirements, we will be entitled to an income tax deduction with respect to the amount of compensation includible as income to the participant.

Internal Revenue Code Section 409A Requirements. The 2006 plan is intended to comply with Section 409A of the Internal Revenue Code. To the extent that Section 409A is deemed to apply to the 2006 plan or any award, the 2006 plan and all such awards will, to the extent practicable, be construed in accordance with Section 409A. Section 409A imposes certain requirements on compensation that is deemed under Section 409A to involve deferred compensation. The 2006 plan imposes certain conditions upon awards that may be subject to Section 409A. These include (but are not limited to) the following:

- Deferrals of shares issuable pursuant to options, SARs settled in shares, restricted awards or other awards otherwise exempt from Section 409A in a manner that would cause Section 409A to apply are not permitted unless such deferrals are otherwise in compliance with Section 409A.
- Awards that are deemed to involve the deferral of compensation under Section 409A are subject to additional restrictions (if and to the extent required under Section 409A):
  - Distributions may not be made earlier than upon the occurrence of one or more of the following: (i) separation from service; (ii) disability; (iii) death; (iv) a specified time or fixed schedule; (v) a change in control (as defined under Section 409A); or (vi) an unforeseeable emergency.
  - Distributions to certain “specified employees” (as defined in Section 409A of the Internal Revenue Code) due to separation from service may not be made for six months after termination (or, if earlier, upon death).
  - Acceleration of the time or schedule of payments due to awards subject to Section 409A is not permitted, unless permitted by the administrator and Section 409A.
  - Distributions generally must be made within two and one-half months after the year in which an award is no longer subject to a substantial risk of forfeiture (unless otherwise permitted under the 2006 plan or by Section 409A).
  - Deferral elections must generally be made (if at all) in the year before the year in which services for an award are performed (subject to certain exceptions permitted under the 2006 plan or Section 409A). Additional restrictions apply to changes to deferral elections.

Performance-Based Compensation—Section 162(m) Requirements. Our 2006 plan is structured to comply with the requirements imposed by Section 162(m) of the Internal Revenue Code and related regulations in order to preserve, to the extent practicable, our tax deduction for awards made under our 2006 plan to covered employees. Section 162(m) of the Internal Revenue Code generally denies an employer a deduction for compensation paid to covered employees, who are generally the named executive officers, of a publicly held corporation in excess of $1,000,000 unless the compensation is exempt from the $1,000,000 limitation because it is performance-based compensation.

In order to qualify as performance-based compensation, we must pay the compensation under our 2006 plan to covered employees under pre-established objective performance goals that a committee comprised of outside directors determines and certifies. In addition to other requirements for the performance-based exception (and subject to certain exceptions), Section 162(m) generally requires that companies disclose to stockholders, and stockholders approve, the material terms or changes in material terms of the performance goals under which compensation is to be paid. Material terms include the individuals eligible to receive compensation, a description of the business criteria on which the performance goals are based, and either the maximum amount of the compensation to be paid or the formula used to calculate the amount of compensation if the performance goals are met.

As proposed, our 2006 plan limits the maximum amount of awards that we may grant to any employee. In particular, (i) we may not grant to any participant options and SARs that are not related to an option for more than 500,000 shares of common stock in any calendar year; (ii) we may not grant to any participant awards for more than 500,000 shares of common stock in any calendar year; and (iii) we may not pay to any participant more than $1,000,000 in cash with respect to awards granted in any single calendar year. Further, with respect to performance-based restricted awards and performance awards, and in some cases, certain other types of awards, payable to covered employees that are intended to be eligible for the compensation limitation exception available under Section 162(m) and related regulations, our 2006 plan limits performance measures to one or more of the following: cash flow, return on equity, return on assets, earnings per share, achievement of clinical development or regulatory milestones, operations expense efficiency milestones, consolidated earnings before or after taxes (including earnings before interest, taxes, depreciation and amortization), net income, operating income, book value per share, return on investment, return on capital, improvements in capital structure, expense management, profitability of an identifiable business unit or product, maintenance or improvement of profit margins, stock price or total stockholder return, market share, revenues or sales, costs, working capital, economic wealth created, strategic business criteria, efficiency ratios, achievement of division, group, function or corporate financial, strategic or operational goals and comparisons with stock market indices or performances of metrics of peer companies.

To the extent that Section 162(m) of the Internal Revenue Code is applicable, the administrator will, within the time and in the manner prescribed by Section 162(m) of the Internal Revenue Code and related regulations, define in an objective fashion the manner of calculating the performance measures it selects to use for participants during any specific performance period. We may adjust or modify such performance factors due to extraordinary items, transactions, events or developments, or in recognition of, or in anticipation of, any other unusual or nonrecurring events affecting us or our financial statements, or in response to, or in anticipation of, changes in applicable laws, regulations, accounting principles or business conditions, in each case as the administrator may determine.

Targacept Retirement Savings Plan—401(k) Plan

Our employees are eligible to participate in our 401(k) plan. Under our 401(k) plan, eligible employees may elect to make a salary reduction contribution up to the statutorily prescribed annual limit. The 401(k) plan is intended to qualify under Section 401 of the Internal Revenue Code, so that the contributions by our employees will be deductible when made and income earned on 401(k) plan contributions will not be taxable to our employees until withdrawals are made. We match the contributions of our eligible employees at up to a maximum of 6% of an eligible employee's salary.

Limitation of Liability and Indemnification

Our certificate of incorporation includes a provision that eliminates the personal liability of our directors for monetary damages to the fullest extent permitted by Section 102(b)(7) of the Delaware General Corporation Law. Under that statute, a director's liability for monetary damages to us or our stockholders may not be limited with respect to:

- a breach of the director's duty of loyalty to us or our stockholders;
- an act or omission not in good faith or involving intentional misconduct or a knowing violation of law;

- an improper distribution to stockholders; or
- a transaction from which the director derived an improper personal benefit.

Our bylaws provide that we will indemnify and hold harmless any person who is made or threatened to be made a party to any matter because he or she is or was our director or officer or was serving as a director, officer or trustee of another entity, employee benefit plan or enterprise at our request to the fullest extent permitted by the Delaware General Corporation Law. Prior to the completion of this offering, we plan to enter into agreements to indemnify our directors and officers. These agreements, among other things, will indemnify our directors and officers for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by any such person in any action or proceeding, including any action by us arising out of such person's services as our director or officer, any of our subsidiaries from time to time or any other company or enterprise to which the person provides services at our request. We believe that these provisions and agreements are necessary to attract and retain qualified persons as directors and officers. Currently, there is no pending litigation or proceeding involving any of our directors, officers or employees for which indemnification is sought, nor are we aware of any threatened litigation that may result in claims for indemnification. We currently maintain directors' and officers' liability insurance for each of our directors and officers.

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Since January 1, 2003, we have engaged in the following transactions with our directors and executive officers and holders of more than 5% of our voting securities and affiliates of our directors, executive officers and 5% stockholders.

Stock Issuances

Issuances of Series C Convertible Preferred Stock

On March 14, 2003, we issued and sold an aggregate of 11,404,958 shares of our series C convertible preferred stock at a purchase price per share of $1.21 for an aggregate purchase price of approximately $13.8 million. The following table sets forth the number of shares of series C convertible preferred stock sold to our 5% stockholders and their affiliates on March 14, 2003.

Name	Number of Shares of Series C Preferred Stock	Aggregate Purchase Price
Entities affiliated with Oxford Bioscience Partners	6,198,347	$ 7,500,000

These shares of our series C convertible preferred stock will convert into an aggregate of 892,857 shares of our common stock concurrently with the completion of this offering.

On December 6, 2004 and May 13, 2005, we issued and sold an aggregate of 27,768,860 additional shares of our series C convertible preferred stock at a purchase price per share of $1.21 for an aggregate purchase price of approximately $33.6 million. The following table sets forth the aggregate number of shares of series C convertible preferred stock sold to our 5% stockholders and their affiliates on December 6, 2004 and May 13, 2005.

Name	Number of Shares of Series C Preferred Stock	Aggregate Purchase Price
New Enterprise Associates 10, Limited Partnership	7,851,240	$ 9,500,000
Nomura Phase4 Ventures L.P.	6,570,248	7,950,000
EuclidSR Partners, L.P.	3,471,074	4,200,000
Burrill Biotechnology Capital Fund, L.P.	1,487,603	1,800,000
Entities affiliated with Advent Private Equity Fund II	1,033,058	1,250,000
R.J. Reynolds Tobacco Holdings, Inc.	1,652,893	2,000,000

These shares of our series C convertible preferred stock will convert into an aggregate of 3,178,571 shares of our common stock concurrently with the completion of this offering.

Dr. Barrett, one of our directors, is a general partner of NEA Partners 10, Limited Partnership, the general partner of New Enterprise Associates 10, Limited Partnership, which is an affiliate of New Enterprise Associates.

Registration Rights

Pursuant to the terms of an investor rights agreement that we entered into with the holders of our series A, series B and series C convertible preferred stock on November 26, 2002, we granted registration rights to these holders. For a more detailed description of these registration rights, see “Description of Capital Stock—Registration Rights.”

Loan Agreement with R.J. Reynolds Tobacco Holdings, Inc.

In May 2002, we borrowed $2.5 million from R.J. Reynolds Tobacco Holdings, Inc. to finance equipment and other fixed assets that we had previously purchased. The borrowing bears a fixed interest rate of 6.6%, is payable in 48 equal monthly installments and matures in May 2006. In January 2004, we amended the terms of our loan facility to permit us to borrow up to an additional $2.0 million in 2004 in up to three separate borrowings. Each borrowing would bear a fixed interest rate equal to a theoretical four-year U.S. Treasury Rate on the disbursement date plus 3.5%, be payable in 48 equal monthly installments and be secured by specified tangible fixed assets that the lender determined to be sufficient at the time of disbursement. We borrowed $1.0 million in April 2004 and $973,000 in December 2004 under the amended loan facility to finance equipment. The April 2004 borrowing bears a fixed interest rate of 5.9%, is payable in 48 equal monthly installments and matures in April 2008. The December 2004 borrowing bears a fixed interest rate of 6.9%, is payable in 48 equal monthly installments and matures in January 2009. All borrowings under the loan facility are secured by specified tangible fixed assets. We believe that the terms of the loan facility are no less favorable than those that we could have obtained from an unaffiliated third party. As of March 1, 2006, the outstanding principal balance under the loan facility was $1.4 million. We are currently in discussions with R.J. Reynolds regarding a potential amendment to the terms of the loan facility to provide up to $2.0 million in new borrowing capacity to finance equipment.

Payments to R.J. Reynolds Tobacco Company

Prior to December 31, 2003, we used the services of an R.J. Reynolds Tobacco Company employee for toxicology studies and purchased materials used for research and development and copy and printing services through R.J. Reynolds Tobacco Company. We paid $201,000 for these services during 2003. During 2004 and 2005, we continued to use only the copy and printing services. We paid $79,000 in 2004 and $71,000 in 2005 for these services.

Director Compensation

For information regarding stock options or restricted stock granted to our non-employee directors or their designees, see “Management—Director Compensation.”

Executive Compensation and Employment Agreements

For information regarding the compensation of our named executive officers, see “Management—Executive Compensation” and “—Stock Options.” For information regarding employment agreements with our named executive officers, see “Management—Employment Agreements.”

PRINCIPAL STOCKHOLDERS

The following table sets forth information regarding the beneficial ownership of our common stock as of February 28, 2006 and on an as adjusted basis to reflect the sale of the common stock offered in this offering by:

- each of our directors;
- each of our named executive officers;
- each person known by us to beneficially own 5% or more of our common stock; and
- all of our directors and executive officers as a group.

The number of shares of common stock beneficially owned by each stockholder is determined under rules issued by the Securities and Exchange Commission and includes voting or investment power with respect to securities. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power and includes any shares that an individual or entity has the right to acquire beneficial ownership of within 60 days of February 28, 2006 through the exercise of any warrant, stock option or other right. Unless otherwise indicated, the address of all listed stockholders is c/o Targacept, Inc., 200 East First Street, Suite 300, Winston-Salem, North Carolina 27101. Each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned (1)	
		Before Offering	After Offering
5% Stockholders	2,921,999	20.7%	15.3%
Entities affiliated with New Enterprise Associates (2) 1119 St. Paul Street Baltimore, Maryland 21202			
Entities affiliated with EuclidSR Partners, L.P. (3) 45 Rockefeller Plaza, Suite 3240 New York, New York 10111	1,887,161	13.4%	9.9%
Entities affiliated with Nomura Phase4 Ventures Limited (4) Nomura House 1 St. Martin's-le-Grand London EC1A 4NP England	2,136,904	15.2%	11.2%
Entities affiliated with Oxford Bioscience Partners (5) 222 Berkeley Street, Suite 1650 Boston, Massachusetts 02116	892,856	6.3%	4.7%
R.J. Reynolds Tobacco Holdings, Inc. (6) 401 North Main Street Winston-Salem, North Carolina 27102	1,129,481	7.9%	5.8%
Entities affiliated with Burrill & Company LLC (7) One Embarcadero Center, Suite 2700 San Francisco, California 94111	784,395	5.6%	4.1%
Entities affiliated with Advent Private Equity Fund II (8) 25 Buckingham Gate London SW1E 6LD England	712,586	5.1%	3.7%

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned (1)	
		Before Offering	After Offering
Executive Officers and Directors			
J. Donald deBethizy, Ph.D. (9)	361,513	2.5%	1.9%
Merouane Bencherif, M.D., Ph.D. (10)	118,788	*	*
Jeffrey P. Brennan (11)	36,088	*	*
William S. Caldwell, Ph.D. (12)	111,207	*	*
Geoffrey C. Dunbar, M.D. (13)	120,865	*	*
Alan A. Musso (14)	100,802	*	*
Mark Skaletsky	11,332	*	*
M. James Barrett, Ph.D. (15)	2,921,999	20.7%	15.3%
Charles A. Blixt (16)	1,129,481	7.9%	5.8%
Errol B. De Souza, Ph.D. (17)	4,333	*	*
Ann F. Hanham (18)	778,062	5.5%	4.1%
Elaine V. Jones, Ph.D. (19)	1,887,161	13.4%	9.9%
John P. Richard (20)	5,333	*	*
All executive officers and directors as a group (14 persons) (21)	7,623,965	50.5%	38.3%

* Indicates less than one percent.

(1) Our calculation of the percentage of shares of common stock beneficially owned before this offering is based on 14,104,838 shares of our common stock and common stock equivalents outstanding as of February 28, 2006, assuming conversion of all outstanding shares of our series A, series B and series C convertible preferred stock. Our calculation of the percentage of shares beneficially owned after this offering is based on 19,104,838 shares of common stock to be outstanding after this offering, including the shares that we are selling in this offering.

(2) Includes 2,913,512 shares owned of record by New Enterprise Associates 10, Limited Partnership, for which voting and investment power is shared by M. James Barrett, Peter J. Barris, C. Richard Kramlich, Peter T. Morris, Charles W. Newhall, III, Mark W. Perry, Scott D. Sandell and Eugene A. Trainor, III, each of whom is a general partner of NEA Partners 10, Limited Partnership, the general partner of New Enterprise Associates 10, Limited Partnership; 3,154 shares owned of record by NEA Ventures 2002, Limited Partnership, for which voting and investment power is held by its general partner, Pamela J. Clark; and 1,000 shares owned of record by, and 4,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006 held by, NEA Development Corp., for which voting and investment power is shared by Charles W. Newhall, III, Mark W. Perry, Peter J. Barris, C. Richard Kramlich and Peter T. Morris through their ownership of New Enterprise Associates, LLC. New Enterprise Associates, LLC is the sole owner of NEA Development Corp. Dr. Barrett, one of our directors, and each of the other general partners of NEA Partners 10, Limited Partnership and NEA Ventures 2002, Limited Partnership disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his or her pecuniary interest therein.

(3) Includes 1,510,080 shares owned of record by, and 5,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006 held by, EuclidSR Partners, L.P., for which voting and investment power is shared by Elaine V. Jones, Graham D.S. Anderson, Barbara J. Dalton, Milton J. Pappas, Stephen K. Reidy and Raymond J. Whitaker, each of whom are general partners of EuclidSR Associates, L.P., the general partner of EuclidSR Partners, L.P.; and 371,748 shares owned of record by EuclidSR Biotechnology Partners, L.P., for which voting and investment power is shared by Elaine V. Jones, Graham D.S. Anderson, Barbara J. Dalton, Milton J. Pappas, Stephen K. Reidy and Raymond J. Whitaker, each of whom are general partners of EuclidSR Biotechnology Associates, L.P., the general partner of EuclidSR Biotechnology Partners, L.P. Dr. Jones, one of our directors, and each of the other general partners of EuclidSR Associates, L.P. and EuclidSR Biotechnology Associates, L.P. disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his or her pecuniary interest therein.

(4) Includes 1,190,476 shares owned of record by Nomura International plc and 946,428 shares owned of record by Nomura Phase4 Ventures L.P. Nomura Phase4 Ventures Limited, as appointee of Nomura International plc and as manager of Nomura Phase4 Ventures L.P., has voting and investment power over the shares held by Nomura International plc and Nomura Phase4 Ventures L.P. Mr. Yoshiki Hashimoto, the Head of Merchant Banking, Nomura International plc, and Dr. Denise Pollard-Knight, the Head of Nomura Phase4 Ventures, are the only two members of the board of directors of Nomura Phase4 Ventures Limited and both of them, acting together, exercise the voting and investment power of Nomura Phase4 Ventures Limited. Mr. Hashimoto exercises these powers in his capacity as director of Nomura Phase4 Ventures Limited and as Head of Merchant Banking, Nomura International plc. Mr. Hashimoto and Dr. Pollard-Knight disclaim beneficial ownership of these shares.

(5) Includes 883,987 shares owned of record by Oxford Bioscience Partners IV L.P. and 8,869 shares owned of record by mRNA Fund II L.P., for which voting and investment power is shared by Alan G. Walton, Jonathan J. Fleming, Jeffrey T. Barnes, Mark P. Carthy and Michael Lytton, each of whom are general partners of OBP Management IV L.P., the sole general partner of Oxford Bioscience Partners IV L.P. and mRNA Fund II L.P. Each of Oxford Bioscience Partners IV L.P. and mRNA Fund II L.P. disclaim beneficial ownership of any shares held of record by the other. Each of the general partners of OBP Management IV L.P. disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his pecuniary interest therein.

(6) Includes 5,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006 and 215,054 shares issuable upon the exercise of an outstanding warrant, assuming that the warrant is exercised in full for cash. Voting and investment power is held by Charles A. Blixt, president of R.J. Reynolds Tobacco Holdings, Inc. and one of our directors. Mr. Blixt disclaims beneficial ownership of these shares.

(7) Includes 778,062 shares owned of record by Burrill Biotechnology Capital Fund, L.P., for which voting and investment power is shared by G. Steven Burrill, John H. Kim, Roger E. Wyse and Ann F. Hanham, members of Burrill & Company (Biotechnology GP), LLC, the general partner of Burrill Biotechnology Capital Fund, L.P.; and 1,000 shares owned of record by, and 5,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006 held by, Burrill & Company LLC, for which voting and investment power is held by G. Steven Burrill, the chief executive officer of Burrill & Company LLC. Ms. Hanham, one of our directors, and each of the other members of Burrill & Company (Biotechnology GP), LLC disclaims beneficial ownership of the shares held by Burrill Biotechnology Capital Fund, L.P. except to the extent of his or her pecuniary interest therein.

(8) Includes 260,685 shares owned of record by Advent Private Equity Fund II 'A' Limited Partnership; 158,989 shares owned of record by Advent Private Equity Fund II 'B' Limited Partnership; 236,694 shares owned of record by Advent Private Equity Fund II 'C' Limited Partnership; and 56,218 shares owned of record by Advent Private Equity Fund II 'D' Limited Partnership. Voting and investment power over the shares held by each of the partnerships constituting Advent Private Equity Fund II is exercised by Advent Venture Partners LLP in its role as manager. The partners of Advent Venture Partners LLP are Sir David James Scott Cooksey (chairman), Jeryl Christine Andrew, Peter Anthony Baines, Jerry Christopher Benjamin, David Cheesman, Leslie Ian Gabb, Mohammed Shahzad Ahmed Malik, Patrick Pak-tin Lee, Martin Alexander McNair, William Harold Neil Pearce and Nicholas James Teasdale. Each partner disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein.

(9) Includes 267,678 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006.

(10) Includes 111,053 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006.

(11) Consists of 36,088 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006.

(12) Includes 103,472 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006.

(13) Includes 98,263 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006.

(14) Includes 98,003 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006.

(15) Includes 2,913,512 shares owned of record by New Enterprise Associates 10, Limited Partnership, for which voting and investment power is shared by M. James Barrett, Peter J. Barris, C. Richard Kramlich, Peter T. Morris, Charles W. Newhall, III, Mark W. Perry, Scott D. Sandell and Eugene A. Trainor, III, each of whom is a general partner of NEA Partners 10, Limited Partnership, the general partner of New Enterprise Associates 10, Limited Partnership; 3,154 shares owned of record by NEA Ventures 2002, Limited Partnership, for which voting and investment power is held by its general partner, Pamela J. Clark; and 1,000 shares owned of record by, and 4,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006 held by, NEA Development Corp., for which voting and investment power is shared by Charles W. Newhall, III, Mark W. Perry, Peter J. Barris, C. Richard Kramlich and Peter T. Morris through their ownership of New Enterprise Associates, LLC. New Enterprise Associates, LLC is the sole owner of NEA Development Corp. Dr. Barrett, one of our directors, and each of the other general partners of NEA Partners 10, Limited Partnership and NEA Ventures 2002, Limited Partnership disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his or her pecuniary interest therein.

(16) Includes 909,094 shares owned of record by R.J. Reynolds Tobacco Holdings, Inc., 5,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006 held by R.J. Reynolds Tobacco Holdings, Inc. and 215,054 shares issuable upon the exercise of an outstanding warrant held by R.J. Reynolds Tobacco Holdings, Inc., assuming that the warrant is exercised in full for cash. Voting and investment power is held by Mr. Blixt, president of R.J. Reynolds Tobacco Holdings, Inc. Mr. Blixt disclaims beneficial ownership of these shares.

(17) Includes 3,333 shares of common stock issuable upon exercise of stock options exercisable within sixty days of February 28, 2006.

(18) Includes 778,062 shares owned of record by Burrill Biotechnology Capital Fund, L.P., for which voting and investment power is shared by G. Steven Burrill, John H. Kim, Roger E. Wyse and Ann F. Hanham, members of Burrill & Company (Biotechnology GP), LLC, the general partner of Burrill Biotechnology Capital Fund, L.P. Ms. Hanham, one of our directors, and each of the other members of Burrill & Company (Biotechnology GP), LLC disclaims beneficial ownership of the shares held by Burrill Biotechnology Capital Fund, L.P. except to the extent of his or her pecuniary interest therein.

(19) Includes 1,510,080 shares owned of record by, and 5,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006 held by, EuclidSR Partners, L.P., for which voting and investment power is shared by Elaine V. Jones, Graham D.S. Anderson, Barbara J. Dalton, Milton J. Pappas, Stephen K. Reidy and Raymond J. Whitaker, each of whom are general partners of EuclidSR Associates, L.P., the general partner of EuclidSR Partners, L.P.; and 371,748 shares owned of record by EuclidSR Biotechnology Partners, L.P., for which voting and investment power is shared by Elaine V. Jones, Graham D.S. Anderson, Barbara J. Dalton, Milton J. Pappas, Stephen K. Reidy and Raymond J. Whitaker, each of whom are general partners of EuclidSR Biotechnology Associates, L.P., the general partner of EuclidSR Biotechnology Partners, L.P. Dr. Jones, one of our directors, and each of the other general partners of EuclidSR Associates, L.P. and EuclidSR Biotechnology Associates, L.P. disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his or her pecuniary interest therein.

(20) Includes 1,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006.

(21) Includes 770,890 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006 and 215,054 shares issuable upon the exercise of an outstanding warrant, assuming that the warrant is exercised in full for cash.

DESCRIPTION OF CAPITAL STOCK

The following description of our capital stock and provisions of our certificate of incorporation and bylaws are summaries and are qualified by reference to the certificate of incorporation and the bylaws that will be in effect upon completion of this offering. Copies of these documents have been filed with the Securities and Exchange Commission as exhibits to our registration statement of which this prospectus forms a part. The descriptions of the common stock and preferred stock reflect changes to our capital structure that will occur concurrently with the completion of this offering.

Upon completion of this offering, our authorized capital stock will consist of 100,000,000 shares of common stock, par value $0.001 per share, and 5,000,000 shares of undesignated preferred stock, par value $0.001 per share.

As of February 28, 2006, we had outstanding:

- 272,823 shares of common stock held by 62 stockholders of record;
- 5,000,000 shares of series A convertible preferred stock;
- 6,567,567 shares of series B convertible preferred stock; and
- 76,937,998 shares of series C convertible preferred stock.

As of February 28, 2006, we also had outstanding a warrant to purchase 215,054 shares of common stock at an exercise price of $14.63 per share.

All of our outstanding shares of preferred stock will convert into 13,832,015 shares of common stock concurrently with the completion of this offering. Also, the warrant will be cancelled if it is not exercised prior to the completion of this offering. If the warrant is exercised in full for cash, we would issue 215,054 shares of common stock and receive cash proceeds of approximately $3.1 million.

Common Stock

Each holder of common stock is entitled to one vote for each share on all matters submitted to a vote of the stockholders, including the election of directors, and there are no cumulative voting rights. Subject to preferences that may be applicable to any shares of preferred stock that may become outstanding from time to time, holders of common stock are entitled to receive, ratably, dividends declared from time to time by our board of directors, if any, out of funds legally available for that purpose. In the event of our liquidation, dissolution or winding up, holders of common stock will be entitled to share ratably in the net assets legally available for distribution to stockholders after the payment of all of our debts and other liabilities and the satisfaction of any liquidation preference granted to the holders of any shares of preferred stock then outstanding. Holders of common stock have no conversion, preemptive or other subscription rights, and there are no redemption or sinking fund provisions applicable to the common stock. The rights, preferences and privileges of the holders of common stock are subject to, and may be adversely affected by, the rights of the holders of shares of any series of preferred stock that we may designate and issue in the future.

Preferred Stock

Upon completion of this offering, our board of directors will be authorized, without stockholder approval, to issue up to an aggregate of 5,000,000 shares of preferred stock in one

or more series and to fix the rights, preferences, designation and powers granted to or imposed upon the preferred stock, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences. We cannot state with certainty the actual effects of the issuance of any shares of preferred stock upon the rights of holders of common stock until the board of directors determines the specific rights of the holders of the preferred stock. Some of these effects might potentially include:

- restricting the declaration or payment of dividends on the common stock;
- diluting the voting power of the common stock;
- impairing the liquidation rights of the common stock; and
- delaying or preventing a change in control of us.

We do not currently have any plans to issue any shares of preferred stock following this offering.

Options

As of February 28, 2006, options to purchase 1,631,110 shares of common stock at a weighted average exercise price of $2.91 per share were outstanding.

Registration Rights

After this offering, holders of approximately 14,043,078 shares of our common stock will have the right to require us to register the sales of their shares under the Securities Act, under the terms of an agreement between us and the holders of these securities. Subject to limitations specified in this agreement, these registration rights include the following:

Demand Registration Rights. Beginning six months after the completion of this offering, subject to specified limitations, two separate constituencies of the holders of registrable securities may require that we register part of these securities for sale under the Securities Act. Each constituency may make one such demand.

Incidental Registration Rights. If we register any of our common stock under the Securities Act, solely for cash, either for our own account or for the account of other security holders, the holders of shares of registrable securities are entitled to notice of the registration and to include their shares of common stock in the registration. These rights have been waived for this offering.

Form S-3 Registration Rights. If we become eligible to file registration statements on Form S-3, holders of registrable securities can require us to register their registrable securities on Form S-3 if the total gross proceeds to be received by them together would be at least $1.0 million.

Limitations and Expenses. With specified exceptions, a holder's right to include shares in a registration statement is subject to the right of the underwriters to limit the number of shares included in the offering. We are generally required to pay all expenses of registration, including the fees and expenses of one legal counsel to the registering security holders up to a prescribed maximum amount, but excluding underwriters' discounts and commissions.

Anti-Takeover Provisions

We are subject to Section 203 of the Delaware General Corporation Law, an anti-takeover statute. Subject to certain exceptions, Section 203 prohibits a publicly held Delaware

corporation from engaging in a business combination with an interested stockholder for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A business combination includes, among other things, a merger or consolidation involving us and the interested stockholder and the sale of more than 10% of our assets. In general, an interested stockholder is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by that entity or person.

Certain provisions of our certificate of incorporation and bylaws that will be in effect upon completion of this offering could make the acquisition of us through a tender offer, proxy contest or other means, or the removal of incumbent officers and directors, more difficult. These provisions may discourage certain types of coercive takeover practices and takeover bids and encourage persons seeking to acquire control of us to first negotiate with our board of directors. We believe that the benefits of retaining the ability to negotiate with a proponent of an unfriendly or unsolicited proposal outweigh the potential disadvantages of discouraging such a proposal. These provisions may make it more difficult for stockholders to take specific corporate actions and could have the effect of delaying or preventing a change in our control.

In particular, our certificate of incorporation or bylaws that will be in effect upon completion of this offering provide for the following:

Staggered Board of Directors and Number of Directors. Our board of directors is divided into three classes of the same or nearly the same number of directors serving staggered three-year terms, which means that only one class of directors may be elected at a particular stockholders meeting. Also, the authorized number of directors comprising our board of directors may only be changed by resolution of our board of directors. As a result, the replacement of incumbent directors may be more difficult and third parties may be discouraged from seeking to circumvent the anti-takeover provisions of our certificate of incorporation and bylaws by replacing our incumbent directors.

Limitations on Calling Special Meetings of Stockholders. Under Delaware law, a special meeting of stockholders may be called by the board of directors or by any other person authorized to do so in the certificate of incorporation or the bylaws. Our certificate of incorporation and bylaws do not permit our stockholders to call a special meeting. As a result, a stockholder could not force stockholder consideration of a proposal over the opposition of the board of directors by calling a special meeting. The restriction on the ability of stockholders to call a special meeting means that a proposal to replace the board of directors also could be delayed until the next annual meeting.

Advance Notice Procedures. Our bylaws establish an advance notice procedure for stockholder proposals to be brought before an annual meeting of our stockholders, including proposed nominations of persons for election to the board of directors. At an annual meeting, stockholders may consider proposals or nominations specified in the notice of meeting or brought before the meeting by or at the direction of the board of directors. Stockholders may also consider a proposal or nomination by a person who was a stockholder of record on the record date for the meeting and on the date that notice of the proposal or nomination was given, who is entitled to vote at the meeting and who has given to our secretary timely written notice, in proper form, of his or her intention to bring that business before the meeting. The bylaws may have the effect of precluding the conduct of certain business at a meeting if the proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer’s own slate of directors or otherwise attempting to obtain control of us.

Prohibition of Stockholder Action by Written Consent. Delaware law provides that, unless prohibited by the certificate of incorporation, stockholders may execute an action by written consent in lieu of a stockholder meeting. Our certificate of incorporation prohibits stockholder action by written consent, which may lengthen the amount of time required to take stockholder actions because actions by written consent are not subject to the minimum notice requirement of a stockholders meeting. The prohibition of stockholder action by written consent may deter hostile takeover attempts because a holder that controlled a majority of our capital stock would not be able to amend our bylaws or remove directors without holding a stockholders meeting and would have to obtain the consent of a majority of our board of directors, our chairman of the board, our chief executive officer or our president to call a stockholders meeting and satisfy the applicable notice periods.

Undesignated Preferred Stock. Our board of directors is authorized to issue up to 5,000,000 shares of our preferred stock in one or more series and to fix the rights, preferences, designation and powers granted to or imposed upon the preferred stock, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences. The existence of this ability could discourage an attempt to take control of us through a merger, tender offer, proxy contest or other means.

With the exception of the provision relating to the issuance of preferred stock, which can be amended with the approval of a majority of the outstanding shares of stock entitled to vote, none of these provisions can be amended without the approval of at least two-thirds of our outstanding shares of stock entitled to vote. In addition, the affirmative vote of two-thirds of our outstanding shares of stock entitled to vote is required to amend provisions of our certificate of incorporation or bylaws relating to exculpation and indemnification of directors and officers, the number, election, qualification, term of office, resignation or removal of directors and the filling of director vacancies.

Transfer Agent and Registrar

The transfer agent and registrar for our common stock is American Stock Transfer & Trust Company.

NASDAQ National Market

Our common stock has been approved for listing on the NASDAQ National Market under the symbol “TRGT.”

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our common stock and we cannot assure you that a liquid trading market for our common stock will develop or be sustained after this offering. Future sales of substantial amounts of our common stock in the public market following this offering, or the anticipation of those sales, could adversely affect market prices prevailing from time to time and could impair our ability to raise capital by the sale of our equity securities.

Upon completion of this offering, we will have outstanding 19,104,838 shares of common stock, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into 13,832,015 shares of common stock concurrently with the completion of this offering.

All of the 5,000,000 shares sold in this offering will be freely tradable without restriction unless purchased by our "affiliates," as that term is defined in Rule 144 under the Securities Act. The remaining 14,104,838 shares of common stock to be outstanding after this offering are "restricted securities" under Rule 144. Substantially all of these restricted securities will be subject to the 180-day lock-up period described below. Immediately after the 180-day lock-up period, 4,605,997 shares will be freely tradable under Rule 144(k) or Rule 701(g)(3) under the Securities Act and 9,498,841 shares will be eligible for resale under Rule 144 or Rule 701(g)(3), subject to volume limitations.

Restricted securities may be sold in the public market only if registered or if they qualify for an exemption from registration under Rules 144 or 701 under the Securities Act. These rules are summarized below.

Rule 144

In general, under Rule 144, beginning 90 days after the date of this prospectus, a person who has beneficially owned shares of our common stock for at least one year would be entitled to sell within any three-month period a number of shares that does not exceed the greater of:

- 1% of the number of shares of common stock then outstanding, which will equal approximately 191,048 shares immediately after the completion of this offering; or
- the average weekly trading volume of the common stock on the NASDAQ National Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

Sales under Rule 144 are also subject to manner of sale provisions and notice requirements and to the availability of current public information about us.

Rule 144(k)

Subject to the lock-up agreements described below, shares of our common stock eligible for sale under Rule 144(k) may be sold immediately after the completion of this offering. In general, under Rule 144(k), a person may sell shares of common stock acquired from us immediately after the completion of this offering, without regard to manner of sale, notice, availability of public information or volume, if:

- the person is not our affiliate and has not been our affiliate at any time during the three months preceding the sale; and
- the person has beneficially owned the shares proposed to be sold for at least two years, including the holding period of any prior owner other than an affiliate.

Rule 701

In general, under Rule 701, any of our employees, consultants or advisors who purchased shares from us in connection with a qualified compensatory benefit plan or other written compensation contract is eligible to resell those shares 90 days after the effective date of this offering in reliance on Rule 144, but without compliance with various restrictions, including the holding period, contained in Rule 144.

Lock-up Agreements

The holders of substantially all of our currently outstanding stock have agreed that, without the prior written consent of Deutsche Bank Securities Inc. on behalf of the underwriters and subject to the exceptions described in the section entitled “Underwriters” in this prospectus they will not, during the period ending 180 days after the date of this prospectus, subject to a possible extension:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for shares of our common stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of shares of our common stock,

whether any transaction described above is to be settled by delivery of shares of our common stock or such other securities, in cash or otherwise. Deutsche Bank Securities does not have any pre-established conditions to waiving the terms of the lock-up agreements. Any determination to release any shares subject to the lock-up agreements would be based on a number of factors at the time of determination, including but not necessarily limited to the market price of the common stock, the liquidity of the trading market for the common stock, general market conditions, the number of shares proposed to be sold and the timing, purpose and terms of the proposed sale.

The lock-up agreements also provide that, if we issue an earnings release or if material news or a material event relating to our company occurs during the last 17 days of the 180-day restricted period or if prior to the expiration of the 180-day restricted period we announce that we will release earnings results during the 16-day period beginning on the last day of the 180-day period, the restricted period will continue for the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

Stock Options

After the completion of this offering, we intend to file a registration statement on Form S-8 under the Securities Act to register all of the shares of common stock subject to issuance upon exercise of outstanding options granted under, or reserved for future issuance under, our 2000 plan and our 2006 plan. Shares of common stock issued under the Form S-8 upon exercise of options will be available for sale in the public market, subject to Rule 144 volume limitations applicable to affiliates and subject to the contractual restrictions described above. As of February 28, 2006, options to purchase 1,631,110 shares of common stock were outstanding under our 2000 plan with a weighted average exercise price of $2.91 per share, of which approximately 975,545 were vested and exercisable with a weighted average exercise price of $3.61 per share and an additional 30,968 shares were reserved for issuance under our 2000 plan. Upon completion of this offering, those shares reserved under our 2000 plan plus an additional 2,700,000 shares of common stock will become reserved for issuance under our 2006 plan.

Registration Rights

Upon completion of this offering, the holders of approximately 14,043,078 shares of our common stock will be entitled to registration rights. Registration of the sale of these shares upon exercise of these rights would make them freely tradable without restriction under the Securities Act. For more information regarding these registration rights, see “Description of Capital Stock—Registration Rights.”

UNDERWRITERS

Under the terms and subject to the conditions contained in an underwriting agreement dated the date of this prospectus, the underwriters named below, for which Deutsche Bank Securities Inc., Pacific Growth Equities, LLC, CIBC World Markets Corp. and Lazard Capital Markets LLC are acting as representatives, have severally agreed to purchase, and we have agreed to sell to them, severally, the number of shares indicated below:

Underwriters	Number of Shares
Deutsche Bank Securities Inc.	
Pacific Growth Equities, LLC	
CIBC World Markets Corp.	
Lazard Capital Markets LLC	
Total	5,000,000

The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of specified legal matters by their counsel and to other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' over-allotment option described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of $ per share under the public offering price. No underwriter may allow, and no dealer may reallow, any concession to other underwriters or to certain dealers. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to an aggregate of 750,000 additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase approximately the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table. If the underwriters' option is exercised in full, the total price to the public would be $, the total underwriters' discounts and commissions would be $ and the total proceeds to us would be $.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed five percent of the total number of shares of common stock offered by them.

We and all of our directors and officers and holders of substantially all of our currently outstanding stock have agreed that, without the prior written consent of Deutsche Bank Securities on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of, directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for shares of our common stock; or
- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of shares of our common stock,

whether any transaction described above is to be settled by delivery of shares of our common stock or such other securities, in cash or otherwise.

The 180-day restricted period described in the preceding paragraph will be extended if:

- during the last 17 days of the 180-day restricted period we issue an earnings release or material news or a material event relating to our company occurs; or
- prior to the expiration of the 180-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 180-day period,

in which case the restrictions described in the preceding paragraph will continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

These restrictions do not apply to:

- the sale of shares to the underwriters;
- the issuance by us of shares of our common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus of which the underwriters have been advised in writing;
- the issuance by us of shares or options to purchase shares of our common stock pursuant to our 2000 plan or our 2006 plan, provided that the recipient of the shares agrees to be subject to the restrictions described above;
- transactions by any person other than us relating to shares of common stock or other securities acquired in open market transactions after the completion of the offering of the shares;
- transfers of shares as a gift or charitable contribution, or by will or intestacy;
- transfers of shares to any trust the sole beneficiaries of which are the transferee or a member of the immediate family of the transferee; or
- transfers to certain entities or persons affiliated with the stockholder;

provided that in the case of each of the last three transactions, each donee, distributee, transferee and recipient agrees to be subject to the restrictions described in the immediately preceding paragraph, no filing under Section 16 of the Securities Exchange Act of 1934, as amended, is required in connection with these transactions, other than a filing on a Form 5 made after the expiration of the 180-day period, and no transaction includes a disposition for value.

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of our common stock.

	Paid by Targacept	
	No Exercise	Full Exercise
Per share	$	$
Total	$	$

In addition, we estimate that the expenses of this offering payable by us, other than underwriting discounts and commissions, will be $.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by exercising the over-allotment option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. In addition, to stabilize the price of the common stock, the underwriters may bid for, and purchase, shares of common stock in the open market. Finally, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the common stock in this offering, if the syndicate repurchases previously distributed common stock in transactions to cover syndicate short positions or to stabilize the price of the common stock. Any of these activities may stabilize or maintain the market price of the common stock above independent market levels. The underwriters are not required to engage in these activities, and may end any of these activities at any time.

Our common stock has been approved for listing on the NASDAQ National Market under the symbol "TRGT."

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

Directed Share Program

At our request, the underwriters have reserved for sale, at the initial public offering price, up to 150,000 shares offered by this prospectus to directors, officers, employees and other individuals associated with us and members of their respective families and friends through a directed share program. The number of shares of our common stock available for sale to the general public in the offering will be reduced to the extent these persons purchase these reserved shares. Any reserved shares not purchased by these persons will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus.

Pricing of the Offering

Prior to the offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations between us and the representatives. Among the factors to be considered in determining the initial public offering price of the shares will be our future prospects and those of our industry in general, our sales, earnings and other financial operating information in recent periods, and the price-earnings ratios, price-sales ratios, market prices of securities and financial and operating information of companies engaged in activities similar to ours. The estimated initial public offering price range set forth on the cover page of this preliminary prospectus is subject to change as a result of market conditions and other factors.

LEGAL MATTERS

Certain legal matters with respect to the validity of the shares of common stock offered hereby will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts and by Womble Carlyle Sandridge & Rice, PLLC, Winston-Salem, North Carolina. Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York, has acted as counsel for the underwriters in connection with certain legal matters related to this offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, have audited our financial statements as of December 31, 2005 and 2004 and for each of the three years in the period ended December 31, 2005, as set forth in their report. We have included our financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock to be sold in this offering. This prospectus does not contain all of the information set forth in the registration statement. You should refer to the registration statement for additional information regarding us and the shares of our common stock to be sold in this offering. Whenever we reference any contract, agreement or other document in this prospectus, the reference is not necessarily complete and you should refer to the exhibits to the registration statement for the actual contract, agreement or other document. In each instance, reference is made to such exhibits and each such statement is qualified in all respects by such reference. In addition, when this offering is completed, we will become subject to the information and reporting requirements of the Exchange Act and, in accordance with the Exchange Act, will file periodic reports, proxy statements and other information with the Securities and Exchange Commission.

You can read the registration statement and our future filings with the Securities and Exchange Commission over the Internet at the Securities and Exchange Commission's website at http://www.sec.gov. You may also read and copy any document that we file with the Securities and Exchange Commission at its public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549.

You may obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the Securities and Exchange Commission at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. Please call the Securities and Exchange Commission at 1-800-SEC-0330 for further information on the operation of the public reference room. Such reports, proxy and information statements and other information may also be inspected at the offices of NASDAQ Operations, 1735 K Street, N.W., Washington, D.C. 20006.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors
Targacept, Inc.

We have audited the accompanying balance sheets of Targacept, Inc. as of December 31, 2004 and 2005, and the related statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2005. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Targacept, Inc. at December 31, 2004 and 2005, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2005, in conformity with U.S. generally accepted accounting principles.

As discussed in Notes 2 and 11 to the financial statements, effective January 1, 2005, the Company adopted the fair value method of accounting provisions of Statement of Financial Accounting Standards (SFAS) No. 123 (revised 2004), *Share-Based Payment*.

/s/ ERNST & YOUNG LLP

Greensboro, North Carolina
February 10, 2006

TARGACEPT, INC.
BALANCE SHEETS

	December 31, 2004	December 31, 2005
ASSETS		
Current assets:		
Cash and cash equivalents	$ 53,075,348	$ 24,851,302
Research fees and accounts receivable	484,565	118,163
Inventories	102,640	41,940
Prepaid expenses	1,727,836	729,241
Total current assets	55,390,389	25,740,646
Property and equipment, net	2,262,698	1,747,524
Intangible assets, net of accumulated amortization of $91,263 and $129,027 at December 31, 2004 and 2005, respectively	550,737	512,973
Total assets	$ 58,203,824	$ 28,001,143
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 1,854,138	$ 1,173,545
Accrued expenses	1,940,836	2,849,747
Current portion of long-term debt	1,113,350	783,895
Current portion of deferred rent incentive	402,647	402,647
Total current liabilities	5,310,971	5,209,834
Long-term debt, net of current portion	3,443,297	1,409,402
Deferred rent incentive, net of current portion	637,524	234,877
Total liabilities	9,391,792	6,854,113
Commitments		
Redeemable convertible preferred stock:		
Series A, $0.001 par value, 5,000,000 shares authorized, issued and outstanding, aggregate liquidation preference of $30,166,741 and $31,836,985 at December 31, 2004, and 2005, respectively, or $4.65 per share plus accreted redemption value	30,166,741	31,836,985
Series B, $0.001 par value, 6,567,567 shares authorized, issued and outstanding, aggregate liquidation preference of $39,622,161 and $41,759,905 at December 31, 2004, and 2005, respectively, or $4.65 per share, plus accreted redemption value	39,622,161	41,759,905
Series C, $0.001 par value, 76,441,866 and 81,741,965 shares authorized at December 31, 2004 and 2005, 76,441,866 and 76,937,998 shares issued and outstanding at December 31, 2004, and 2005, respectively, aggregate liquidation preference of $101,988,994 and $110,031,263 at December 31, 2004, and 2005, respectively, or $1.21 per share, plus accreted redemption value	101,988,994	110,031,263
Total redeemable convertible preferred stock	171,777,896	183,628,153
Stockholders' equity (deficit):		
Common stock, $0.001 par value, 16,666,666 shares authorized at December 31, 2004, and 2005, 256,816 and 270,427 shares issued and outstanding at December 31, 2004, and 2005, respectively	257	270
Capital in excess of par value	11,573,677	12,287,904
Common stock warrants	213,710	213,710
Accumulated deficit	(134,753,508)	(174,983,007)
Total stockholders' equity (deficit)	(122,965,864)	(162,481,123)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 58,203,824	$ 28,001,143

See accompanying notes

TARGACEPT, INC.
STATEMENTS OF OPERATIONS

	Year ended December 31,		
	2003	2004	2005
Revenue:			
Research fee revenue	$ 1,302,500	$ 337,500	$ —
License fee revenue	269,532	1,917,224	—
Product sales	814,724	766,583	681,285
Grant revenue	71,529	717,067	498,632
Net revenue	2,458,285	3,738,374	1,179,917
Operating expenses:			
Research and development ($0, $0 and $457,670 stock-based compensation in 2003, 2004 and 2005, respectively)	18,179,542	22,770,881	24,251,463
General and administrative ($65,325, $50,623 and $232,784 stock-based compensation in 2003, 2004 and 2005, respectively)	3,599,673	5,162,474	6,388,437
Cost of product sales	742,941	198,446	480,933
Total operating expenses	22,522,156	28,131,801	31,120,833
Loss from operations	(20,063,871)	(24,393,427)	(29,940,916)
Other income (expense):			
Interest and dividend income	791,339	504,986	1,174,398
Interest expense	(122,789)	(132,749)	(225,005)
Loss on disposal of fixed assets	—	(4,199)	—
Total other income (expense)	668,550	368,038	949,393
Net loss	(19,395,321)	(24,025,389)	(28,991,523)
Deemed dividend—beneficial conversion feature for Series C redeemable convertible preferred stock issued December 2004	—	(10,312,499)	—
Preferred stock accretion	(8,340,628)	(8,743,559)	(11,237,976)
Net loss attributable to common stockholders	$ (27,735,949)	$ (43,081,447)	$ (40,229,499)
Basic and diluted net loss attributable to common stockholders per share	$ (254.33)	$ (196.53)	$ (153.54)
Weighted average common shares outstanding—basic and diluted	109,053	219,213	262,013
Unaudited pro forma basic and diluted net loss per share attributable to common stockholders assuming conversion of preferred stock and conversion of convertible debt			$ (2.06)
Unaudited pro forma weighted average shares outstanding—basic and diluted			14,068,182

See accompanying notes

TARGACEPT, INC.

STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

	Redeemable Convertible Preferred Stock			Common Stock		Capital in Excess of Par Value	Common Stock Warrants	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Deficit
	Series A	Series B	Series C	Shares	Amount					
Balances at December 31, 2002	$26,826,253	$35,346,675	$ 45,853,329	83,278	$ 83	$ 387,396	$213,710	$ (63,936,112)	$ —	$ (63,334,923)
Stock issuance costs	—	—	(32,548)	—	—	—	—	—	—	—
Issuance of 11,404,958 shares of Series C redeemable convertible preferred stock at $1.21 per share	—	—	13,800,000	—	—	—	—	—	—	—
Issuance of 61,092 shares of common stock at $0.001 per share par value, related to exercise of stock options	—	—	—	61,092	61	304,218	—	—	—	304,279
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock	42,744	—	—	—	—	—	—	(42,744)	—	(42,744)
Accreted redemption value for Series A, Series B, and Series C redeemable convertible preferred stock	1,627,500	2,137,744	4,532,640	—	—	—	—	(8,297,884)	—	(8,297,884)
Net change in unrealized holding loss on available-for-sale securities	—	—	—	—	—	—	—	—	(29,282)	(29,282)
Net loss	—	—	—	—	—	—	—	(19,395,321)	—	(19,395,321)
Comprehensive loss										(19,424,603)
Balances at December 31, 2003	28,496,497	37,484,419	64,153,421	144,370	144	691,614	213,710	(91,672,061)	(29,282)	(90,795,875)
Stock issuance costs	—	—	(100,000)	—	—	—	—	—	—	—
Issuance of 27,272,728 shares of Series C redeemable convertible preferred stock at $1.21 per share	—	—	33,000,000	—	—	—	—	—	—	—
Deemed dividend—beneficial conversion feature for Series C redeemable convertible preferred stock issued December 2004	—	—	—	—	—	10,312,499	—	(10,312,499)	—	—
Issuance of 112,446 shares of common stock at $0.001 per share par value, related to exercise of stock options	—	—	—	112,446	113	569,564	—	—	—	569,677
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock	42,744	—	—	—	—	—	—	(42,744)	—	(42,744)
Accreted redemption value for Series A, Series B, and Series C redeemable convertible preferred stock	1,627,500	2,137,742	4,935,573	—	—	—	—	(8,700,815)	—	(8,700,815)
Net change in unrealized holding loss on available-for-sale securities	—	—	—	—	—	—	—	—	29,282	29,282
Net loss	—	—	—	—	—	—	—	(24,025,389)	—	(24,025,389)
Comprehensive loss										(23,996,107)
Balances at December 31, 2004	$30,166,741	$39,622,161	$101,988,994	256,816	$ 257	$ 11,573,677	$213,710	$(134,753,508)	$ —	$ (122,965,864)

See accompanying notes

TARGACEPT, INC.

STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)—(CONTINUED)

	Redeemable Convertible Preferred Stock			Common Stock		Capital in Excess of Par Value	Common Stock Warrants	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Deficit
	Series A	Series B	Series C	Shares	Amount					
Balances as of December 31, 2004 (carried forward)	$ 30,166,741	$ 39,622,161	$ 101,988,994	256,816	$ 257	$ 11,573,677	$ 213,710	$ (134,753,508)	$ —	$ (122,965,864)
Issuance of 496,132 shares of Series C redeemable convertible preferred stock at $1.21 per share	—	—	612,281	—	—	—	—	—	—	—
Issuance of 13,611 shares of common stock at $0.001 per share par value, related to exercise of stock options	—	—	—	13,611	13	23,773	—	—	—	23,786
Stock-based compensation	—	—	—	—	—	690,454	—	—	—	690,454
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock	42,744	—	—	—	—	—	—	(42,744)	—	(42,744)
Accreted redemption value for Series A, Series B, and Series C redeemable convertible preferred stock	1,627,500	2,137,744	7,429,988	—	—	—	—	(11,195,232)	—	(11,195,232)
Net loss	—	—	—	—	—	—	—	(28,991,523)	—	(28,991,523)
Comprehensive loss										(28,991,523)
Balances at December 31, 2005	$ 31,836,985	$ 41,759,905	$ 110,031,263	270,427	$ 270	$ 12,287,904	$ 213,710	($ 174,983,007)	$ —	($ 162,481,123)

See accompanying notes

TARGACEPT, INC.
STATEMENTS OF CASH FLOWS

	Year ended December 31,		
	2003	2004	2005
Operating activities			
Net loss	$ (19,395,321)	$ (24,025,389)	$ (28,991,523)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	672,927	766,335	803,185
Loss on disposal of equipment	—	4,199	—
Non-cash compensation expense	65,325	50,623	690,454
Recognition of deferred rent incentive	(402,647)	(402,647)	(402,647)
Realized loss on sale of investments	20,978	87,948	—
Changes in operating assets and liabilities:			
Research fees and accounts receivable	517,030	334,053	366,402
Inventories	51,016	15,880	60,700
Prepaid expenses	(205,054)	(1,091,627)	998,595
Accounts payable and accrued expenses	(326,451)	1,141,221	228,318
Deferred license fee revenue	(269,532)	(1,917,224)	—
Net cash used in operating activities	(19,271,729)	(25,036,628)	(26,246,516)
Investment activities			
Purchase of investments	(84,796,103)	(6,191,930)	(25,500,000)
Proceeds from sale of investments	58,500,000	37,379,107	25,500,000
Purchase of property and equipment	(545,254)	(660,624)	(250,247)
Proceeds from sale of property and equipment	—	38,191	—
Net cash (used in) provided by investing activities	(26,841,357)	30,564,744	(250,247)
Financing activities			
Proceeds from borrowing of long-term debt	—	3,250,000	—
Principal payments on long-term debt	(637,483)	(730,979)	(2,363,350)
Proceeds from issuance of redeemable convertible preferred stock, net of transaction costs	13,767,452	32,900,000	612,281
Proceeds from issuance of common stock	238,954	519,054	23,786
Net cash provided by (used in) financing activities	13,368,923	35,938,075	(1,727,283)
Net (decrease) increase in cash and cash equivalents	(32,744,163)	41,466,191	(28,224,046)
Cash and cash equivalents at beginning of period	44,353,320	11,609,157	53,075,348
Cash and cash equivalents at end of period	$ 11,609,157	$ 53,075,348	$ 24,851,302

See accompanying notes

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS
DECEMBER 31, 2005

1. The Company and Nature of Operations

Targacept, Inc., a Delaware corporation (the Company), was formed on March 7, 1997. The Company is a biopharmaceutical company engaged in the design, discovery and development of a new class of drugs to treat multiple diseases and disorders by selectively targeting a class of receptors known as neuronal nicotinic receptors, or NNRs. Its facilities are located in Winston-Salem, North Carolina.

The accompanying financial statements have been prepared on a going concern basis. The Company has incurred operating losses since its inception and expects to incur substantial additional losses for the foreseeable future. As a result, the Company will require substantial additional funds and plans to seek collaborative agreements, research funding, and private or public equity or debt financing to meet such needs. If such funds are not available, management may need to reassess its plans. Even if the Company does not have an immediate need for additional cash, it may seek access to the private or public equity markets if and when conditions are favorable. There is no assurance that such additional funds will be available for the Company to finance its operations on acceptable terms, if at all.

2. Summary of Significant Accounting Policies

Cash and Cash Equivalents

The Company considers cash equivalents to be those investments, which are highly liquid, readily convertible to cash, and which mature within three months from the date of purchase.

Investments

In accordance with the Company's investment policy, surplus cash is invested with high quality financial institutions in money market accounts, certificates of deposit, and certain other high credit quality financial investments including Government National Mortgage Association and other mortgage-backed securities, Student Loan Auction Rate Securities, United States Government debt and other asset-backed securities with AAA credit ratings. The Company determines the appropriate classification of marketable securities at the time of purchase and reevaluates such designation as of each balance sheet date. All marketable securities entered into during 2004 and 2005 were classified as available-for-sale. Interest and dividend income on investments, as well as realized gains and losses, are included in "Interest and dividend income." There were no unrealized holding gains or losses at December 31, 2004 or 2005. The cost of securities sold is based on the specific identification method.

Research Fees and Accounts Receivable

Substantially all of the Company's research fees and accounts receivable are related to the collaborative research and license agreements discussed in Note 14 and trade sales of Inversine, the Company's sole approved product. All of the Company's trade accounts receivable are due from customers located within the United States. The Company makes judgments with respect to the collectability of trade accounts receivable based on historical experience and current economic trends. Actual collections could differ from those estimates.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

During 2003, 2004 and 2005, the Company recognized revenues of $1,572,000, $2,255,000 and $0, respectively, or 64%, 60% and 0% of net revenues, respectively, from two collaborative research and license agreements discussed in Note 14.

Inventories

Inventories are stated at the lower of cost or market. Cost is determined by the weighted-average method.

Property and Equipment and Intangible Assets

Property and equipment consists primarily of lab equipment, office furniture and fixtures and leasehold improvements and is recorded at cost. Depreciation is computed using the straight-line method over the estimated useful lives of the assets ranging from three to ten years. Lab equipment is typically depreciated over 3-5 years, office furniture and fixtures are typically depreciated over 5-10 years, and leasehold improvements are amortized over the life of the applicable lease.

Intangible assets consist of patents acquired from Layton Bioscience, Inc. The intangible assets are being amortized to research and development expense on a straight-line basis over the remaining useful life of the patents, or a period of 17 years from the date of acquisition.

The Company assesses the net realizable value of its long-lived assets and evaluates such assets for impairment whenever events or changes in business circumstances indicate that the carrying amount of an asset may not be recoverable. An impairment would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. An impairment, if recognized, would be based on the excess of the carrying value of the impaired asset over its fair value. Through December 31, 2005, there has been no such impairment in the Company's long-lived assets.

Patents

The Company capitalizes the costs of patents purchased from external sources. The Company expenses all other patent-related costs.

Research and Development Expense

Research and development costs are expensed as incurred and include related salaries of, and stock-based compensation for, personnel involved in research and development activities, contractor fees, administrative expenses and allocations of research-related overhead costs. Administrative expenses and research-related overhead costs included in research and development consist of allocations of facility and equipment lease charges, depreciation and amortization of assets, and insurance, legal and supply costs that are directly related to research and development activities.

The Company directly reduces research and development expenses for amounts reimbursed pursuant to cost-sharing agreements. During 2003, 2004 and 2005, research and development expenses were reduced by $131,000, $23,000 and $0, respectively, for costs reimbursed primarily by Dr. Falk Pharma, GmbH under the terms of the collaboration agreement described in Note 14.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

Clinical Trials Accruals

The Company records accruals based on estimates of the services received, efforts expended and amounts owed pursuant to contracts with numerous clinical trial centers and contract research organizations. In the normal course of business, the Company contracts with third parties to perform various clinical trial activities in the ongoing development of potential products. The financial terms of these agreements are subject to negotiation and variation from contract to contract and may result in uneven payment flows. Payments under the contracts depend on factors such as the achievement of certain events, the successful recruitment of patients, the completion of portions of the clinical trial or similar conditions. The objective of the Company's accrual policy is to match the recording of expenses in its financial statements to the actual services received and efforts expended. As such, expense accruals related to clinical trials are recognized based on the Company's estimate of the degree of completion of the event or events specified in the specific clinical study or trial contract.

Transaction Charges

In the first quarter of 2005, the Company recognized general and administrative expense of $1,635,000 for expenses incurred in connection with a terminated public offering, including $1,146,000 in prepaid expenses at December 31, 2004. As of December 31, 2005, the Company had $99,000 of IPO charges in prepaid expenses.

Deferred Rent Incentive

In August 2002, the Company received $2,013,000 as an incentive to lease its current office space. The incentive is being recognized monthly over the life of the lease on a straight-line basis as a reduction to the lease expense in general and administrative expenses. The Company recognized $403,000 of the incentive during each of 2003, 2004 and 2005.

Redeemable Convertible Preferred Stock

The carrying value of redeemable convertible preferred stock is increased by periodic accretions so that the carrying amount will equal the redemption amount at the earliest redemption date. These increases are affected through charges to accumulated deficit.

Fair Value of Financial Instruments

The carrying amounts of cash and cash equivalents, accounts receivable, accounts payable, accrued expenses and redeemable convertible preferred stock are considered to be representative of their respective fair values. The fair value of long-term debt was $4,504,000 and $2,162,000 at December 31, 2004 and 2005, respectively, as compared to the book value of $4,557,000 and $2,193,000 at December 31, 2004 and 2005, respectively. The difference between fair value and book value was attributable to the benefit of the interest grace period on the Company's loan from the City of Winston-Salem. The Company estimates the fair value of long-term debt using discounted cash flows based on its incremental borrowing rates for similar debt.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

Credit Risk

Financial instruments that potentially subject the Company to credit risk consist principally of cash and short-term investments. The Company places its cash and cash equivalents with high-credit quality financial institutions. The Company has established guidelines for investment of its excess cash designed to emphasize safety, liquidity and preservation of capital. At December 31, 2004 and 2005, the Company had deposits with a high credit quality major financial institution in excess of federally insured limits of approximately $53,000,000 and $24,800,000, respectively.

Revenue Recognition

The Company uses revenue recognition criteria in Staff Accounting Bulletin No. 101, *Revenue Recognition in Financial Statements,* as amended by Staff Accounting Bulletin No. 104, *Revenue Recognition (replacement of SAB 101)*. The Company considers a variety of factors in determining the appropriate method of revenue recognition under its collaboration agreements, such as whether the elements of the agreement are separable, whether there are determinable fair values and whether there is a unique earnings process associated with a particular element of an agreement. Research fee revenues are earned and recognized as research is performed and related expenses are incurred. License fees for access to the Company's intellectual property are recognized ratably over the contracted period in accordance with the provisions of the contract. Amounts received in advance of performance are recorded as deferred revenue and amortized in the statement of operations into revenue over the estimated life of the research and development period. Revenues based on the achievement of development and regulatory milestones that carry substantive performance risk are only recognized upon achievement of the milestone event. Product sales revenues are recorded when goods are shipped, at which point title has passed. Revenues from grants are recognized as the Company performs the work and incurs reimbursable costs in accordance with the objectives of the award.

Shipping and Handling Costs

During 2003, 2004 and 2005, $173,000, $174,000 and $175,000, respectively, of shipping and handling costs were included in cost of product sales.

Income Taxes

The liability method is used in accounting for income taxes as required by Statement of Financial Accounting Standards (SFAS) No. 109, *Accounting for Income Taxes*. Under this method, deferred tax assets and liabilities are recognized for operating loss and tax credit carryforwards and for the future tax consequences attributable to the differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the results of operations in the period that includes the enactment date. A

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

valuation allowance is recorded to reduce the carrying amounts of deferred tax assets unless it is more likely than not that such assets will be realized. Currently there is no provision for income taxes, as the Company has incurred net losses to date.

Comprehensive Loss

SFAS No. 130, *Reporting Comprehensive Income*, requires components of other comprehensive loss, including unrealized gains and losses on available-for-sale securities, to be included as part of total comprehensive loss. The components of comprehensive loss are included in the statements of redeemable convertible preferred stock and stockholders' equity (deficit).

Net Loss Per Share Attributable to Common Stockholders

The Company computes net loss per share attributable to common stockholders in accordance with SFAS No. 128, *Earnings Per Share* (SFAS 128). Under the provisions of SFAS 128, basic net loss per share attributable to common stockholders (Basic EPS) is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding. Diluted net loss per share attributable to common stockholders (Diluted EPS) is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares and dilutive common share equivalents then outstanding. Common share equivalents consist of the incremental common shares issuable upon the conversion of preferred stock, shares issuable upon the exercise of stock options and shares issuable upon the exercise of warrants. For the periods presented, Diluted EPS is identical to Basic EPS because common share equivalents are excluded from the calculation, as their effect is antidilutive.

Unaudited Pro Forma Stockholders' Equity and Pro Forma Net Loss Per Share

The Company's Board of Directors has authorized management of the Company to file a registration statement with the Securities and Exchange Commission permitting the Company to sell shares of its common stock to the public in an initial public offering (the IPO). If the IPO is closed at a price per share of at least $11.00 and gross proceeds to the Company are not less than $50,000,000, all of the redeemable convertible preferred stock outstanding at the time of the IPO will automatically convert into 13,832,015 shares of common stock. Unaudited pro forma basic and diluted net loss per share is computed using the weighted average number of common shares outstanding, including the pro forma effects of the conversion of outstanding redeemable convertible preferred stock into shares of the Company's common stock effective upon the completion of the Company's planned IPO as if such conversion had occurred at January 1, 2005, or the date of issuance, if later.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

The following table sets forth the computation of Basic EPS and Diluted EPS:

	Year ended December 31,		
	2003	2004	2005
Historical			
Numerator:			
Net loss attributable to common stockholders	$ (27,735,949)	$ (43,081,447)	$ (40,229,499)
Denominator:			
Weighted average common shares outstanding	109,053	219,213	262,013
Basic and diluted net loss per share attributable to common stockholders	$ (254.33)	$ (196.53)	$ (153.54)
Unaudited pro forma			
Numerator:			
Net loss attributable to common stockholders			$ (28,991,523)
Denominator:			
Shares used above			262,013
Pro forma adjustment to reflect assumed conversion of preferred stock, on a weighted average basis			13,806,169
Shares used to compute pro forma basic and diluted net loss per share attributable to common stockholders			14,068,182
Unaudited pro forma basic and diluted net loss per share attributable to common stockholders			$ (2.06)

The Company has excluded all outstanding stock options and warrants from the calculation of net loss per share attributable to common stockholders because such securities are antidilutive for all periods presented. Had the Company been in a net income position, these securities may have been included in the calculation. These potentially dilutive securities consist of the following on a weighted average basis:

	Year ended December 31,		
	2003	2004	2005
Outstanding common stock options	613,503	1,010,716	1,466,715
Redeemable convertible preferred stock	9,373,431	10,111,066	13,806,169
Outstanding warrants	215,054	215,054	215,054
Total	10,201,988	11,336,836	15,487,938

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

Stock-Based Compensation

The Company has an equity incentive plan, which is described more fully in Note 11. Prior to January 1, 2005, the Company accounted for the plan under the recognition and measurement provisions of APB Opinion No. 25, *Accounting for Stock Issued to Employees,* and related Interpretations, as permitted by FASB Statement No. 123, *Accounting for Stock-Based Compensation (SFAS 123)*. No stock-based employee compensation cost was recognized in the Statement of Operations for the years ended December 31, 2004 as all options granted under the plan to employees had an exercise price equal to the fair market value of the underlying common stock on the date of grant.

Effective January 1, 2005, the Company adopted the fair value recognition provisions of FASB Statement No. 123 (revised 2004), *Share-Based Payment* (SFAS 123R), using the modified-prospective-transition method. Under that transition method, compensation cost recognized in 2005 includes: (a) compensation cost for all stock-based payments granted prior to, but not yet vested as of, January, 1, 2005, based on the grant date fair value estimated in accordance with the original provisions of Statement 123; (b) compensation cost for all stock-based payments granted subsequent to January 1, 2005, based on the grant date fair value estimated in accordance with the provisions of SFAS 123R; and (c) compensation cost for awards modified on April 7, 2005, based on the modification provisions in accordance with SFAS 123R. Results for prior periods have not been restated.

As a result of adopting SFAS 123R effective January 1, 2005, the Company's net loss for the year ended December 31, 2005, is $645,000 higher than if it had continued to account for stock-based compensation under APB Opinion 25.

SFAS 123R also requires the benefits of tax deductions in excess of recognized compensation cost to be reported as a financing cash flow, rather than as an operating cash flow as required under pre-existing literature. This requirement will reduce net operating cash flows and increase net financing cash flows in periods after adoption. While the Company cannot estimate what those amounts will be in the future (because they depend on, among other things, when employees exercise stock options and the tax deductions for the Company at those times), no amount of operating cash flows have been recognized in prior periods for such excess tax deductions because of net operating losses generated since inception.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

The following table illustrates the effect on net income and earnings per share if the Company had applied the fair value recognition provisions of SFAS 123 to options granted under the Company's equity incentive plan in all periods presented. For purposes of this pro forma disclosure, the value of the options is estimated using a Black-Scholes-Merton option pricing formula and amortized to expense over the options' vesting periods.

	Year Ended December 31	
	2003	2004
Net loss attributable to common stockholders, as reported	$ (27,735,949)	$ (43,081,447)
Add: stock-based employee compensation expense included in reported net income, net of related tax effects of $0	65,325	50,623
Deduct: stock-based employee compensation expense determined under fair value based method for all awards, net of related tax effects	(515,405)	(916,988)
Pro forma net loss	$ (28,186,029)	$ (43,947,812)
Net loss per share:		
Basic and diluted, as reported	$ (254.33)	$ (196.53)
Basic and diluted, pro forma	$ (258.46)	$ (200.48)

Recent Accounting Pronouncements

In June 2005, the FASB issued SFAS No. 154, Accounting Changes and Error Corrections, a replacement of ABP Opinion No. 20, Accounting Changes, and FASB Statement No. 3, Reporting Accounting Changes in Interim Financial Statements (SFAS 154). SFAS 154 requires retrospective application to prior periods' financial statements for all voluntary changes in accounting principle, unless impracticable. SFAS 154 is effective for accounting changes and corrections of errors made in fiscal years beginning after December 15, 2005. SFAS 154 will have no immediate impact on our consolidated financial statements, although it would impact our presentation of future voluntary accounting changes, should such changes occur.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ materially from those estimates.

Reclassifications

Certain reclassifications have been made to the prior year financial statements to conform to the current year presentation. These reclassifications had no impact on net loss.

TARGACEPT, INC.
NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

3. Inventories

Inventories consisted of the following:

	December 31, 2004	December 31, 2005
Raw materials	$ 53,388	$ 6,400
Finished goods	49,252	35,540
	$ 102,640	$ 41,940

4. Property and equipment

Property and equipment consists of the following:

	December 31, 2004	December 31, 2005
Lab equipment	$ 4,795,050	$ 5,006,167
Office furniture and fixtures	1,438,329	1,474,655
Leasehold improvements	138,790	138,790
	6,372,169	6,619,612
Less: accumulated depreciation	4,109,471	4,872,088
Property and equipment, net	$ 2,262,698	$ 1,747,524

The Company recorded approximately $635,000, $729,000 and $765,000 of depreciation expense during 2003, 2004 and 2005, respectively.

5. Intangible Assets

Intangible assets consist of the following:

	December 31, 2004	December 31, 2005
Patents	$642,000	$ 642,000
Less: accumulated amortization	(91,263)	(129,027)
Total	$550,737	$ 512,973

The Company recognized amortization expense of approximately $38,000 per year in 2003, 2004 and 2005. Based on the Company's current intangible assets, the Company expects to recognize $38,000 of amortization expense in each of the next five years.

6. Accrued Expenses

Accrued expenses consists of the following:

	December 31, 2004	December 31, 2005
Clinical trials costs	$ 965,407	$ 1,688,277
Employee compensation	850,503	1.045.967
Other	124,926	115,503
	$ 1,940,836	$ 2,849,747

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

7. Long-term debt

During 2002, the Company entered into agreements to borrow $500,000 from the City of Winston-Salem and $2,500,000 from R.J. Reynolds Tobacco Company (RJRT). The note payable to the City of Winston-Salem matures on April 19, 2012, is non-interest bearing until April 2007 and, thereafter, bears interest between 5% and 7% depending on the gross revenues of the Company until maturity. No payments are due on the City of Winston-Salem note until the 5-year anniversary of the loan. At that time the Company will initiate monthly repayments of $9,000 over the five-year period until maturity, at which time any remaining principal and interest is then due. The note payable to RJRT accrues interest at 6.6%, and is repayable in monthly payments of $59,403 through the maturity date of May 1, 2006. In January 2004, the Company amended the note agreement with RJRT to allow additional borrowings for up to a total of $2,000,000. The Company was advanced an additional tranche on April 1, 2004 in the amount of $1,027,000. This additional tranche accrues interest at 5.87% and is repayable in monthly payments of $24,000 through the maturity date of April 1, 2008. The Company was advanced the final tranche on December 23, 2004 in the amount of $973,000. This tranche accrues interest at 6.89% and is repayable in monthly payments of $23,000 through the maturity date of January 1, 2009. The Company paid approximately $135,000, $133,000 and $146,000 for interest under the RJRT note during 2003, 2004 and 2005, respectively.

The notes with RJRT are secured by equipment owned by the Company with a book value of approximately $1,488,000, net of accumulated depreciation, at December 31, 2005.

On December 15, 2004, the Company entered into a development agreement with The Stanley Medical Research Institute (SMRI). In connection with the agreement, SMRI paid the Company $1,250,000 in return for the issuance by the Company of a convertible promissory note in an equal principal amount. The note bore interest at 10% per annum. The note's principal balance plus accrued interest of $84,000 was paid in full on August 18, 2005 and the development agreement with SMRI was terminated in December 2005.

Maturities of long-term debt are as follows at December 31, 2005:

2006	$ 783,895
2007	593,070
2008	455,813
2009	121,297
2010	103,182
Thereafter	136,040
	$ 2,193,297

8. Redeemable Preferred Stock

In August 2000, the Company issued 5,000,000 shares of its Series A redeemable convertible preferred stock (the Series A) to RJRT, and completed a private placement of 6,537,634 of its Series B redeemable convertible preferred stock (the Series B) generating cash of $29,073,000, net of offering costs.

In January 2001, the Company issued 29,933 shares of Series B to three consultants in partial payment of consulting fees owed by the Company.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

8. Redeemable Preferred Stock (continued)

In November 2002, the Company completed a private placement of 37,764,180 shares of its Series C redeemable convertible preferred stock (the Series C) and received cash of $45,488,000, net of offering costs.

In March 2003, the Company completed a private placement of an additional 11,404,958 shares of Series C and received cash of $13,767,000, net of offering costs.

In December 2004, the Company completed a private placement of an additional 27,272,728 shares of Series C and received cash of $32,900,000 net of offering costs. Pursuant to EITF Issue No. 98-5, *Accounting for Convertible Securities with Beneficial Conversion Features*, and EITF 00-27, *Application of Issue No. 98-5 to Certain Convertible Instruments*, the Company recorded a deemed dividend at the date of issuance of $10,312,499, which is the difference in the $8.40 conversion price of the Series C and the underlying value of the common stock issuable upon conversion of the Series C of $11.03.

In May 2005, the Company completed a private placement of an additional 496,132 shares of Series C and received cash of $612,000, net of offering costs.

The following is a summary of the rights, preferences and terms of the Company's outstanding series of redeemable convertible preferred stock:

Conversion

Each share of Series A, Series B and Series C is convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into fully paid and nonassessable shares of the Company's common stock. As of December 31, 2005, conversion of the Series A, Series B and Series C would result in the issuance of 666,667, 2,082,623 and 11,082,725 shares of common stock, respectively. Future sales of equity at prices below the respective conversion prices could result in adjustments to the number of shares of common stock into which each series of preferred stock is convertible.

Automatic conversion of the Series A, Series B and Series C into fully paid and nonassessable shares of common stock, without the payment of additional consideration by the holders thereof, would occur immediately upon the closing of the sale of the Company's common stock in a firm commitment, underwritten public offering registered under the Securities Act of 1933 in which (i) the price per share equals or exceeds $11.00 (subject to certain adjustments) or such lesser amount as is approved by the holders of (a) a majority of then outstanding shares of Series A and Series B, considered together as a single class on an as-converted basis, and (b) at least sixty-five percent (65%) of the then outstanding shares of Series C, and (ii) the gross proceeds to the Company are not less than $50,000,000 or such lesser amount as is approved by the holders of (a) a majority of then outstanding shares of Series A and Series B, considered together as a single class on an as-converted basis, and (b) at least sixty-five percent (65%) of the then outstanding shares of Series C. The accrued but unpaid cumulative dividend on the Series C shall, if not yet declared, be forfeited upon conversion of the Series C.

Dividends

Dividends accrue daily on each share of Series C on a cumulative basis at the rate of 8% per annum and are recorded as an increase to Series C and an increase to accumulated deficit. Cumulative dividends may be declared and paid at any time and shall be payable upon

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

8. Redeemable Preferred Stock (continued)

liquidation or redemption. At December 31, 2004 and 2005, cumulative accrued dividends on the Series C stock totaled $9,834,000 and $17,264,000, respectively.

Dividends on the Series A, Series B and Series C are payable when and if declared by the Company's Board of Directors. No dividend may be paid on the common stock without the approval of the holders of a majority of the then outstanding shares of Series A and Series B, considered together on an as-converted basis, and the holders of 65% of the Series C. No dividend may be declared or paid on either the Series A or the Series B unless, simultaneously with such declaration or payment, the same dividend per share is declared or paid on both the Series A and the Series B, as well as the Series C, and any unpaid cumulative dividends on the Series C are declared and paid in full.

Voting

Each holder of the Series A, Series B and Series C is entitled to the number of votes equal to the number of shares of common stock into which such holder's shares are convertible on the applicable record date. In addition, certain actions by the Company require the approval of one or more of (i) the holders of a majority of the outstanding shares of Series A, (ii) the holders of at least two-thirds of the outstanding shares of Series B, (iii) the holders of a majority of the outstanding shares of Series A and Series B, considered together on an as-converted basis, and/or (iv) the holders of at least 65% of the outstanding shares of Series C.

Liquidation Preference

In the event of any liquidation, dissolution or winding up of the Company, the holders of the Series C shares have preference and are entitled to receive an amount per share equal to the greater of (i) their initial purchase price per share plus any accrued or declared and unpaid dividends on such share or (ii) the amount per share of Series C that such holders would receive if all of the Series A, Series B and Series C were converted to common stock immediately prior to such liquidation, dissolution or winding up.

Next, the holders of Series A and Series B are entitled to receive, on a *pari passu* basis, an amount equal to their initial purchase price per share plus any declared and unpaid dividends on such shares. Any assets of the Company remaining after the payments specified above shall be distributed on a *pari passu* basis among the holders of common stock and, on an as-converted to common stock basis, Series A, Series B and Series C. Unless the holders of a prescribed number of shares of Series A, Series B and/or Series C otherwise elect, certain fundamental transactions involving the Company shall be treated as a liquidation for the Series A, Series B and/or Series C, as the case may be.

Mandatory Redemption

At any time after November 26, 2008, upon demand by the holders of at least 65% of the outstanding shares of Series C, all of the outstanding shares of Series C shall be redeemed in cash in an amount per share equal to the initial purchase price per share (subject to certain adjustments) plus any accrued or declared and unpaid dividends on such shares.

At any time after the later of August 22, 2005 or the date on which no shares of Series C are outstanding, a number of outstanding shares of Series A or Series B elected upon demand by

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

8. Redeemable Preferred Stock (continued)

the holders of a majority of the outstanding shares of Series A (in the case of Series A) or a majority of the outstanding shares of Series B (in the case of Series B) shall be redeemed in an amount per share equal to $4.65 (subject to certain adjustments) plus (i) any previously declared but unpaid dividends on such share and (ii) an amount equal to $0.081375 per share (subject to certain adjustments) multiplied by the number of complete three-month periods that have elapsed from the date such share was originally issued to the redemption date. The Company may satisfy its redemption obligation with respect to the Series A and/or the Series B in cash or by paying a portion in cash and issuing a promissory note that meets certain prescribed conditions for the remaining amount.

9. Stockholders' Equity (Deficit)

On March 14, 2003, the Company amended its Certificate of Incorporation to increase the number of authorized shares of common stock to 11,333,333 and preferred stock to 60,736,705 and issued 11,404,958 shares of Series C.

On December 6, 2004, the Company amended its Certificate of Incorporation to increase the number of authorized shares of common stock to 16,666,666 and preferred stock to 93,309,532 and issued 27,272,728 shares of Series C.

On February 2, 2005, the Company's Board of Directors adopted, and on February 2, 2005 the stockholders approved, a one-for-7.5 share reverse stock split of the Company's common stock effective as of February 3, 2005. All common stock and per common share amounts for all periods presented in the accompanying financial statements have been restated to reflect the effect of this reverse common stock split.

In conjunction with the issuance of Series A, the Company issued a warrant to purchase 215,054 shares of the Company's common stock at an original exercise price of $34.88 per share (subject to certain adjustments). In connection with the Company's issuance of Series C and price adjustment provisions of the warrant, the conversion price of the warrant was adjusted to $14.63. The warrant is exercisable only upon the earlier of an initial public offering or a change in control. The fair value of the warrant is a direct cost of obtaining capital. As such, the fair value has been recorded in stockholders' equity, with the offset recorded as a decrease in the redemption value of the Series A. The Company will accrete to the redemption value of the Series A at the earliest date of redemption, or until November 2008, through an increase in redemption value to Series A and an increase to retained deficit. The fair value of the warrant to purchase 215,054 shares of the Company's common stock was estimated at the grant date to be $213,710 or $0.99 per share. The Company considered the anti-dilution features, the contingencies surrounding the limited opportunities for exercise, and the warrant's priorities over common stock options in relation to the fair value of the Company's common stock at the date of issuance when estimating the fair value of the warrant.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

9. Stockholders' Equity (Deficit) (continued)

At December 31, 2004 and 2005, the Company had reserved shares of common stock for future issuance as follows:

	December 31,	
	2004	2005
Convertible preferred stock	13,760,548	13,832,015
Warrant	215,054	215,054
Options	1,028,086	1,664,474
	15,003,688	15,711,543

10. Income Taxes

There is no income tax provision (benefit) for federal or state income taxes as the Company has incurred operating losses since inception.

The Company's effective tax rate differs from the federal income tax rate for the following reasons:

	Year Ended December 31,		
	2003	2004	2005
Expected federal income tax benefit at statutory rate	(34)%	(34)%	(34)%
Increase (decrease) resulting from:			
Research and development credits	(6)	(3)	(3)
State income tax expense, net of federal benefit	(5)	(5)	(4)
Net operating loss and credit limitations	3	—	—
Change in valuation allowance	41	42	41
Other	1	—	—
	— %	— %	— %

At December 31, 2003, 2004 and 2005, the Company had net operating loss carryforwards for federal income tax purposes of approximately $45,606,000, $70,866,000 and $98,333,000, respectively, and for state income tax purposes of approximately $45,627,000, $70,887,000 and $98,349,000, respectively, and research and development federal income tax credits of approximately $638,000, $1,357,000 and $2,131,000, respectively. The federal net operating loss carryforwards begin to expire in 2020. State net operating loss carryforwards begin to expire in 2015. The research and development tax credits begin to expire in 2021.

Utilization of the net operating loss carryforwards and credits may be subject to a substantial annual limitation due to ownership change limitations provided by Section 382 of the Internal Revenue Code of 1986, as amended, and similar state provisions. As a result of a series of stock issuances, the Company had such an ownership change on November 30, 2002. Consequently, an annual limitation is imposed on the Company's use of net operating loss and credit carryforwards attributable to periods before the change.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

10. Income Taxes (continued)

for income tax purposes. The Company's net deferred tax assets relate primarily to its net operating loss carryforwards. A valuation allowance has been recognized to offset the deferred tax assets related primarily to its net operating loss carryforward. If and when recognized, the tax benefit for those items will be reflected in current operations of the period in which the benefit is recorded as a reduction of income tax expense. The utilization of the loss carryforwards to reduce future income taxes will depend on the Company's ability to generate sufficient taxable income prior to the expiration of the net operating loss carryforwards. For the years ended December 31, 2003, 2004 and 2005, the valuation allowance increased approximately $8,050,000, $9,600,000 and $11,750,000, respectively.

Significant components of the Company's deferred tax assets (liabilities) are as follows:

	December 31,	
	2004	2005
Deferred tax assets:		
Net operating loss carryforward	$ 24,787,121	$ 35,299,808
Research and development tax credit	1,357,135	2,130,640
Patents	577,974	914,069
Stock based compensation	—	88,129
Total gross deferred tax assets	26,722,230	38,432,646
Valuation allowance	(26,599,098)	(38,347,057)
Net deferred tax asset	123,132	85,589
Deferred tax liabilities:		
Equipment and other	(123,132)	(85,589)
Net deferred tax asset	$ —	$ —

11. Equity Incentive Plan

On August 22, 2000, the Company established an equity incentive plan (the Plan) and authorized the issuance of up to 268,168 shares under the Plan to attract and retain employees, directors and certain independent contractors, consultants and advisors and to allow them to participate in the growth of the Company. During 2001, the number of shares authorized for issuance under the Plan was increased to 348,168. In conjunction with the November 2002 Series C financing, the Company authorized the issuance of an additional 400,000 shares, increasing the number of authorized shares to 748,168. Upon the issuance of the additional Series C shares in March 2003, the number of authorized shares was increased to 1,228,888. In March 2005, the number of authorized shares was increased to 1,878,888. Awards may be made to participants under the Plan in the form of incentive and nonqualified stock options, restricted stock, stock appreciation rights, stock awards, and performance awards. Eligible participants under the Plan include employees, directors and certain independent contractors, consultants or advisors of the Company or a related corporation. The vesting periods for awards made under the Plan are determined at the discretion of the Plan administrator and range from 0 to 5 years. Awards made under the Plan have 10-year contractual terms or, in some cases, shorter terms designed to comply with Section 409A of the Internal Revenue Code. The exercise price of incentive options granted under the Plan may not be less than 100% of the fair market value of the common stock on the date of grant, as determined by the Plan administrator.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

11. Equity Incentive Plan (continued)

On April 7, 2005 the Company's Board of Directors authorized an amendment to each stock option agreement held by current employees that changed the exercise price per share for each unvested portion as of March 31, 2005 to $1.75. As of March 31, 2005, there were 354,672 shares issued to 75 employees subject to the unvested portions of employee options ranging from an original option price of $5.10 to $5.63 that were affected by the amendments. Each affected option is required to be accounted for as a modification of an award under SFAS 123R. The fair market value was calculated immediately prior to the modification and immediately after the modification to determine the incremental fair market value. This incremental value of $147,000 and the fair market value of each modified option will be expensed as compensation on a quarterly basis, until the date that the option is exercised or forfeited or expires unexercised.

The Company uses the Black-Scholes-Merton formula to estimate the fair value of its stock-based payments. The volatility assumption used in the Black-Scholes-Merton formula is based on the calculated historical volatility of twelve benchmark biotechnology companies that have been identified as comparable public entities. The expected term of options granted is derived from the simplified method allowable under SEC Staff Accounting Bulletin No. 107. Under this approach, the expected term would be the mid-point between the weighted average of vesting period and the contractual term. The risk-free rate for periods within the contractual life of the option is based on the U.S. Treasury yield curve in effect at the time of grant.

The following table illustrates the weighted-average assumptions for the Black-Scholes-Merton model used in determining the fair value of options granted to employees:

	Year Ended December 31,	
	2004	2005
Dividend yield	—	—
Risk-free interest rate	3.0%	4.1%
Volatility	0.8	0.7
Expected life	4 years	6.25-6.5 years

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

11. Equity Incentive Plan (continued)

A summary of option activity under the Plan and changes during the periods are presented below:

	Options Granted	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at January 1, 2003	307,548	$ 4.43		
Granted	799,479	5.03		
Forfeited	(4,797)	1.95		
Exercised	(61,092)	3.90		
Outstanding at December 31, 2003	1,041,138	4.88		
Granted	65,200	5.33		
Forfeited	(6,066)	21.53		
Exercised	(112,472)	4.73		
Outstanding at December 31, 2004	987,800	4.88		
Granted	653,743	1.76		
Forfeited	(17,923)	5.00		
Exercised	(13,611)	1.75		
Outstanding at December 31, 2005	1,610,009	$ 2.88	8.0	$ 46,764
Vested and exercisable at December 31, 2005	979,784	$ 3.61	7.6	$ 37,614

The weighted average grant date fair value for an option granted during 2003, 2004 and 2005 was $3.08, $5.33 and $1.20, respectively. The total intrinsic value of options exercised during the year ended December 31, 2005 was $13,047.

A summary of the status of the Company's non-vested shares as of December 31, 2005, and changes during year ended December 31, 2005, is presented below:

Non-vested Options	Options Granted	Weighted-Average Grant-Date Fair Value
Non-vested at January 1, 2005	401,148	$ 3.00
Granted	653,743	1.20
Vested	(418,913)	2.93
Forfeited	(5,753)	3.06
Non-vested at December 31, 2005	630,225	1.18(a)

(a) Reflects the April 7, 2005 amendment that decreased the weighted average fair value of 354,672 shares subject to unvested options from $3.08 to $1.02 per option.

As of December 31, 2005, there was $989,000 of total unrecognized compensation cost related to non-vested stock-based compensation arrangements granted under the Plan. That cost is expected to be recognized over a weighted-average period of 3.3 years. The total fair value of shares vested during the twelve months ended December 31, 2005 was $1,016,000.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

11. Equity Incentive Plan (continued)

During 2004, the Company granted options to purchase 10,333 shares of common stock at an exercise price of $0.08, below the fair value of $5.63 per share of common stock. During 2005, the Company granted options to purchase 6,000 shares of common stock at an exercise price of $0.08, below the fair value of $1.75 per share of common stock. The fair value of these shares was recorded as compensation expense in the amounts of $51,000 and $46,000 during the twelve months ended December 31, 2004 and 2005, respectively.

12. Leases

On March 1, 2002, the Company entered into an agreement with Wake Forest University to lease an office and research facility in Winston-Salem, North Carolina with an initial term that extends through July 31, 2007. The lease contains a renewal option for up to one additional five-year term, with a lease rate similar to the original agreement. In December 2004, the Company amended the terms of the lease to include 1,000 square feet and an option on additional space in this facility. The lease amendment increased annual rent by $15,000 per year and included a $37,000 hold fee in the first year. Rent expense incurred by the Company under this lease was approximately $1,456,000, $1,456,000 and $1,500,000 for the years ended December 31, 2003, 2004 and 2005, respectively. Rent expense is offset by the monthly recognition of the deferred rent incentive discussed in Note 2. At December 31, 2005, the Company has the following future minimum lease payments in relation to this lease:

2006	$ 1,470,552
2007	857,822
2008 and thereafter	—
	$ 2,328,374

13. Retirement Savings Plan

The Company has a 401(k) retirement plan that covers substantially all of its employees. This plan provides for the Company to make 100% matching contributions up to a maximum of 6% of employees' eligible compensation. The Company contributed approximately $298,000, $368,000 and $412,000 to the plan for the years ended December 31, 2003, 2004 and 2005, respectively.

14. Collaborative Research and License Agreements

Aventis Pharma

In December 1998, the Company entered into a collaborative research and license agreement with Aventis Pharma whereby the Company and Aventis agreed to collaborate on the discovery, development and commercialization of nicotinic agonists for use in prevention of certain human diseases. Under the agreement, as restated in January 2002, Aventis was granted a license under certain patent rights and knowledge to develop, manufacture and commercialize certain compounds. The agreement provided for the payment of research fees on a "fee for service" basis for development work that the Company agreed to perform. For the years ended December 31, 2003, 2004 and 2005, these fees were approximately $1,303,000, $338,000 and $0, respectively. The Company was entitled to receive milestone payments under the contract at

14. Collaborative Research and License Agreements (continued)

specified dates during the development period. The Company did not receive milestone payments under the agreement during 2003, 2004 or 2005. In addition, Aventis agreed to make royalty payments based on net sales of products developed and sold. In general, either party could terminate the agreement in the event of a material breach by the other party, including a material breach of research obligations or the issuance of third-party patent rights to a competitor. Additionally, Aventis could terminate the agreement without cause by providing the Company with 30 days, written notice at any time after the research term, in which case all rights to the product candidate would revert to the Company. All royalty and other payment obligations of the parties survive any termination of the agreement.

During 1999, the Company received a one-time non-refundable license fee payment of $2,000,000 to enter into this agreement. During 2003 and 2004, the product candidate subject to the agreement had not completed the research and clinical development process. Accordingly, the Company has deferred recognition of the license fee and was amortizing it over the expected term of the research and development period. On December 3, 2004, Aventis provided the Company with 30 days advance written notice of Aventis' plans to terminate the collaborative research and license agreement. The agreement was terminated effective January 2, 2005 and was within the provisions of termination clauses of the agreement. As a result of the termination of the agreement, the Company recognized the remaining deferred revenue of $825,000 related to the agreement during the fourth quarter of 2004, as there were no further responsibilities or duties to be performed under the agreement as of December 31, 2004.

On January 21, 2002, the Company entered into a second collaborative research and license agreement with Aventis to discover and develop drugs, derived from the Aventis library of compounds for the treatment of Alzheimer's disease and other disorders of the central nervous system. The second agreement was structured similarly to the first agreement. The research term of the agreement expired in December 2004. The Company was eligible to receive milestone payments and royalties from Aventis for any compounds that are selected for further development within six months after the expiration of the research term.

Dr. Falk Pharma

On January 26, 2001, the Company entered into a collaborative research development and license agreement with Dr. Falk Pharma GmbH, a German corporation, pursuant to which the parties agreed to collaborate to research, develop and commercialize nicotinic therapeutics for use in the prevention or treatment of ulcerative colitis and other gastrointestinal and liver diseases. Upon execution of the agreement, Dr. Falk Pharma paid the Company a $1,000,000 upfront license fee and purchased 14,815 shares of the Company's common stock for $1,000,000. The Company deferred recognition of the upfront license fee payment and was amortizing it over the expected term of the research and development period. To account for the $1,000,000 in proceeds for the common stock, the Company used the estimated fair value of the common stock to value the shares issued to arrive at a total equity value of $76,000, with the remaining proceeds of $924,000 allocated to deferred revenue. This deferred revenue was also being amortized over the expected term of the research and development period.

The Company and Dr. Falk Pharma mutually agreed to discontinue the development of the lead compound subject to the collaboration agreement, resulting in the recognition of the

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

14. Collaborative Research and License Agreements (continued)

remaining deferred revenue of $890,000 during the fourth quarter of 2004, and terminated the collaboration agreement in November 2005. The Company recognized $170,000 and $1,017,000 of deferred revenue under this agreement during 2003 and 2004, respectively.

Stanley Medical Research Institute

On December 15, 2004, the Company entered into a development agreement with The Stanley Medical Research Institute (SMRI). In connection with the agreement, SMRI paid the Company $1,250,000 in return for the issuance by the Company of a convertible promissory note in an equal principal amount. The note bore interest at 10% per annum. In August 2005, the Company re-paid the promissory note in full. The Company and SMRI terminated the development agreement in December 2005.

AstraZeneca AB

In December 2005, the Company entered into a collaborative research and license agreement with AstraZeneca AB under which the Company granted AstraZeneca exclusive development and worldwide commercialization rights to the Company's product candidate known as TC-1734 as a treatment for Alzheimer's disease, cognitive deficits in schizophrenia and potentially other conditions marked by cognitive impairment such as attention deficit hyperactivity disorder, age associated memory impairment and mild cognitive impairment. The collaboration agreement also provides for a multi-year preclinical research collaboration to be conducted by the Company and AstraZeneca.

The Company is eligible to receive future research fees, license fees and milestone payments under its collaboration agreement with AstraZeneca. The amount of research fees, license fees and milestone payments will depend on the extent of the Company's research activities and the timing and achievement of development, regulatory and first commercial sale milestone events. AstraZeneca paid the Company an initial fee of $10 million in February 2006. Based on the collaboration agreement terms, the Company allocated $5 million of the initial fee to the research collaboration, which the Company expects to recognize as revenue over the four-year term of the research collaboration. The Company deferred recognition of the remaining $5 million of the initial fee, which was allocated to the TC-1734 license grants, until AstraZeneca makes a determination whether to conduct Phase II clinical development of TC-1734 following the completion of additional safety and product characterization studies that AstraZeneca is conducting. If AstraZeneca decides to conduct a Phase II clinical trial of TC-1734 following the completion of the safety and product characterization studies, the Company would recognize the deferred $5 million of the initial fee as revenue over the expected development period for TC-1734. The Company expects to recognize any revenue based on the achievement of milestones under the collaboration agreement upon achievement of the milestone event, if the Company determines that the revenue satisfies the revenue recognition requirements of SEC Staff Accounting Bulletin, or SAB, No. 101, *Revenue Recognition Financial Statements*, as amended by SAB No. 104. SAB No. 101 requires that four basic criteria must be met before revenue can be recognized: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed and determinable; and collectability is reasonably assured. The Company will record research fees that the Company receives from

14. Collaborative Research and License Agreements (continued)

AstraZeneca while it is conducting the safety and product characterization studies on TC-1734 as deferred revenue. The Company expects to receive approximately $2.5 million (unaudited) in research fees from AstraZeneca while AstraZeneca is conducting the safety and product characterization studies of TC-1734. If the agreement continues in effect following the completion of the additional safety and product characterization studies that AstraZeneca is conducting, the Company will recognize all research fees previously recorded as deferred revenue and recognize future research fee revenues as the research is performed and related expenses are incurred. In that event, the Company would be entitled to receive at least an additional $21.2 million (unaudited) in research fees. Based on the current research budget, the Company would expect to receive an additional $23.9 million (unaudited) in research fees.

If AstraZeneca terminates the collaboration agreement upon completion of any or all of the additional safety and product characterization studies, the Company would be required to reimburse AstraZeneca for the amount of all research fees that it paid to the Company under the research collaboration under the agreement while AstraZeneca conducted the studies. In addition, the Company would be required to pay AstraZeneca an additional $5 million as compensation for assigning to it the data and any intellectual property generated in the studies. In that event, upon final termination by AstraZeneca in accordance with the terms of the Agreement, the Company would reduce deferred revenue by $5 million.

The Company's collaboration agreement with AstraZeneca became effective on January 20, 2006. AstraZeneca paid the Company an initial fee of $10 million in February 2006.

15. Related Party Transactions

RJRT is the holder of 5,000,000 shares of Series A redeemable preferred stock convertible to 666,667 shares of common stock, 1,652,893 shares of Series C redeemable preferred stock convertible to 238,095 shares of common stock, a warrant to purchase 215,054 shares of common stock, 3,333 shares of common stock, and options to purchase 5,230 shares of common stock. The Company has entered into the following transactions and agreements with RJRT in the ordinary course of business.

During 2002, the Company entered into an agreement to borrow $2,500,000 from RJRT accruing interest at 6.6%. The note is repayable in monthly installments of $59,000 through the maturity date of May 1, 2006. In January 2004, the Company amended the note agreement with RJRT to allow for up to three additional tranches to be advanced to the Company for up to a total of $2,000,000. Each of the additional tranches will accrue interest at the 4-year U.S. Treasury rate plus 3.5% determined as at the day the additional tranche is advanced and will be repayable in 48 equal monthly installments. The Company was advanced an additional tranche on April 1, 2004 in the amount of $1,027,000. This additional tranche accrues interest at 5.87% and is repayable in monthly payments of $24,000 through the maturity date of April 1, 2008.

The Company was advanced the final tranche on December 23, 2004 in the amount of $973,000. This tranche accrues interest at 6.89% and is repayable in monthly payments of $23,000 through the maturity date of January 1, 2009. Under this related party note payable, the Company paid RJRT $772,000, $846,000 and $1,259,000 during 2003, 2004 and 2005, respectively.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

15. Related Party Transactions (continued)

The notes are secured by equipment owned by the Company with a book value of approximately $1,488,000 net of accumulated depreciation, at December 31, 2005.

A member of the Company's board of directors serves as an officer of RJRT. Equity compensation for such director's service has been made, at the director's request, directly to RJRT. The numbers of shares subject to stock options granted to RJRT during the years ended December 31, 2003, 2004 and 2005 in connection with the director's services are 1,000 shares per year. In connection with the issuance of the stock options, the Company recognized compensation expense of $2,512, $4,247 and $4,656 during 2003, 2004 and 2005, respectively.

Prior to December 31, 2003, the Company used the services of a RJRT employee for toxicology studies and purchased materials used for research and development and copy and print services through RJRT. The Company paid RJRT $201,000 for these services during 2003. During 2004 and 2005 the Company continued to use copy and print services totaling $79,000 and $71,000, respectively.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

16. Selected Quarterly Financial Data (unaudited)

	2004 Quarter			
	First	Second	Third	Fourth
Net revenue	$ 496,939	$ 528,026	$ 555,583	$ 2,157,826
Gross profit on product sales	6,060	494,780	55,697	11,600
Operating loss	(6,843,593)	(6,485,006)	(6,664,381)	(4,400,447)
Net loss	(6,637,935)	(6,481,318)	(6,617,687)	(4,288,449)
Net loss attributable to common stockholders	(8,779,826)	(8,623,208)	(8,759,577)	(16,918,836)
Basic and diluted net loss per share attributable to common stockholders(1)	$ (59.18)	$ (38.76)	$ (34.94)	$ (66.46)
Weighted average common shares outstanding—basic and diluted	148,345	222,504	250,710	254,556

	2005 Quarter			
	First	Second	Third	Fourth
Net revenue	$ 303,233	$ 299,646	$ 338,310	$ 238,728
Gross profit (loss) on product sales	157,518	62,477	39,768	(59,411)
Operating loss(2)	(7,656,423)	(8,339,228)	(7,170,082)	(6,775,183)
Net loss	(7,437,771)	(8,105,493)	(6,920,200)	(6,528,059)
Net loss attributable to common stockholders	(10,239,660)	(10,913,785)	(9,734,099)	(9,341,955)
Basic and diluted net loss per share attributable to common stockholders(1)	$ (39.51)	$ (41.95)	$ (37.28)	$ (35.29)
Weighted average common shares outstanding—basic and diluted	259,173	260,140	261,094	264,739

Diluted EPS is identical to Basic EPS since common stock equivalent shares are excluded from the calculation, as their effect is anti-dilutive.

(1) Per common share amounts for the quarters and full years have been calculated separately. Accordingly, quarterly amounts do not add to the annual amount because of differences in the weighted average common shares outstanding during each period principally due to the effect of the Company's issuing shares of its common stock during the year.

(2) Net loss for the first quarter of 2005 includes $1,635,000 of expenses incurred in connection with a public offering that was terminated.

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You should rely only on the information contained in this prospectus. We have not authorized anyone to provide information different from that contained in this prospectus. We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock.

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Until , 2006 (25 days after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to unsold allotments or subscriptions.

5,000,000 Shares

Common Stock

Deutsche Bank Securities

Pacific Growth Equities, LLC

CIBC World Markets

Lazard Capital Markets

Prospectus

, 2006

Part II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the expenses in connection with the offering, all of which will be borne by us. All amounts shown are estimates except for the Securities and Exchange Commission registration fee, the NASDAQ National Market listing fee and the NASD filing fee.

Securities and Exchange Commission registration fee	$ 7,999
NASDAQ National Market listing fee	100,000
NASD filing fee	7,975
Blue sky fees and expenses	5,000
Accounting fees and expenses	300,000
Legal fees and expenses	285,000
Transfer agent and registrar fees and expenses	3,500
Printing and engraving expenses	300,000
Miscellaneous	50,526
Total	$ 1,060,000

Item 14. Indemnification of Directors and Officers.

Our Third Amended and Restated Certificate of Incorporation, as amended and in effect as of the date of this registration statement, and our Fourth Amended and Restated Certificate of Incorporation to be in effect upon completion of this offering (as may be in effect from time to time, the Certificate) provide that, except to the extent prohibited by the Delaware General Corporation Law, as amended (the DGCL), our directors shall not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty while serving as our directors. Under the DGCL, our directors have a fiduciary duty to us that is not eliminated by this provision of the Certificate and, in appropriate circumstances, equitable remedies such as injunctive or other forms of non-monetary relief will remain available. In addition, each director will continue to be subject to liability under the DGCL for breach of the director's duty of loyalty to us or our stockholders, for acts or omissions that are found by a court of competent jurisdiction to be not in good faith or involving intentional misconduct, for knowing violations of law, for actions leading to improper personal benefit to the director and for payment of dividends or approval of stock repurchases or redemptions that are prohibited by the DGCL. This provision also does not affect our directors' responsibilities under any other laws, such as federal securities laws or state or federal environmental laws.

Section 145 of the DGCL empowers a corporation to indemnify its directors and officers against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by them in connection with any action, suit or proceeding brought by third parties by reason of the fact that they were or are directors or officers of the corporation, if they acted in good faith, in a manner they reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reason to believe that their conduct was unlawful. The DGCL provides further that the indemnification permitted thereunder shall not be deemed exclusive of any other rights to which the directors and officers may be entitled under the corporation's bylaws, any agreement, a vote of stockholders or otherwise. The Certificate provides that, to the fullest extent permitted by Section 145 of the DGCL, we shall indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding (whether civil, criminal, administrative or investigative) by reason of the fact that

such person is or was a director or officer of us, or is or was serving at our request as a director, officer or trustee of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding. At present, there is no pending litigation or proceeding involving any director or officer as to which indemnification will be required or permitted under the Certificate and we are not aware of any threatened litigation or proceeding that may result in a claim for such indemnification.

Section 145 of the DGCL also empowers a corporation to purchase insurance for its officers and directors for such liabilities. We maintain liability insurance for our officers and directors.

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding shares of common stock and preferred stock issued, and options and warrants granted, by us since January 1, 2003. Also included is the consideration, if any, received by us for such shares, options and warrants and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuance of Securities

1. On March 14, 2003, we issued and sold an aggregate of 11,404,958 shares of our series C convertible preferred stock at a purchase price per share of $1.21 to investors affiliated with JAFCO G-9(A) Venture Capital Investment Limited Partnership, Rock Castle Ventures, Cogene Biotech Ventures Five, Bison Capital, LLC and Oxford Bioscience Partners IV L.P. for an aggregate purchase price of approximately $13.8 million. These shares will convert into common stock at the rate of approximately 0.144 shares of common stock for each share of series C convertible preferred stock concurrently with the completion of this offering.

2. On December 6, 2004, we issued and sold an aggregate of 27,272,728 shares of our series C convertible preferred stock at a purchase price per share of $1.21 to New Enterprise Associates 10, Limited Partnership, EuclidSR Partners, L.P., Burrill Biotechnology Capital Fund, L.P., R.J. Reynolds Tobacco Holdings, Inc., Nomura Phase4Ventures LP and investors affiliated with CDIB Bioscience Ventures I, Inc., Genavent Fund, FCPR SGAM AI Biotechnology Fund, FCPR CDC-Innovation 2000, Advent Private Equity Fund II and JAFCO G-9(A) Venture Capital Investment Limited Partnership for an aggregate purchase price of approximately $33.0 million. These shares will convert into common stock at the rate of approximately 0.144 shares of common stock for each share of series C convertible preferred stock concurrently with the completion of this offering.

3. On December 15, 2004, we issued a $1.25 million convertible promissory note to The Stanley Medical Research Institute. In August 2005, we repaid the note in full.

4. On May 13, 2005, we issued and sold an aggregate of 496,132 shares of our series C convertible preferred stock at a purchase price per share of $1.21 to Cogene Biotech Ventures, L.P. for an aggregate purchase price of approximately $600,320. These shares will convert into common stock at the rate of approximately 0.144 shares of common stock for each share of series C convertible preferred stock concurrently with the completion of this offering.

5. In December 2005, upon the exercise of stock options at an exercise price per share of $0.08 per share, we issued and sold an aggregate of 5,999 shares of common stock to NEA Development Corp., EuclidSR Partners, L.P., EuclidSR Biotechnology Partners, L.P., Burrill & Company LLC, R.J. Reynolds Tobacco Holdings, Inc., John P. Richard and Errol B. De Souza.

6. From January 1, 2003 to April 5, 2006, we granted:

- options to purchase an aggregate of 1,522,751 shares of common stock at exercise prices ranging from $0.08 to $5.63 per share under our 2000 Equity Incentive Plan, as amended, with a weighted average exercise price of $3.26 per share, to employees, directors and individual consultants;
- restricted stock awards for an aggregate of 8,331 shares of common stock at a purchase price of $0.08 per share under our 2000 Equity Incentive Plan, as amended; and
- options to purchase an aggregate of 13,999 shares of common stock at an exercise price of $0.08 per share to non-individual consultants under our 2000 Equity Incentive Plan, as amended.

The weighted average exercise price of all options to purchase shares of common stock granted since January 1, 2003 and outstanding on April 5, 2006 is $2.91 per share. As of April 5, 2006, there were 62 holders of record of shares of our common stock.

(b) No underwriters were involved in the foregoing sales of securities. The securities described in paragraphs (a)(1), (2), (3) and (4), and a portion of the securities described in paragraphs (5) and (6) of this Item 15 were issued to a combination of foreign and U.S. investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Sections 3(a)(9) or 4(2) under the Securities Act and Rule 506 of Regulation D promulgated thereunder relative to sales by an issuer not involving any public offering, or in reliance upon Regulation S promulgated under the Securities Act, to the extent an exemption from such registration was required. All purchasers of shares of our convertible preferred stock described in paragraphs (a)(1), (2), (3) and (4), and the purchasers of a portion of the securities described in paragraphs (5) and (6) of this Item 15 represented to us in connection with their purchase that they were accredited investors and were acquiring the shares for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. The purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration.

All of the foregoing securities are deemed restricted securities for purposes of the Securities Act. All certificates representing the issued shares of common stock described in this Item 15 included appropriate legends setting forth that the securities had not been registered and the applicable restrictions on transfer.

The restricted stock and a portion of the stock options and the common stock issuable upon the exercise of such options described in paragraphs (5) and (6) of this Item 15 were issued pursuant to written compensatory benefit plans or arrangements with our employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

Exhibit No.	Description
1.1**	Form of Underwriting Agreement.
3.1(a)**	Third Amended and Restated Certificate of Incorporation of the Company.
3.1(a)(1)	Certificate of Amendment to Third Amended and Restated Certificate of Incorporation of the Company filed February 3, 2005.
3.1(a)(2)	Certificate of Amendment to Third Amended and Restated Certificate of Incorporation of the Company filed April 3, 2006.
3.1(b)**	Form of Fourth Amended and Restated Certificate of Incorporation of the Company, to be effective upon completion of this offering.
3.2(a)**	Amended and Restated Bylaws of the Company.
3.2(b)**	Form of Bylaws of the Company, to be effective upon completion of this offering.
4.1**	Specimen common stock certificate.
4.2(a)**	Third Amended and Restated Investor Rights Agreement, dated May 12, 2004, by and among the Company and certain stockholders of the Company.
4.2(b)**	Amendment No. 1, dated December 6, 2004, to Third Amended and Restated Investor Rights Agreement, dated May 12, 2004.
4.2(c)**	Amendment No. 2, dated March 16, 2006, to Third Amended and Restated Investor Rights Agreement, dated May 12, 2004.
4.3**	Warrant to Purchase Common Stock, dated August 22, 2000, granted to R.J. Reynolds Tobacco Company and subsequently assigned to R.J. Reynolds Tobacco Holdings, Inc.
5.1**	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
10.1**	Form of Indemnification Agreement between the Company and each of its directors and officers.
10.2(a)**	Lease Agreement, dated as of August 1, 2002, by and between the Company and Wake Forest University Health Sciences.
10.2(b)**	First Lease Amendment to Lease Agreement, dated as of August 1, 2002, by and between the Company and Wake Forest University Health Sciences.
10.3**	Loan Agreement, dated as of April 19, 2002, between the Company and the City of Winston-Salem.
10.4**	Amended and Restated Note and Security Agreement, dated January 30, 2004, issued by the Company in favor of R.J. Reynolds Tobacco Holdings, Inc.
10.5**#	Amended and Restated Targacept, Inc. 2000 Equity Incentive Plan.
10.5(a)**	Form of Incentive Stock Option Agreement under Targacept, Inc. 2000 Equity Incentive Plan.
10.5(b)**	Form of Nonemployee Director Nonqualified Stock Option Agreement under Targacept, Inc. 2000 Equity Incentive Plan.
10.5(c)**	Form of Restricted Stock Award Agreement under Targacept, Inc. 2000 Equity Incentive Plan.
10.6**	Targacept, Inc. 2006 Stock Incentive Plan.
10.6(a)**	Form of Incentive Stock Option Agreement under Targacept, Inc. 2006 Stock Incentive Plan.

Exhibit No.	Description
10.6(b)**	Form of Nonqualified Stock Option Agreement under Targacept, Inc. 2006 Stock Incentive Plan.
10.6(c)**	Form of Nonemployee Director Nonqualified Stock Option Agreement under Targacept, Inc. 2006 Stock Incentive Plan.
10.6(d)**	Form of Restricted Stock Award Agreement under Targacept, Inc. 2006 Stock Incentive Plan.
10.7**	Employment Agreement, dated as of August 22, 2000, by and between the Company and J. Donald deBethizy.
10.8**	Employment Agreement, dated as of August 22, 2000, by and between the Company and Merouane Bencherif.
10.9**	Employment Agreement, dated as of August 22, 2000, by and between the Company and William S. Caldwell.
10.10**	Employment Agreement, dated as of April 24, 2001, by and between the Company and Geoffrey Dunbar.
10.11**	Employment Agreement, dated as of February 8, 2002, by and between the Company and Alan Musso.
10.12**	Employment Agreement, dated as of September 1, 2003, by and between the Company and Jeffrey P. Brennan.
10.13(a)**+	Collaborative Research and License Agreement, dated as of January 21, 2002, by and between the Company and Aventis Pharma SA.
10.13(b)**+	Amended and Restated Collaborative Research and License Agreement, dated as of January 21, 2002, by and between the Company and Aventis Pharma SA.
10.13(c)**	Letter Agreement, dated March 18, 2003, amending the Amended and Restated Collaborative Research and License Agreement, dated as of January 21, 2002, by and between the Company and Aventis Pharma SA and the Collaborative Research and License Agreement, dated as of January 21, 2002, by and between the Company and Aventis Pharma SA.
10.14**	Asset Purchase Agreement, dated as of June 28, 2002, by and between the Company and Layton Bioscience, Inc.
10.15**+	Asset Purchase and Trademark Assignment Agreement, dated March 19, 1998, by and between the Company (as assignee of Layton Bioscience, Inc.) and Merck & Co., Inc.
10.16**+	Amended and Restated License Agreement, dated as of March 9, 2004, by and between the Company and the University of South Florida Research Foundation, Inc.
10.17(a)**+	License Agreement, dated October 6, 1997, by and between the Company (as assignee of R.J. Reynolds Tobacco Company) and Virginia Commonwealth University Intellectual Property Foundation.
10.17(b)**+	Amendment to License Agreement, dated February 11, 2004, to the License Agreement, dated October 6, 1997, by and between the Company (as assignee of R.J. Reynolds Tobacco Company) and Virginia Commonwealth University Intellectual Property Foundation.
10.18(a)**+	License Agreement, dated May 26, 1999, by and between the Company and the University of Kentucky Research Foundation.

Exhibit No.	Description
10.18(b)++	Amendment No. 1, dated August 16, 2005, to License Agreement, dated May 26, 1999, by and between the Company and the University of Kentucky Research Foundation.
10.19**+	License Agreement, dated as of August 12, 2002, between the Company and Wake Forest University Health Sciences.
10.20**+	Development and Production Agreement for Active Pharmaceutical Ingredients, dated as of February 1, 2004, by and between the Company and Siegfried Ltd.
10.21++	Collaborative Research and License Agreement, dated as of December 27, 2005, by and between the Company and AstraZeneca AB.
23.1	Consent of Ernst & Young LLP.
23.2**	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in Exhibit 5.1).
24.1**	Power of Attorney (included on signature page).

** Previously filed.
+ Confidential treatment has been granted with respect to certain portions of this Exhibit, which portions have been omitted and filed separately with the Securities and Exchange Commission as part of an application for confidential treatment pursuant to the Securities Act of 1933, as amended.
++ Portions of this Exhibit have been omitted and filed separately with the Securities and Exchange Commission as part of an application for confidential treatment pursuant to the Securities Act of 1933, as amended.
# Replaces Exhibit 10.5(a) filed with the Company's Registration Statement on Form S-1 dated January 17, 2006.

(b) Financial Statement Schedules.

All information for which provision is made in the applicable accounting regulations of the Securities and Exchange Commission is either included in the financial statements or is not required under the related instructions or is inapplicable, and therefore has been omitted.

Item 17. Undertakings.

The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the provisions described herein, or otherwise, the registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as a part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this Amendment No. 5 to the registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Winston-Salem, State of North Carolina, on April 6, 2006.

TARGACEPT, INC.

By: /S/ J. DONALD DEBETHIZY

J. Donald deBethizy
Chief Executive Officer and President

Pursuant to the requirements of the Securities Act of 1933, this Amendment No. 5 to the registration statement has been signed by the following persons in the capacities indicated on April 6, 2006.

/S/ J. DONALD DEBETHIZY	/S/ ALAN A. MUSSO
Name: **J. Donald deBethizy** **Title:** **Chief Executive Officer, President and Director (Principal Executive Officer)**	**Name:** **Alan A. Musso** **Title:** **Vice President and Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)**
*	*
Name: **Mark Skaletsky** **Title:** **Chairman of the Board of Directors**	**Name:** **M. James Barrett** **Title:** **Director**
*	*
Name: **Charles A. Blixt** **Title:** **Director**	**Name:** **Errol B. De Souza** **Title:** **Director**
*	*
Name: **Ann F. Hanham** **Title:** **Director**	**Name:** **Elaine V. Jones** **Title:** **Director**
*	
Name: **John P. Richard** **Title:** **Director**	

*By: /S/ J. DONALD DEBETHIZY

J. Donald deBethizy
Attorney-in-fact

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Exhibit No.	Description
10.20**+	Development and Production Agreement for Active Pharmaceutical Ingredients, dated as of February 1, 2004, by and between the Company and Siegfried Ltd.
10.21++	Collaborative Research and License Agreement, dated as of December 27, 2005, by and between the Company and AstraZeneca AB.
23.1	Consent of Ernst & Young LLP.
23.2**	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in Exhibit 5.1).
24.1**	Power of Attorney (included on signature page).

** Previously filed.
+ Confidential treatment has been granted with respect to certain portions of this Exhibit, which portions have been omitted and filed separately with the Securities and Exchange Commission as part of an application for confidential treatment pursuant to the Securities Act of 1933, as amended.
++ Portions of this Exhibit have been omitted and filed separately with the Securities and Exchange Commission as part of an application for confidential treatment pursuant to the Securities Act of 1933, as amended.
# Replaces Exhibit 10.5(a) filed with the Company's Registration Statement on Form S-1 dated January 17, 2006.

CERTIFICATE OF AMENDMENT
TO
THIRD AMENDED AND RESTATED CERTIFICATE OF INCORPORATION
OF
TARGACEPT, INC.

TARGACEPT, INC., a corporation duly organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "Corporation"), hereby certifies as follows:

1. That the Board of Directors of the Corporation has duly adopted the following resolution:

RESOLVED, that the Board hereby declares it advisable and in the best interest of the Corporation to amend its Third Amended and Restated Certificate of Incorporation, as amended, in accordance with Section 242(b) of the DGCL, as follows:

(a) by adding the following four paragraphs to Article FOURTH immediately preceding the existing opening clause of such Article:

"At the Effective Time, a 1-for-7.5 reverse stock split of the corporation's common stock shall become effective, pursuant to which all common stock issued and outstanding immediately prior to the Effective Time ("**Old Common Stock**") shall automatically, without any action on the part of the holders thereof, be reclassified such that each 7.5 shares of Old Common Stock held of record by each stockholder of the corporation immediately prior to the Effective Time shall be combined into one share of Common Stock (as defined below) from and after the Effective Time.

Following the Effective Time, each holder of Old Common Stock shall be entitled to receive upon surrender of such holder's certificate(s) representing Old Common Stock (whether one or more, "**Old Certificates**") for cancellation pursuant to procedures adopted by the corporation, a certificate(s) (whether one or more, "**New Certificates**") representing the number of whole shares of Common Stock as provided above ("**New Common Stock**") into which and for which the shares of Old Common Stock formerly represented by such Old Certificates so surrendered are combined under the terms hereof. From and after the Effective Time, Old Certificates shall represent only the right to receive New Certificates and, if applicable, cash in lieu of fractional shares as provided below.

No fractional shares of Common Stock shall be issued. No stockholder of the corporation shall transfer any fractional shares of Common Stock. The corporation shall not recognize on its stock record books any purported transfer of any fractional share of Common Stock. A holder of Old Certificates at the Effective Time who would otherwise be entitled to a fraction of a share of New Common Stock (after aggregating all fractions of a share to which such stockholder would otherwise be entitled) shall, in lieu thereof, be entitled to

receive a cash payment in an amount equal to the fraction to which the stockholder would otherwise be entitled multiplied by the fair value per share as determined by the Board.

For purposes hereof, the "**Effective Time**" shall mean 3:00 p.m. eastern time on the date of filing of a Certificate of Amendment setting forth the foregoing with the Secretary of State of the State of Delaware."

(b) by deleting the first paragraph of Article FOURTH, Section A in its entirety and replacing it with the following (leaving the second paragraph unchanged):

"A. The number of shares that the corporation is authorized to issue is One Hundred Nine Million, Nine Hundred Seventy-Six Thousand, One Hundred Ninety-Eight (109,976,198), of which: (1) Sixteen Million, Six Hundred Sixty-Six Thousand, Six Hundred Sixty-Six (16,666,666) shares shall be designated as Common Stock, $0.001 par value per share ("**Common Stock**"); and (2) Ninety-Three Million, Three Hundred Nine Thousand, Five Hundred Thirty-Two (93,309,532) shares shall be designated as Preferred Stock, $0.001 par value per share ("**Preferred Stock**"). Of the Preferred Stock, (i) Five Million (5,000,000) shares shall be designated Series A Convertible Preferred Stock ("**Series A Preferred**"), (ii) Six Million, Five Hundred Sixty-Seven Thousand, Five Hundred Sixty-Seven (6,567,567) shares shall be designated Series B Convertible Preferred Stock ("**Series B Preferred**") and (iii) Eighty-One Million, Seven Hundred Forty-One Thousand, Nine Hundred Sixty-Five (81,741,965) shares shall be designated Series C Convertible Preferred Stock ("**Series C Preferred**"). Each of Series A Preferred, Series B Preferred and Series C Preferred may be referred to herein individually as a "**Preferred Series**.""

(c) by replacing "except for Company Equity issued:" in Article FOURTH, Section B.3.(e)(iii) with "except in connection with a Qualified IPO and except for Company Equity issued:"

(d) by deleting Article FOURTH, Section B.4.(b) in its entirety and replacing it with the following:

"(b) Automatic Conversion. Each share of all the Preferred Series shall automatically be converted into shares of Common Stock in the manner provided for in Sections 4(a)(i), 4(a)(ii) and 4(a)(iii), respectively, immediately upon the closing of the sale of Common Stock in a firm commitment, underwritten public offering registered under the Securities Act of 1933, as amended (the "**1933 Act**") (other than a registration relating solely to a transaction under Rule 145 under such Act or any successor rule thereto) in which (i) the public offering price per share of Common Stock equals or exceeds Eleven Dollars and 00/100 ($11.00) (subject to adjustment for stock splits, stock dividends, reverse stock splits and other similar corporate reorganizations occurring after the Effective Time) or such lesser amount as is approved in writing after the Effective Time by the holders of (A) a majority of the then outstanding shares of Series A Preferred and Series B Preferred, considered together as a single class on an as-converted basis, and (B) at least sixty-five percent (65%) of the then outstanding shares of Series C Preferred, and (ii) the gross proceeds to the corporation are not less than (A) Fifty Million Dollars ($50,000,000) or (B) such lesser amount as is approved in writing after the Effective Time by the holders of (1) a majority of the then outstanding shares of Series A Preferred and Series B Preferred, considered together as a single class on an as-converted basis, and (2) at least sixty-five percent (65%) of the then outstanding shares of Series C Preferred, in

either case before the deduction of expenses and before applying any underwriter's discounts or commission (a "**Qualified IPO**")."

2. That this Certificate of Amendment will become effective at 3:00 p.m. eastern time (the "Effective Time") on the date of filing of this Certificate of Amendment with the Secretary of State of the State of Delaware.

3. That this Certificate of Amendment was duly adopted in accordance with the applicable provisions of Sections 228 and 242(b) of the General Corporation Law of the State of Delaware.

4. That the capital of the Corporation will not be reduced under or by reason of said amendments.

IN WITNESS WHEREOF, TARGACEPT, INC., has caused this Certificate of Amendment to be executed by J. Donald deBethizy, its President and Chief Executive Officer, this 3rd day of February 2005.

TARGACEPT, INC.

By: /S/ J. DONALD DEBETHIZY
J. Donald deBethizy
President and CEO

CERTIFICATE OF AMENDMENT

TO

THIRD AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

OF

TARGACEPT, INC.

TARGACEPT, INC., a corporation duly organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "Corporation"), hereby certifies as follows:

1. That the Board of Directors of the Corporation has duly adopted the following resolution:

"RESOLVED that the Board hereby declares it advisable and in the best interest of the Corporation to amend its Third Amended and Restated Certificate of Incorporation, as amended, in accordance with Section 242(b) of the DGCL by deleting the first paragraph of Article FOURTH, Section A in its entirety and replacing it with the following (leaving the second paragraph unchanged) (the "**Amendment**"):

"A. The number of shares that the corporation is authorized to issue is One Hundred Sixteen Million, Three Hundred Nine Thousand, Five Hundred Thirty-Two (116,309,532), of which: (1) Twenty-Three Million (23,000,000) shares shall be designated as Common Stock, $0.001 par value per share ("**Common Stock**"); and (2) Ninety-Three Million, Three Hundred Nine Thousand, Five Hundred Thirty-Two (93,309,532) shares shall be designated as Preferred Stock, $0.001 par value per share ("**Preferred Stock**"). Of the Preferred Stock, (i) Five Million (5,000,000) shares shall be designated Series A Convertible Preferred Stock ("**Series A Preferred**"), (ii) Six Million, Five Hundred Sixty-Seven Thousand, Five Hundred Sixty-Seven (6,567,567) shares shall be designated Series B Convertible Preferred Stock ("**Series B Preferred**") and (iii) Eighty-One Million, Seven Hundred Forty-One Thousand, Nine Hundred Sixty-Five (81,741,965) shares shall be designated Series C Convertible Preferred Stock ("**Series C Preferred**"). Each of Series A Preferred, Series B Preferred and Series C Preferred may be referred to herein individually as a "**Preferred Series**."

2. That this Certificate of Amendment will become effective at 3:00 p.m. eastern time (the "Effective Time") on the date of filing of this Certificate of Amendment with the Secretary of State of the State of Delaware.

3. That this Certificate of Amendment was duly adopted in accordance with the applicable provisions of Sections 228 and 242 of the General Corporation Law of the State of Delaware.

4. That the capital of the Corporation will not be reduced under or by reason of said amendments.

IN WITNESS WHEREOF, TARGACEPT, INC., has caused this Certificate of Amendment to be executed by J. Donald deBethizy, its President and Chief Executive Officer, this 3rd day of April 2006.

TARGACEPT, INC.

By: /s/ J. Donald deBethizy

J. Donald deBethizy
President and CEO

Exhibit 10.18(b)

[********] Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

August 16, 2005

University of Kentucky Research Foundation
[207 Administration Building]
A144 ASTeCC Building
University of Kentucky
Lexington, Kentucky 40506-0286
Attention: Donald Keach

Re: Amendment No. 1 to License Agreement

Dear Mr. Keach:

Reference is made to the License Agreement between Targacept, Inc. ("**Targacept**") and University of Kentucky Research Foundation ("**UKRF**") dated May 26, 1999 (the "**Agreement**").

Targacept and UKRF believe it is in their mutual best interest to amend the Agreement to clarify the intent of certain provisions. Section 13.2 of the Agreement provides that the Agreement is not subject to any change or modification except by execution of a written instrument by the parties. Accordingly, for good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, Targacept and UKRF agree as follows:

1. the Agreement is hereby amended by:

   a. deleting Section 1.2 in its entirety and replacing it with the following:

      "1.2 "Patent Rights" shall mean, collectively, (i) the patents listed on Attachment A, (ii) all patents that issue or have issued from patent applications that resulted in the patents listed on Attachment A and all reexaminations, reissues, revisions, substitutes, renewals or extensions thereof, and (iii) all other United States and foreign patents that issue or have issued from applications that claim priority to patent applications that resulted in the patents listed on Attachment A, including, without limitation, continuation applications, continuation-in-part applications, divisional applications, substitute applications, reissue applications or requests for examination and foreign applications of any of the foregoing.";

   b. adding the following as Section 1.4:

      "1.4 "Assigned Rights" shall mean, collectively, (i) the patent applications listed on Attachment B, (ii) all patents that issue or have issued from patent applications listed on Attachment B and all reexaminations, reissues, revisions, substitutes, renewals or extensions thereof, and (iii) all other United States and foreign patents that issue or have issued from applications that claim priority to patent applications listed on Attachment B, including, without limitation, continuation applications, continuation-in-part applications, divisional applications, substitute applications, reissue applications or requests for examination and foreign applications of any of the foregoing.";

c. adding the following as Section 1.5

"1.5 "Excluded Amount" shall mean any amount received by TARGACEPT from a sublicensee in the case of the Patent Rights or a licensee in the case of the Assigned Rights: (i) to fund research and development; (ii) as payment for the manufacture or supply of any compound or chemical entity; (iii) that TARGACEPT is required to repay (e.g., a loan); (iv) as payment for securities of TARGACEPT; or (v) based on or determined by reference to sales of any compound or product in any country in which there is no Valid Claim included in the Patent Rights or Assigned Rights, as the case may be, that covers such compound or product.

d. adding the following as Section 1.6:

"1.6 "Valid Claim" shall mean: (i) any claim of an issued patent that has not expired and that has not been held invalid or unenforceable by decision of a court or other governmental agency of competent jurisdiction or been admitted to be invalid through reissue, disclaimer or otherwise; or (ii) any claim of a pending patent application that has not expired or become canceled, abandoned or otherwise disallowed.

e. deleting from Section 2.1 the words "set forth in Attachment A";

f. amending Section 4.1 by deleting "to the end of the term of the Patent Rights" from the first sentence thereof;

g. deleting Sections 4.1(b) and 4.1(c) in their entirety and replacing them with the following:

"(b) [********] of any amount received by TARGACEPT from a third party for a sublicense to the Patent Rights, specifically excluding any and all Excluded Amounts and subject to Sections 4.1(d) and (e). In the event TARGACEPT ever sells Licensed Product directly, the parties agree to negotiate an equitable royalty rate, taking into consideration the existing sublicense rates.

(c) [********] ([********] until the amount paid by TARGACEPT under this Section 4.1(c) is at least $[********]) of any amount received by TARGACEPT from a third party for a license to the Assigned Rights, specifically excluding any and all Excluded Amounts and subject to Sections 4.1(d) and (e).

(d) For the avoidance of doubt, in the event that (i) TARGACEPT sublicenses Patent Rights or licenses Assigned Rights to a third party (A) together with any other rights of TARGACEPT or (B) in connection with any agreement by TARGACEPT to collaborate with such third party to discover, research, develop or commercialize, or to license to such third party, any compound or product that is not claimed or covered by the sublicensed Patent Rights or the licensed Assigned Rights, as the case may be, whether in the same agreement or in separate agreements, and (ii) TARGACEPT receives (or would receive pursuant to a collaboration agreement) any amount from such third party that is not specifically attributable to a particular compound or product (such amount, a "Broad Collaboration Payment"), an equitable percentage of such Broad Collaboration Payment actually received by TARGACEPT, based on the relative value to such third party of the

sublicensed Patent Rights or licensed Assigned Rights, as the case may be, and all other rights licensed by or agreements of TARGACEPT, and no more, shall be considered received by TARGACEPT for the sublicensed Patent Rights or the licensed Assigned Rights, as the case may be, and therefore taken into account for purposes of Section 4.1(b) and Section 4.1(c). TARGACEPT and UKRF agree to negotiate such equitable percentage in good faith prior to, or as soon as practicable after, receipt of such Broad Collaboration Payment by TARGACEPT.

(e) TARGACEPT's obligations pursuant to Section 4.1(b) shall expire upon expiration of the last to expire Valid Claim included in the Patent Rights, and TARGACEPT's obligations pursuant to Section 4.1(c) shall expire upon expiration of the last to expire Valid Claim included in the Assigned Rights.";

h. amending Section 4.2 by deleting its text in its entirety and replacing it with "Reserved.";

i. amending Section 5.2 by deleting the second sentence thereof in its entirety; and

j. adding the following as Section 13.5:

"13.5 Notwithstanding anything herein to the contrary, each of UKRF and TARGACEPT acknowledges and agrees that: (i) for good and valuable consideration received, UKRF has previously assigned to TARGACEPT all of its right, title and interest in and to the Assigned Rights (the "Assignment"); (ii) the Assignment is valid and binding and not dependent on the license grant to the Patent Rights hereunder or on this Agreement; (iii) all references herein to a "sublicense" by, or a "sublicensee" or "sublicensee agreement" of, TARGACEPT shall be applicable only to a sublicense of Patent Rights by TARGACEPT and, for the avoidance of doubt, not to a license of Assigned Rights by TARGACEPT that does not also include a sublicense of Patent Rights; and (iv) this Agreement represents the parties' intent to comply with Section 14 of the agreement dated August 15, 1996 between R.J. Reynolds Tobacco Company (TARGACEPT's former parent company) and the University of Kentucky, an affiliate of UKRF ("UK"), with regard to consideration due to UK in respect of the Assigned Rights."

2. As expressly amended hereby, all of the terms and conditions of the Agreement shall continue in full force and effect.

3. This letter agreement may be executed in two counterparts, each of which shall be deemed an original and both of which, taken together, shall be deemed a single document.

Please indicate your acceptance of, and agreement with, the foregoing by executing the duplicate copies of this letter agreement and returning one fully-executed original to my attention.

Sincerely,

TARGACEPT, INC.

By: /s/ J. Donald deBethizy

J. Donald deBethizy
President and Chief Executive Officer

Accepted and agreed:

University of Kentucky Research Foundation

By: /s/ John B. Parks

Name: John Parks
Title: Assoc. V.P. for Research & Economic Development

Exhibit 10.21

Execution Copy

[********] Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

COLLABORATIVE RESEARCH AND LICENSE AGREEMENT

by and between

TARGACEPT, INC.

and

ASTRAZENECA AB

December 27, 2005

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List of Exhibits and Schedules

[********] Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 406 of the Securities Act of 1933, as amended.

COLLABORATIVE RESEARCH AND LICENSE AGREEMENT

This COLLABORATIVE RESEARCH AND LICENSE AGREEMENT (this "**Agreement**") is entered into as of December 27, 2005 (the "**Execution Date**"), by and between Targacept, Inc., a Delaware corporation having an address of 200 East First Street, Suite 300, Winston-Salem, NC 27101-4165 ("**Targacept**"), and AstraZeneca AB, a company limited by shares organized and existing under the laws of Sweden, having its principal place of business at V-Malarehamnen 9, S-151 85 Södertälje, Sweden ("**AstraZeneca**"), effective as of the Effective Date, except for those provisions that are expressly stated to be effective as of the Execution Date, which shall be effective as of the Execution Date. Each of AstraZeneca and Targacept is sometimes referred to individually herein as a "**Party**" and collectively as the "**Parties**."

WHEREAS, Targacept Controls certain Technology and Proprietary Materials related to the discovery and optimization of compounds that target NNRs; and

WHEREAS, AstraZeneca is engaged in the development and commercialization of human therapeutics; and

WHEREAS, the Parties desire to enter into a collaboration for purposes of identifying and developing Candidate Drugs and commercializing Products in the Field and in Schizophrenia.

NOW, THEREFORE, in consideration of the mutual covenants contained herein, and for other good and valuable consideration, the Parties hereto, intending to be legally bound, hereby agree as follows:

1. DEFINITIONS

Whenever used in this Agreement with an initial capital letter, the terms defined in this Section 1 shall have the meanings specified.

1.1 **"AAA"** means the American Arbitration Association.

1.2 **"AAMI"** means (a) age associated memory impairment, a condition in which persons at least 50 years old experience memory impairment (as compared with younger adults) that is not accompanied by substantial impairment in the normal activities of daily living or in thinking or reasoning skills and is not otherwise part of a pathological illness or other separately-defined medical condition (such as, by way of example only, Dementia, delirium, stroke, inflammatory brain disease, depression or a history of alcohol or psychotropic drug use), unless and until, (b) age associated memory impairment (or age related cognitive decline, age associated cognitive decline or any other substantially equivalent term that connotes memory impairment associated with age or aging) becomes included in DSM-IV, ICD-10 or any other Diagnostic Manual in any country in the Territory or becomes recognized as a distinct diagnosable condition by general consensus in the applicable medical community in any country in the Territory, or a product receives Product Regulatory Approval from the applicable Regulatory Authority in any country in the Territory for AAMI, in each case after the Execution Date, in which case, a condition with the diagnostic characteristics included in DSM-IV, ICD-10 or such other Diagnostic Manual or as recognized by such medical community in such country or such Regulatory Authority, as applicable, from time to time.

1.3 **"Acceptance"** means, with respect to an NDA, the date on which the FDA issues a notice of acceptance of such NDA for filing.

1.4 **"Achievement of Proof of Concept"** means, with respect to any Candidate Drug, the first to occur after the Effective Date of (a) achievement of the **[********]** (as set forth in the applicable Product Development Plan or clinical trial protocol) in a **[********]** Clinical Trial of such Candidate Drug in any Primary Indication or Schizophrenia (as the case may be) (but excluding, in the case of Ispronicline, the Ongoing Ispronicline Trial) at a dose range that is shown to be safe and tolerable in the patient group of interest and that is acceptable from each of a scientific, statistical, medical, regulatory and commercial perspective or (b) the **[********]** Clinical Trial of such Candidate Drug. For purposes of clarity, whether achievement of a

[********] in a **[********]** Clinical Trial at a dose range that is shown to be safe and tolerable in the patient group of interest and that is acceptable from each of a scientific, statistical, medical, regulatory and commercial perspective has occurred shall be determined as soon as practicable after reliable information from such trial is available following database lock and shall not require the availability of the final report for such trial. "Achieve Proof of Concept" shall be interpreted accordingly.

1.5 **"Active+ Compound"** means each Collaboration Candidate that is not a Terminated Compound that is determined by the JRC or AstraZeneca during the Research Program Term or the Tail Period to satisfy the Active+ Criteria (unless and until (a) Targacept challenges such determination pursuant to Section 4.3.2 and (b) such Collaboration Candidate is finally determined by the ESC (in accordance with Section 2.1.5(c)(iii)) or, if applicable, an Expert (in accordance with Section 14.3) to not satisfy the Active+ Criteria), including any salt form, polymorph, crystalline form, hydrate, solvate or formulation thereof. For purposes of clarity, all Active+ Compounds are also Collaboration Candidates. Notwithstanding the foregoing, unless the Parties otherwise agree in writing, the Compounds known to Targacept as of the Execution Date as **[********]** and, **[********]**, including any salt form, polymorph, crystalline form, Prodrug, metabolite (other than any such metabolite that is an Excluded Zone Compound), hydrate, solvate or formulation thereof, shall not be Active+ Compounds.

1.6 **"Active+ Criteria"** means the assays and other tests, and the success criteria for those assays and tests, set forth in the Research Plan, as such assays, tests or success criteria may be amended from time to time in any Annual Research Plan in accordance with the terms hereof.

1.7 **"AD"** means Alzheimer's disease (or Dementia of the Alzheimer's type), a condition having the diagnostic criteria identified in DSM-IV, ICD-10 or any other Diagnostic Manual from time to time.

1.8 **"ADD"** means adult attention deficit disorder, a condition having the diagnostic criteria identified in DSM-IV, ICD-10 or any other Diagnostic Manual from time to time.

1.9 **"Additional Compound"** means, subject to Section 4.11, with respect to any Collaboration Compound, Candidate Drug or Product, any compound or product that has the

same Framework as such Collaboration Compound, Candidate Drug or Product and, if such Collaboration Compound, Candidate Drug or Product is:

(a) an Alpha4Beta2 Agonist, (i) has an **[********]** at least equal to **[********]**, (ii) has **[********]** and (iii) has activity in **[********]** at a dose of less than or equal to **[********]** or activity in a Replacement Assay at the applicable dose if and as agreed pursuant to Section 4.11.3 or, if applicable, determined by an Expert pursuant to Section 14.3 (accelerated arbitration);

(b) a Selective Alpha7 Compound, (i) has **[********]** at least equal to **[********]**, (ii) has **[********]** and (iii) has activity in **[********]**or activity in a Replacement Assay at the applicable dose if and as agreed pursuant to Section 4.11.3 or, if applicable, determined by an Expert pursuant to Section 14.3 (accelerated arbitration);

(c) a Dual Pharmacology Compound, (i) has an **[********]** at least equal to **[********]**, (ii) has **[********]** and (iii) has activity in either (A) **[********]**, or (B) **[********]** or, in either case ((A) or (B)), activity in a Replacement Assay at the applicable dose if and as agreed pursuant to Section 4.11.3 or, if applicable, determined by an Expert pursuant to Section 14.3 (accelerated arbitration); or

(d) an Other NNR Compound, (i) has an **[********]** at least equal to **[********]**, (ii) has **[********]** based on a functional assay designated and approved by the Parties, subject to referral of any disputes to an Expert pursuant to Section 14.3, in accordance with Section 4.11.2 for the applicable NNR (or, if there is no such functional assay designated and approved by the Parties (or by an Expert pursuant to Section 14.3) for the applicable NNR, such Other NNR Compound has a **[********]**, **[********]**; provided that this clause (ii) shall not apply to (A) a Collaboration Candidate that does not meet Minimum Binding Affinity or a Licensed Derivative of any Collaboration Compound, Candidate Drug (other than an Option Compound Candidate Drug) or Product (other than an Option Compound Product) that is not itself an Alpha4Beta2 Agonist or (B) an Option Compound Candidate Drug that is not a **[********]** but that is a Licensed Derivative of an Option Compound Candidate Drug that is a **[********]**; and (iii) has activity in an **[********]** assay (such assay, and the criteria for activity in such assay, to be designated and approved by the Parties, subject to referral of any disputes to

an Expert pursuant to Section 14.3 (accelerated arbitration), in accordance with Section 4.11.2) for the applicable NNR at a dose of less than or equal to **[********]** or has activity in a Replacement Assay at the applicable dose if and as agreed pursuant to Section 4.11.3 or, if applicable, determined by an Expert pursuant to Section 14.3 (accelerated arbitration). For purposes of this Section 1.9(d), the applicable NNR for: (A) a Collaboration Candidate that does not meet Minimum Binding Affinity or a Licensed Derivative of any Collaboration Compound, Candidate Drug (other than an Option Compound Candidate Drug) or Product (other than an Option Compound Product) that is not itself an Alpha4Beta2 Agonist shall be the Alpha4Beta2 NNR and the **[********]** assay shall be as provided in clause (iii) of Section 1.9(a); (B) an Option Compound Candidate Drug that is a Licensed Derivative of an Option Compound Candidate Drug that is a **[********]** shall be the **[********]** and the **[********]** assay shall be as provided in clause (iii) of Section 1.9(b); (C) an Option Compound Candidate Drug that is a Licensed Derivative of an Option Compound Candidate Drug that is a **[********]** shall be the **[********]** and the **[********]** assay shall be as provided in clause (iii) of Section 1.9(c); and (D) an Option Compound Candidate Drug that is an Other NNR Compound or a Licensed Derivative of an Other NNR Compound shall be the applicable NNR.

Any salt form, polymorph, crystalline form, Prodrug, metabolite, hydrate, solvate or formulation of an Additional Compound shall also be an Additional Compound. Additional Compounds shall also include:

(x) any compound or product **[********]** is Ispronicline, a Lead Collaboration Compound, a Related Collaboration Compound, an IND-Ready Option Candidate Drug or a POC Option Candidate Drug;

(y) any Terminated Compound (other than a Terminated AZ Compound) or an Unexercised Option Compound **[********]** (i) is an Additional Compound with respect to a Collaboration Compound or Candidate Drug, or (ii) is the same **[********]** (A) a Collaboration Compound, (B) Candidate Drug (other than a Licensed Derivative) or (C) to the extent AstraZeneca notifies Targacept thereof, a Licensed Derivative or an Additional Compound with respect to a Collaboration Compound or a Candidate Drug, in each case ((A), (B) and (C)), that satisfies Section 1.9(a)(iii), 1.9(b)(iii), 1.9(c)(iii) or 1.9(d)(iii), whichever is applicable to such compound; and

(z) any compound or product **[********]** is (i) a Collaboration Compound or a Candidate Drug (other than Ispronicline, a Lead Collaboration Compound, a Related Collaboration Compound, an IND-Ready Option Candidate Drug or a POC Option Candidate Drug) or an Additional Compound with respect to a Collaboration Compound or Candidate Drug or (ii) the same **[********]** (A) a Collaboration Compound, (B) Candidate Drug or (C) an Additional Compound with respect to a Collaboration Compound or a Candidate Drug, in each case ((A), (B) and (C)), that satisfies Section 1.9(a)(iii), 1.9(b)(iii), 1.9(c)(iii) or 1.9(d)(iii), whichever is applicable to such compound or product, in each case ((i) and (ii)), solely for purposes of this clause (z), to the extent AstraZeneca notifies Targacept of such Collaboration Compound, Candidate Drug, Additional Compound **[********]**, in writing, prior to the date, if any, that Targacept or its Affiliates or licensees has commenced **[********]** for such compound or product, the commencement of which (or the fact that it has not done so) Targacept shall confirm with respect to each such Collaboration Compound, Candidate Drug, Additional Compound **[********]** (with such support as AstraZeneca may reasonably request) within **[********]** after receipt of AstraZeneca's notice with respect thereto (and any failure by Targacept to provide any such notice within such **[********]** period shall mean, for purposes of this Section 1.9, that AstraZeneca retains rights hereunder with respect to any such compound or product).

With respect to each of the foregoing assays, Additional Compounds shall be determined within the margins of error for each such assay.

Notwithstanding the foregoing, unless the Parties otherwise agree in writing, the Compounds known to Targacept as of the Execution Date as **[********]**, **[********]** and, **[********]**, including any salt form, polymorph, crystalline form, Prodrug, metabolite (other than any such metabolite that is an Excluded Zone Compound), hydrate, solvate or formulation thereof, shall not be Additional Compounds. For purposes of clarity, the Compound known to Targacept as of the Execution Date as TC-1827 is an Additional Compound with respect to Ispronicline.

1.10 **"Additional Primary Indication"** means any indication that is not a Primary Indication as of the Execution Date that the Parties agree in writing shall be a Primary Indication, other than a Newly-Defined Cognitive Disorder or an Associated Cognitive Impairment.

1.11 **"Additional Product"** means any product that contains an Additional Compound as an active ingredient.

1.12 **"Additional Research Plan"** has the meaning set forth in Section 4.8.2.

1.13 **"Additional Research Program"** has the meaning set forth in Section 4.8.1.

1.14 **"Additional Research Program Term"** means the period during which an Additional Research Program is conducted pursuant to an Additional Research Plan; provided that, if earlier, the last day of the Term shall be the last day of each Additional Research Program Term.

1.15 **"Additional Small Market Indication"** means any indication that is not a Small Market Indication as of the Execution Date that the Parties agree in writing shall be a Small Market Indication.

1.16 **"ADHD"** means attention deficit hyperactivity disorder, a condition having the diagnostic criteria identified in DSM-IV, ICD-10 or any other Diagnostic Manual from time to time. For purposes of this Agreement, ADHD shall include ADD.

1.17 **"Adverse Event"** means the development of an undesirable medical condition or the deterioration of a pre-existing medical condition in a patient or clinical investigation subject following or during exposure to a pharmaceutical product or investigational drug, whether or not considered causally related to such product or drug, the exacerbation of any pre-existing condition(s) occurring during the use of such product or drug, or any other adverse experience or adverse drug experience described in the FDA's Investigational New Drug safety reporting and NDA post-marketing reporting regulations, 21 C.F.R. 312.32 and 314.80, respectively, and any applicable corresponding regulations outside of the United States, in each case as may be amended from time to time. For purposes of this Agreement, "undesirable medical condition" shall include symptoms (e.g., nausea, chest pain), signs (e.g., tachycardia, enlarged liver) or the

abnormal results of an investigation (e.g., laboratory findings, electrocardiogram), including unfavorable side effects, toxicity, injury, overdose or sensitivity reactions. Failure of a product to exhibit its expected pharmacologic/biologic effect in a clinical study is not considered an Adverse Event.

1.18 **"Affiliate"** means, with respect to any Person, any other Person that, directly or through one or more Affiliates, controls, or is controlled by, or is under common control with, such first Person. For purposes of this definition, "control" means (a) ownership of more than fifty percent (50%) of the shares of stock entitled to vote for the election of directors in the case of a corporation, or more than fifty percent (50%) of the equity interests in the case of any other type of legal entity, (b) status as a general partner in any partnership, or (c) any other arrangement whereby a Person controls or has the right to control the board of directors of a corporation or equivalent governing body of an entity other than a corporation.

1.19 **"Agreement"** has the meaning set forth in the preamble.

1.20 **"Alpha4Beta2 Agonist"** means any compound with Minimum Binding Affinity.

1.21 **"Alpha4Beta2 NNR"** means any NNR that is comprised, in whole or in part, of one or more Alpha4 subunits and one or more Beta2 subunits.

1.22 **"Alpha7 NNR"** means any NNR comprised, in whole or in part, of Alpha7 subunits.

1.23 **"Annual Research Plan"** means, with respect to any Contract Year in the Research Program Term, the written plan for the Research Program for such Contract Year, as may be amended from time to time in accordance with the terms hereof.

1.24 **"Applicable Laws"** means federal, state, local, national and supra-national laws, statutes, rules and regulations, including any rules, regulations, guidance, guidelines or requirements of Regulatory Authorities, national securities exchanges or securities listing organizations, that may be in effect from time to time during the Term and applicable to a particular activity hereunder.

1.25 **"Arbitration Matter"** has the meaning set forth in Section 14.1.

1.26 **"ARP Budget"** has the meaning set forth in Section 4.8.2.

1.27 **"ARP Selection Date"** has the meaning set forth in Section 4.8.1.

1.28 **"Associated Cognitive Impairment"** means any Cognitive Impairment that: (a) is not otherwise a Primary Indication and is not a Small Market Indication; (b) is specifically caused by or associated with a separately defined and widely recognized disease or condition; (c) is, as of the Execution Date, neither included in DSM-IV or ICD-10 nor recognized as a distinct diagnosable condition by general consensus in the medical community in the United States or Europe, and for which no product has received Product Regulatory Approval from the FDA in the United States or the EMEA in Europe prior to the Execution Date; (d) either becomes included in DSM-IV, ICD-10 or any other Diagnostic Manual in any Major Market Country during the Term, becomes recognized as a distinct diagnosable condition by general consensus in the applicable medical community in any Major Market Country during the Term or for which a product receives Product Regulatory Approval from the applicable Regulatory Authority in any Major Market Country during the Term; and (e) **[********]** as an Associated Cognitive Impairment. For purposes of clarity, the separately defined and widely recognized disease or condition shall not itself be an Associated Cognitive Impairment. For purposes of further clarity, an Associated Cognitive Impairment **[********]** shall apply throughout the Territory, even if such Associated Cognitive Impairment is not included in DSM-IV, ICD-10 or any other Diagnostic Manual in all Major Market Countries, is not recognized as a distinct diagnosable condition by general consensus in the applicable medical community in all Major Market Countries or a product has not received Product Regulatory Approval for Associated Cognitive Impairment from the applicable Regulatory Authority in all Major Market Countries.

1.29 **"AstraZeneca"** has the meaning set forth in the preamble.

1.30 **"AstraZeneca Assigned Patent Rights"** means any Patent Rights Controlled by AstraZeneca containing only claim(s) that cover the AstraZeneca Assigned Technology. For purposes of clarity, AstraZeneca Assigned Patent Rights are Targacept Patent Rights.

1.31 **"AstraZeneca Assigned Technology"** means any: (x) Technology Controlled by AstraZeneca as of the applicable dates set forth in clauses (a) and (b) below that solely relates to

(a) compounds that (i) are Derived by or on behalf of AstraZeneca from a Collaboration Candidate, Active+ Compound, Collaboration Compound or Candidate Drug (other than Ispronicline or a Licensed Derivative with respect thereto, or an Option Compound Candidate Drug) and (ii) then become Terminated Compounds during the Research Program or Tail Period or as of the end of the Tail Period (or, if later, the resolution of any dispute pursuant to Section 4.3.2 or as provided in Section 4.9), when and as such compounds become Terminated Compounds, or (b) Excluded Derivatives that are Derived by or on behalf of AstraZeneca during the applicable Restricted Derivative Period, on the date each such Excluded Derivative is determined to be an Excluded Derivative, provided in each case ((a) and (b)) that such compounds are Derived during the Term; and (y) Technology made, developed or conceived by or on behalf of AstraZeneca in the conduct of any Pre-IND Study conducted pursuant to Section 5.10.2(a) other than by or on behalf of Targacept. For purposes of further clarity, AstraZeneca Assigned Technology is Targacept Technology.

1.32 **"AstraZeneca Change of Control Notice"** has the meaning set forth in Section 15.2.1.

1.33 **"AstraZeneca Derivative Patent Rights"** means any Patent Rights Controlled by AstraZeneca containing one or more claims that claim as a composition of matter a Licensed Derivative Derived by AstraZeneca during the applicable Restricted Derivative Period. For purposes of clarity, AstraZeneca Derivative Patent Rights are AstraZeneca Patent Rights. For purposes of further clarity, AstraZeneca Derivative Patent Rights shall include any Patent Rights Controlled by AstraZeneca containing one or more claims that claim as a composition of matter a Licensed Derivative of Ispronicline Derived by AstraZeneca during the Restricted Derivative Period for Ispronicline.

1.34 **"AstraZeneca Development Program Patent Rights"** means any AstraZeneca Patent Rights containing one or more claims that cover AstraZeneca Development Program Technology. For purposes of clarity, AstraZeneca Development Program Patent Rights are AstraZeneca Patent Rights.

1.35 **"AstraZeneca Development Program Technology"** means any Technology made, developed or conceived by employees or consultants of AstraZeneca, alone or jointly with

Third Parties, in the conduct of a Development Program or any additional research or Development activities conducted by AstraZeneca pursuant to Section 4.1 or Section 5.2.1 (excluding AstraZeneca Research Program Technology) with respect to Collaboration Compounds, Candidate Drugs and Products, but in each case only if not AstraZeneca Assigned Technology.

1.36 **"AstraZeneca Excluded Patent Rights"** means, collectively, all AstraZeneca Patent Rights that would not be infringed (and, with respect to any applications included in the Patent Rights, that, if issued, would not be infringed) by the Exploitation of a Collaboration Compound, Candidate Drug, Product, Terminated Compound or Product to the extent it contains a Terminated Compound in the Field or Schizophrenia (but, with respect to each such Terminated Compound or Product that contains a Terminated Compound, only as it exists on the date on which such Terminated Compound became a Terminated Compound), by a Third Party in the absence of a license.

1.37 **"AstraZeneca Indemnitees"** has the meaning set forth in Section 13.1.

1.38 **"AstraZeneca Other Patent Rights"** means any Patent Rights Controlled by AstraZeneca containing one or more claims that cover AstraZeneca Other Technology.

1.39 **"AstraZeneca Other Technology"** means any Technology Controlled by AstraZeneca that is necessary to Exploit Terminated AZ Compounds (or any Product that contains a Terminated AZ Compound) in the Field or Schizophrenia, as applicable (but, with respect to each such Terminated AZ Compound (or Product that contains such Terminated AZ Compound), only with respect to such Technology as (a) is incorporated into, used to manufacture, or used to manufacture the formulation (if any) of such Terminated AZ Compound (or Product that contains such Terminated AZ Compound), in each case as of the date on which such Terminated AZ Compound became a Terminated Compound, or (b) was generated in the Development or Commercialization of, and that relates to, such Terminated AZ Compound (or Product that contains such Terminated AZ Compound), if such Technology was generated on or prior to the date on which such Terminated AZ Compound became a Terminated Compound); provided that AstraZeneca Other Technology excludes AstraZeneca Pre-Phase IIb Program

Technology, AstraZeneca Research Program Technology and AstraZeneca Development Program Technology.

1.40 **"AstraZeneca Patent Rights"** means any: (a) Patent Rights Controlled by AstraZeneca containing one or more claims that cover (i) AstraZeneca Technology, (ii) any Terminated AZ Compound (or any Product that contains a Terminated AZ Compound), or (iii) the Exploitation of any Terminated AZ Compound (or any Product that contains a Terminated AZ Compound) in the Field or Schizophrenia, as applicable (but, with respect to each such Terminated AZ Compound (or Product that contains such Terminated AZ Compound), only with respect to such Technology as (x) is incorporated into, used to manufacture, or used to manufacture the formulation (if any) of such Terminated AZ Compound (or Product that contains such Terminated AZ Compound), in each case as of the date on which such Terminated AZ Compound became a Terminated Compound, or (y) was generated in the Development or Commercialization of, and that relates to, such Terminated AZ Compound (or Product that contains such Terminated AZ Compound), and only if such Technology was generated on or prior to the date on which such Terminated AZ Compound became a Terminated Compound); or (b) AstraZeneca Derivative Patent Rights, to the extent not included in clause (a) above. For purposes of clarity, AstraZeneca Assigned Patent Rights are not AstraZeneca Patent Rights.

1.41 **"AstraZeneca Pre-Phase IIb Program Patent Rights"** means any AstraZeneca Patent Rights containing one or more claims that cover AstraZeneca Pre-Phase IIb Program Technology. For purposes of clarity, AstraZeneca Pre-Phase IIb Program Patent Rights are AstraZeneca Patent Rights.

1.42 **"AstraZeneca Pre-Phase IIb Program Technology"** means any Technology made, developed or conceived by employees or consultants of AstraZeneca, alone or jointly with Third Parties, in the conduct of the Pre-Phase IIb Program.

1.43 **"AstraZeneca Proprietary Materials"** means any Proprietary Materials Controlled by AstraZeneca and used by AstraZeneca, or provided by AstraZeneca for use, in the Pre-Phase IIb Program, the Research Program, any Additional Research Program or any Development Program.

1.44 **"AstraZeneca Research Activities"** means, collectively: (a) all activities specified to be conducted by AstraZeneca pursuant to the Research Plan, any Annual Research Plan or Additional Research Plan (or amendment thereto); (b) all activities in the Research Program that, as contemplated by Section 4.1.1, are conducted by AstraZeneca or its Affiliates in lieu of Targacept appointing a Third Party to conduct such activities; and (c) such other activities as AstraZeneca, in its sole discretion (but subject to the notice, coordination and oversight set forth in Sections 4.1.1, 4.3, 4.6 and 4.11) and at its sole expense, elects to conduct with respect to Collaboration Candidates and Active+ Compounds (other than Terminated Compounds and Candidate Drugs) during the Research Program Term or the Tail Period to further the goals of the Collaboration; provided, however, in no event shall AstraZeneca Research Activities include Development activities. For purposes of clarity, (i) AstraZeneca Research Activities may, subject to the notice, coordination and oversight set forth in Sections 4.1.1, 4.3, 4.6 and 4.11 and subject to Section 1.309, include generating Derivatives from Collaboration Candidates (including Active+ Compounds, Collaboration Compounds and Candidate Drugs (other than Option Compound Candidate Drugs and Ispronicline)) during the Research Program Term and Tail Period, and otherwise Exploiting such Derivatives, in an effort to identify additional Collaboration Candidates to further the goals of the Collaboration and (ii) any activities that AstraZeneca conducts with respect to Ispronicline (or any Licensed Derivatives with respect thereto) or an Option Compound Candidate Drug (or any Additional Compounds with respect to Ispronicline (or any Licensed Derivatives with respect thereto) or any Option Compound Candidate Drug) shall not be AstraZeneca Research Activities.

1.45 **"AstraZeneca Research Program Patent Rights"** means any AstraZeneca Patent Rights containing one or more claims that cover AstraZeneca Research Program Technology. For purposes of clarity, AstraZeneca Research Program Patent Rights are AstraZeneca Patent Rights.

1.46 **"AstraZeneca Research Program Technology"** means any Technology made, developed or conceived by employees or consultants of AstraZeneca, alone or jointly with Third Parties, in the conduct of the AstraZeneca Research Activities, but in each case only if not AstraZeneca Assigned Technology. For purposes of clarity, Technology with respect to

Ispronicline made, developed or conceived by employees or consultants of AstraZeneca, alone or jointly with Third Parties, shall not be AstraZeneca Research Program Technology.

1.47 **"AstraZeneca Technology"** means, collectively, AstraZeneca Pre-Phase IIb Program Technology, AstraZeneca Research Program Technology, AstraZeneca Development Program Technology and AstraZeneca Other Technology. For purposes of clarity, AstraZeneca Assigned Technology is not AstraZeneca Technology.

1.48 **"AZ Compounds"** has the meaning set forth in Section 8.9.1.

1.49 **"AZ Co-Promotion Opportunity"** has the meaning set forth in Section 5.11.1.

1.50 **"AZ Net Sales"** means Net Sales by AstraZeneca, its Affiliates or Sublicensees.

1.51 **"AZ Proposal"** has the meaning set forth in Section 5.10.2(e)(2).

1.52 **"Back-Up Option Compound"** means, with respect to any Option Compound for a particular Primary Indication or for Schizophrenia, another Option Compound for such indication that possesses (a) the same Framework when compared with such first Option Compound and (b) a more favorable Option Compound Profile when compared to such first Option Compound, but excluding any Excluded Zone Compounds.

1.53 **"Business Day"** means a day that is not a Saturday, Sunday or a day on which banking institutions in New York, New York, London, England or Stockholm, Sweden are authorized or required by law to close.

1.54 **"Calendar Quarter"** means the period beginning on the Effective Date and ending on the last day of the calendar quarter in which the Effective Date falls, and thereafter each successive period of three (3) consecutive calendar months ending on March 31, June 30, September 30 or December 31.

1.55 **"Calendar Year"** means the period beginning on the Effective Date and ending on December 31, 2006 and thereafter each successive period of twelve (12) months commencing on January 1 and ending on December 31.

1.56 **"Candidate Drug"** means each of (a) Ispronicline, (b) each Active+ Compound that is not a Terminated Compound, (c) each Collaboration Compound for which AstraZeneca commences GLP Toxicology Studies as provided in Section 5.1.2 or for which AstraZeneca does not commence GLP Toxicology Studies but Initiates a Clinical Trial, (d) each Option Compound for which AstraZeneca exercises an Option, (e) each Licensed Derivative with respect to (i) any such Option Compound made by or on behalf of AstraZeneca or its Affiliates or Sublicensees or (ii) Ispronicline or any such Active+ Compound or Collaboration Compound made by or on behalf of (A) AstraZeneca, Targacept or any of their respective Affiliates or Sublicensees during the Research Program Term or the Tail Period or (B) AstraZeneca or its Affiliates or Sublicensees after the Tail Period and (f) in each case ((a) through (e)), any salt form, polymorph, crystalline form, hydrate, solvate or formulation thereof.

1.57 **"CDS"** means cognitive deficiency in schizophrenia, an impairment in humans that (a) affects any or all of memory, attention, diligence, reasoning, problem solving, judgment and language and (b) is associated specifically with, but is a separate condition from the non-cognitive symptoms of, Schizophrenia.

1.58 **"Change of Control"** means, with respect to a Party, (a) a merger, consolidation, acquisition, share exchange or other similar transaction involving such Party and any Third Party which results in the holders of the outstanding voting securities of such Party immediately prior to such merger, consolidation, share exchange or other similar transaction ceasing to hold more than fifty percent (50%) of the combined voting power of the surviving, purchasing or continuing entity immediately after such merger, consolidation, share exchange or other similar transaction, (b) any transaction or series of related transactions in which any "person", as such term is used in Sections 13(d) and 14(d) of the Securities Exchange Act of 1934, as amended (the "**Exchange Act**"), together with any of such person's "affiliates" or "associates", as such terms are used in the Exchange Act, becomes the beneficial owner of fifty percent (50%) or more of the combined voting power of the outstanding securities of such Party or (c) the sale or other transfer to a Third Party of all or substantially all of such Party's assets which relate to this Agreement.

1.59 **"Claims"** has the meaning set forth in Section 13.1.

1.60 **"Clinical Trials"** means, collectively, Phase I Clinical Trials, Phase II Clinical Trials, Phase III Clinical Trials, and such other tests and studies in human subjects that are required by any Regulatory Authority, from time to time, pursuant to Applicable Laws or otherwise, to obtain or maintain Product Regulatory Approval for a product.

1.61 **"Cognitive Impairment"** means a clinically significant deficit in cognition in humans that (a) affects the ability to learn new information or to recall previously learned information and (b) represents (i) a change from a previous level of cognitive functioning or (ii) an impairment relative to age-matched peers.

1.62 **"Collaboration"** means the alliance of Targacept and AstraZeneca established pursuant to this Agreement for purposes of identifying and Developing Candidate Drugs and Commercializing Products in the Territory in the Field and in Schizophrenia.

1.63 **"Collaboration Candidate"** means each (a) Compound that Targacept determines during the Research Program Term to have Minimum Binding Affinity or (b) compound Derived therefrom by or on behalf of AstraZeneca or Targacept (including, for clarification, any compounds Derived from an Active+ Compound, Collaboration Compound or Candidate Drug (excluding Ispronicline (or any Licensed Derivatives with respect thereto) and Option Compound Candidate Drugs)) during the Research Program Term or the Tail Period if such Derived compound (i) itself has Minimum Binding Affinity or (ii) is not the **[********]** where an objective of the **[********]**, in whole or in part, was to **[********]**; including in each case ((a) and (b)) any salt form, polymorph, crystalline form, hydrate, solvate or formulation thereof. Notwithstanding the foregoing, unless the Parties otherwise agree in writing, the Compounds known to Targacept as of the Execution Date as **[********]** and **[********]**and, **[********]**, including any salt form, polymorph, crystalline form, Prodrug, metabolite (other than any such metabolite that is an Excluded Zone Compound), hydrate, solvate or formulation thereof, shall not be Collaboration Candidates.

1.64 **"Collaboration Compound"** means each Lead Collaboration Compound, each Related Collaboration Compound with respect thereto, each Licensed Derivative with respect to any of the foregoing first Derived by or on behalf of AstraZeneca or its Affiliates or Sublicensees after the Tail Period and, only under the circumstances provided in Section 3.3.2(b)(A), Ispronicline. For purposes of clarity, all Collaboration Compounds are also Collaboration Candidates.

1.65 **"Collaboration Compound Designation"** has the meaning set forth in Section 4.7.1.

1.66 **"Collaboration Compound Pool"** means the pool consisting of (a) no more than [********] Lead Collaboration Compounds and (b) all Related Collaboration Compounds with respect to each such Lead Collaboration Compound.

1.67 **"Collaboration Compound Pool Satisfaction Date"** means the date, if any, on which the JRC or AstraZeneca designates the [********]Active+ Compound to be a Lead Collaboration Compound.

1.68 **"Collaboration Manager"** has the meaning set forth in Section 2.5.1.

1.69 **"Combination Product"** means a Product (or a Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product) that contains a Candidate Drug (or a Royalty-Bearing Terminated Compound or a Terminated AZ Compound) as an active ingredient together with one or more other active ingredients, including Other Licensed Compounds or Other Licensed Products, that are sold either as a fixed dose or as separate doses in a single package.

1.70 **"Commencement Date"** has the meaning set forth in Section 3.3.1.

1.71 **"Commercial Coordination Committee"** or **"CCC"** means the committee of Targacept and AstraZeneca representatives to be established pursuant to Section 2.4 if Targacept exercises a Co-Promotion Option.

1.72 **"Commercialization"** or **"Commercialize"** means any and all lawful activities directed to the commercialization of a product (whether before or after Product Regulatory Approval has been obtained), including marketing, manufacturing for commercial sale, promoting, detailing, distributing, offering to sell and selling a product, importing a product for sale, conducting additional human clinical studies with respect to an indication for which Product Regulatory Approval has been obtained and interacting with Regulatory Authorities regarding

the foregoing. When used as a verb, "Commercializing" means to engage in Commercialization and "Commercialized" has a corresponding meaning.

1.73 **"Commercialization Regulatory Approval"** means, with respect to any product for an indication, the granting or approval by the applicable Regulatory Authority(ies) of (a) a Drug Approval Application and (b) all other Regulatory Approvals, if any, required by Applicable Laws, in each case ((a) and (b)) to market and sell such product for use in such indication in a country or region. For purposes of clarity, "Commercialization Regulatory Approval" for a product for an indication in a country or region shall include Product Regulatory Approval for such product for such indication in such country or region.

1.74 **"Commercially Reasonable Efforts"** means:

(a) with respect to the Development of a particular Candidate Drug or the Commercialization of a particular Product by AstraZeneca, the efforts and resources typically used by **[********]** in the development of product candidates or the commercialization of products of comparable market potential, taking into account all relevant factors (including, as applicable and without limitation, stage of development, mechanism of action, efficacy and safety relative to competitive products in development or in the marketplace, actual or anticipated Regulatory Authority approved labeling, the nature and extent of market exclusivity (including patent coverage and regulatory exclusivity), cost of development and likelihood of obtaining Regulatory Approvals, actual or projected profitability (which may take into account, if and as applicable, pricing or reimbursement approvals or authorizations) (provided that in assessing such profitability the royalties, milestones or other payments due or potentially due to Targacept with respect to such Candidate Drug or Product pursuant to this Agreement shall not be taken into account), other products or product candidates (including any **[********]**) that AstraZeneca is researching, developing or commercializing and availability of capacity to manufacture and supply for commercial sale); provided that **[********]**, the effect of diverting effort or resources to Developing **[********]** on any product or product candidate of AstraZeneca that is optimized to act through any Exclusivity Mechanism (other than other Candidate Drug(s) or Product(s)) shall not be taken into account; and

(b) with respect to the performance by Targacept of the Research Program, any Additional Research Program, any Targacept Development Activities, an Option Compound Development Plan or its Manufacturing (as defined in Section 16.18(f)) obligations under Article 16 from time to time, the efforts and resources typically used by companies in the **[********]** industry, with resources and expertise comparable to those of Targacept (or any successor thereto) at such time, to perform such activities on their own behalf (and not as a contract research organization), provided that (i) in no event shall such efforts and resources be less than those typically used by companies in the **[********]** industry with resources and expertise comparable to those of Targacept **[********]** and (ii) with respect to Targacept's obligation to use Commercially Reasonable Efforts to conduct its Manufacturing obligations under Article 16, Targacept's other obligations under the Research Program shall be taken into account.

1.75 **"Competitive Entity"** means any Third Party in the **[********]** companies ranked by worldwide pharmaceutical sales in the most recently completed Calendar Year for which such ranking is readily available from IMS Health Incorporated or such other source as may be agreed by the Parties.

1.76 **"Competitive Program"** means any research, development or commercialization activity of a Third Party that involves a compound or product (other than a Secondary Pharmacology Compound) for which its prophylactic or therapeutic activity is known to be derived in any material respect through any Exclusivity Mechanism for use in the Field or, prior to the Schizophrenia Expiration Date, Schizophrenia that would (a) were such Third Party to undergo a Change of Control transaction with Targacept, cause Targacept to be in breach of any of its exclusivity obligations under Section 8.6.1, or (b) were such Third Party to undergo a Change of Control transaction with AstraZeneca, cause AstraZeneca to be in breach of any of its exclusivity obligations under Section 8.6.3 or terminate or limit any of Targacept's exclusivity obligations under Section 8.6.1.

1.77 **"Compound"** means any compound Controlled by Targacept.

1.78 **"Compound Family"** means (a) with respect to each Lead Collaboration Compound, such Lead Collaboration Compound, all Related Collaboration Compounds with

respect to such Lead Collaboration Compound, and all Licensed Derivatives with respect to either of the foregoing, (b) with respect to Ispronicline, Ispronicline and all Licensed Derivatives with respect thereto, (c) with respect to each IND-Ready Option Candidate Drug, such IND-Ready Option Candidate Drug and all Licensed Derivatives with respect thereto and (d) with respect to each POC Option Candidate Drug, such POC Option Candidate Drug and all Licensed Derivatives with respect thereto.

1.79 **"Confidential Information"** means (a) with respect to Targacept, all tangible embodiments of Targacept Technology, (b) with respect to AstraZeneca, all tangible embodiments of AstraZeneca Technology and the Excluded Data and (c) with respect to each Party, (i) all tangible embodiments of Joint Technology (other than the Excluded Data) and (ii) all information, Technology and Proprietary Materials (other than Targacept Technology, AstraZeneca Technology or Joint Technology) disclosed or provided by or on behalf of such Party (the "**disclosing Party**") to the other Party (the "**receiving Party**") or to any of the receiving Party's employees, consultants, Affiliates or Sublicensees (including, by way of example only, information, Technology and, if applicable, Proprietary Materials regarding an actual or potential future Option Compound provided pursuant to Section 5.10.2 or regarding an ROFN Indication Opportunity provided pursuant to Section 5.10.3); provided that none of the foregoing shall be Confidential Information if: (A) as of the date of disclosure or delivery, it is known to, or in the possession of, the receiving Party or its Affiliates as demonstrated by credible written documentation, other than by virtue of a prior confidential disclosure to such receiving Party; (B) as of the date of disclosure or delivery, it is in the public domain or is otherwise publicly available, or it subsequently enters the public domain or becomes otherwise publicly available through no fault of the receiving Party; (C) it is obtained by the receiving Party from a Third Party having a lawful right to make such disclosure or delivery free from any obligation of confidentiality to the disclosing Party unless disclosed to the receiving Party by such Third Party at the direction, or with the consent of, the disclosing Party; (D) with respect to any Proprietary Materials, it is supplied by a Third Party without breach of any obligation to the disclosing Party, or (E) it is independently developed by or for the receiving Party without reference to or use of any Confidential Information of the disclosing Party as demonstrated by credible written documentation. Notwithstanding anything herein to the contrary, but subject to Section 7.5, (x) the terms of this Agreement shall constitute Confidential Information of each Party, (y) to the

extent Joint Technology solely claims or covers one or more Collaboration Candidates, Active+ Compounds, Collaboration Compounds, Candidate Drugs or Products (other than Terminated Compounds or Products containing Terminated Compounds) or the Exploitation of one or more Collaboration Candidates, Active+ Compounds, Collaboration Compounds, Candidate Drugs or Products (other than Terminated Compounds or Products containing Terminated Compounds), such Joint Technology shall constitute Confidential Information of AstraZeneca and (z) to the extent Joint Technology solely claims or covers one or more Terminated AZ Compounds or the Exploitation thereof, such Joint Technology shall constitute Confidential Information of Targacept.

1.80 **"Contract Quarter"** means (a) the period beginning on the Effective Date and ending on the last day of the third full calendar month after the Effective Date and (b) each succeeding three (3)-month period thereafter.

1.81 **"Contract Year"** means (a) the period beginning on the Effective Date and ending on the first anniversary of the last day of the calendar month in which the Effective Date occurs and (b) each succeeding twelve (12)-month period thereafter.

1.82 **"Control" or "Controlled"** means (a) with respect to Technology (other than Proprietary Materials) or Patent Rights or other intellectual property rights, the possession by a Party of the right, whether by ownership, license or otherwise (other than pursuant to this Agreement), to assign, or to grant a license or sublicense or other right to or under, such Technology, Patent Rights or other intellectual property rights as provided herein without violating the terms of any agreement or arrangement with any Third Party and (b) with respect to Proprietary Materials, the possession by a Party of the right to supply such Proprietary Materials to the other Party as provided herein without violating the terms of any agreement or arrangement with any Third Party.

1.83 **"Co-Promote"** or **"Co-Promotion"** means, with respect to any Co-Promoted Product, the joint promotion and Detailing of such Co-Promoted Product to the Co-Promotion Target Audience in the Co-Promoted Territory using a coordinated sales force consisting of representatives of both Parties.

1.84 **"Co-Promoted Product"** has the meaning set forth in Section 5.11.2(a).

1.85 **"Co-Promotion Activities"** means the activities to be undertaken by either Party pursuant to a Co-Promotion Agreement.

1.86 **"Co-Promotion Agreement"** has the meaning set forth in Section 5.11.2(b)(1).

1.87 **"Co-Promotion Option"** has the meaning set forth in Section 5.11.2(a).

1.88 **"Co-Promotion Option Notice"** has the meaning set forth in Section 5.11.2(a).

1.89 **"Co-Promotion Target Audience"** means, with respect to each Co-Promoted Product, any or all of those classes of specialist physicians and other specialist medical professionals that customarily prescribe or purchase, or that would reasonably be expected to prescribe or purchase, products to treat or prevent any Primary Indication, Schizophrenia or Small Market Indication for which the Co-Promoted Product receives Regulatory Approval in the Co-Promotion Territory. For purposes of clarity, Co-Promotion Target Audience shall include nursing homes or comparable facilities if they would reasonably be expected to purchase a particular Co-Promoted Product but shall not include primary care physicians or medical professionals, including family and general practitioners, internists (regardless of whether they have subspecialty in psychiatry or geriatrics) and pediatricians (except that pediatricians shall not be so excluded in the case of a Co-Promoted Product for which Regulatory Approval is obtained in the United States for ADHD).

1.90 **"Co-Promotion Territory"** means the United States of America (excluding its territories and possessions), including the District of Columbia.

1.91 **"CREATE Act"** has the meaning set forth in Section 10.1.6.

1.92 **"Cure Period"** has the meaning set forth in Section 11.2.4.

1.93 **"Data Exclusivity Period"** means the period of data exclusivity for a Product in a country that is granted when such Product first receives Product Regulatory Approval based on such Product's status as a new chemical entity (and not based on a use or application of such Product, such as, for example, orphan drug exclusivity (unless a Product is only approved for

orphan indications), new uses or pediatric exclusivity) that is, with respect to the United States, listed in the FDA's Orange Book or outside the United States, under the national implementations of Article 10.1(a)(iii) of Directive 2001/EC/83 or other international equivalents. If during the Data Exclusivity Period with respect to a Product in a country, a generic version of such Product (or, with respect to orphan exclusivity, a product for use in the same indication) is approved by the applicable Regulatory Authority(ies) for sale in such country, then, notwithstanding the preceding sentence, the Data Exclusivity Period shall be deemed to have expired with respect to such Product in such country.

1.94 **"Defaulting Party"** has the meaning set forth in Section 11.2.4.

1.95 **"Dementia"** means dementia, a condition having the diagnostic criteria identified in DSM-IV, ICD-10 or any other Diagnostic Manual in a country or recognized by general consensus in the applicable medical community in such country as a distinct diagnosable condition or for which a product has received Product Regulatory Approval from the applicable Regulatory Authority in such country, as applicable, from time to time.

1.96 **"Derived"** means, with respect to a compound, directly (but not necessarily by means of a single step) obtained, developed, created, synthesized, designed, derived or otherwise generated from (whether in whole or in substantial part) another compound, including with the use of any Technology of a Party with respect thereto. "Derivative" and "Derive" shall be interpreted accordingly.

1.97 **"Detail"** means that part of an in person, face-to-face sales call during which a sales representative, who is fully trained with respect to a Co-Promoted Product, including its labeling and any promotional materials, makes a full presentation of the Co-Promoted Product to a medical professional with prescribing authority or to a potential purchaser of the Co-Promoted Product (such as nursing homes or comparable facilities) such that the relevant characteristics of the Co-Promoted Product are described by the sales representative in a fair and balanced manner consistent with the requirements of the applicable Co-Promotion Agreement and Applicable Laws and in a manner that is customary in the industry for the purpose of promoting a prescription pharmaceutical product. Any activities performed by medical information scientists, market development specialists, managed care account directors and other personnel that are not

conducting face-to-face sales calls as provided in the preceding sentence shall not constitute a "Detail" and E-details and presentations made at conventions or similar gatherings shall not constitute a "Detail." When used as a verb, "Detail" means to engage in a Detail.

1.98 **"Development"** or **"Develop"** means, with respect to a Collaboration Compound, Candidate Drug or Product for a Primary Indication, Schizophrenia or a Small Market Indication, all non-clinical and clinical activities required to obtain Commercialization Regulatory Approval of such Product (including any Product that contains such Collaboration Compound or Candidate Drug) in accordance with this Agreement up to and including the obtaining of Commercialization Regulatory Approval of such Product for such Primary Indication, Schizophrenia or Small Market Indication. For purposes of clarity, these activities include test method development and stability testing, regulatory toxicology studies, formulation, process development, manufacturing, manufacturing scale-up, development-stage manufacturing, quality assurance/quality control development, statistical analysis and report writing, Clinical Trial design and operations, preparing and filing Drug Approval Applications, and all regulatory affairs related to the foregoing. When used as a verb, "Developing" means to engage in Development and "Developed" has a corresponding meaning.

1.99 **"Development Program"** means, with respect to each Candidate Drug, the Development program to be conducted by the Parties during the Term with respect to such Candidate Drug pursuant to the Product Development Plan for such Candidate Drug.

1.100 **"Development Program Technology"** means, collectively, Targacept Development Program Technology, AstraZeneca Development Program Technology and, if made, developed or conceived in the conduct of a Development Program, Joint Technology.

1.101 **"Development Project Team"** means a team established by AstraZeneca pursuant to Section 2.3.5.

1.102 **"Development Workaround"** has the meaning set forth in Section 5.5.2.

1.103 **"Diagnostic Manual"** means DSM-IV, ICD-10 or such other similar diagnostic manual or tool as may be a standard used by the medical community in a country to identify or diagnose medical conditions in such country.

1.104 **"Diligence Cure Period"** has the meaning set forth in Section 11.2.5.

1.105 **"Disputed Matter"** has the meaning set forth in Section 2.1.5.

1.106 **"Distributor"** has the meaning set forth in Section 8.3.2.

1.107 **"Drug Approval Application"** means, with respect to a product in a particular country or region in the Territory, an application to the applicable Regulatory Authority(ies) to market and sell such product in such country or region, including: (a) an NDA or sNDA; (b) a counterpart of an NDA or sNDA in any country or region in the Territory; and (c) all supplements and amendments to any of the foregoing.

1.108 **"DSM-IV"** means the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, published by the American Psychiatric Association, as amended and as supplemented or superseded by subsequent editions published from time to time during the Term (e.g., DSM-V).

1.109 **"Dual Pharmacology Compound"** means a compound that **[********]**, including any salt form, polymorph, crystalline form, hydrate, solvate or formulation thereof.

1.110 **"Effective Date"** means the first date on which the condition precedent set forth in Section 17.14 is satisfied.

1.111 **"Effectiveness of IND"** means, with respect to any IND, thirty (30) days after the date such IND is received by the FDA if no clinical hold is issued by the FDA with respect thereto or, if a clinical hold is issued, such later date on which such IND is no longer subject to that clinical hold.

1.112 **"Election Period"** has the meaning set forth in Section 15.1.2(a).

1.113 **"Europe"** means the countries comprising the European Union as it may be constituted from time to time.

1.114 **"European Union"** means the economic, scientific and political organization of member states, which, as of the Execution Date, consists of Austria, Belgium, Czech Republic,

Denmark, Estonia, Finland, France, Germany, Greece, Hungary, Ireland, Italy, Latvia, Lithuania, Luxembourg, Malta, The Netherlands, Poland, Portugal, Slovakia, Slovenia, Spain, Sweden and the United Kingdom of Great Britain and Northern Ireland, and that certain portion of Cyprus included in such organization.

1.115 **"Excepted Decision"** has the meaning set forth in Section 2.1.5.

1.116 **"Excluded Data"** means, with respect to each of the Compounds known to Targacept as of the Execution Date as **[********]**, **[********]** and **[********]** or with respect to each Terminated Compound or Excluded Derivative or with respect to each Collaboration Compound, Candidate Drug, Product or Other Licensed Compound (or product containing any of the foregoing), any results, data or other information generated or otherwise resulting from any of the following activities with respect thereto: (a) **[********]**, **[********]**, and the **[********]** known, as of the Execution Date, as **[********]** and any other **[********]** that after the Execution Date becomes generally accepted in the scientific community as validated for cognitive performance; (b) the **[********]** known, as of the Execution Date, as **[********]**; (c) the **[********]** known, as of the Execution Date, as **[********]** and any other **[********]** that after the Execution Date becomes generally accepted in the scientific community as validated for the **[********]**; (d) **[********]** to measure the **[********]** and any other **[********]** study that after the Execution Date becomes generally accepted in the scientific community as validated for the **[********]**; (e) **[********]** testing for **[********]**; (f) **[********]** known, as of the Execution Date, as (i) **[********]**or **[********]** or **[********]** or (ii) **[********]** or **[********]** and any other **[********]** that after the Execution Date becomes generally accepted in the scientific community as validated for the **[********]**; and (g) any **[********]** or other **[********]** tests or **[********]**, provided that, for purposes of this clause (g), in no event shall **[********]** be Excluded Data.

1.117 **"Excluded Derivative"** means, with respect to a Collaboration Compound, Candidate Drug or Product, any compound Derived therefrom with the use of any AstraZeneca Research Program Technology or Targacept Technology during the applicable Restricted Derivative Period, other than a Licensed Derivative.

1.118 **"Excluded Zone Compound"** means: (a) any Terminated Compound that is not a Terminated AZ Compound or any Unexercised Option Compound, in each case for which a Major Metabolite (i) is a Collaboration Compound or Candidate Drug, (ii) is an Additional Compound with respect to a Collaboration Compound or Candidate Drug or (iii) is the same as a Major Metabolite of (A) a Collaboration Compound, (B) a Candidate Drug (other than a Licensed Derivative) or (C) to the extent Known by Targacept, a Licensed Derivative or an Additional Compound with respect to a Collaboration Compound or a Candidate Drug, in each case ((A), (B) and (C)) that satisfies Section 1.9(a)(iii), 1.9(b)(iii), 1.9(c)(iii) or 1.9(d)(iii), whichever is applicable to the Terminated Compound or Unexercised Option Compound, as applicable; (b) any metabolite of any Terminated AZ Compound, any Partially-Terminated Product or **[********]**, **[********]** or **[********]** that (i) is a Collaboration Compound or Candidate Drug, (ii) is an Additional Compound with respect to a Collaboration Compound or Candidate Drug or (iii) is the same as a Major Metabolite of (A) a Collaboration Compound, (B) a Candidate Drug (other than a Licensed Derivative) or (C) to the extent Known by Targacept, a Licensed Derivative or an Additional Compound with respect to a Collaboration Compound or a Candidate Drug, in each case ((A), (B) and (C)) that satisfies Section 1.9(a)(iii), 1.9(b)(iii), 1.9(c)(iii) or 1.9(d)(iii), whichever is applicable to the Terminated AZ Compound, Partially-Terminated Product or **[********]**, **[********]** or **[********]**, as applicable; and (c) any Prodrug of an Unexercised Option Compound that is made, developed or conceived by or on behalf of Targacept prior to Initiation of a Phase II Clinical Trial of such Unexercised Option Compound. For purposes of clarity, the **[********]**, which is known by Targacept as of the Execution Date as **[********]**, shall not be an Excluded Zone Compound.

1.119 **"Exclusivity Mechanism"** means any mechanism of action involving the **[********]** an NNR **[********]** such NNR. For purposes of clarity, any mechanism of action involving the **[********]** an NNR **[********]** such NNR shall not be an Exclusivity Mechanism.

1.120 **"Execution Date"** has the meaning set forth in the preamble.

1.121 **"Executive Steering Committee"** or **"ESC"** means the committee comprised of Targacept and AstraZeneca representatives established pursuant to Section 2.1.

1.122 **"Expanded Field Indication"** has the meaning set forth in Section 8.9.1.

1.123 **"Expert"** has the meaning set forth in Section 14.3.1.

1.124 **"Exploit"** means to make, have made, import, use, sell or offer for sale, including to discover, research, develop, modify, enhance, improve, manufacture, have manufactured, hold or keep (whether for disposal or otherwise) store, formulate, optimize, have used, export, transport, distribute, promote and market or have sold or otherwise dispose or offer to dispose of, a product or process. **"Exploitation"** means the act of Exploiting a product or process.

1.125 **"External Targacept R&D Costs"** means costs or expenditures incurred by Targacept (or for its account by an Affiliate) in connection with the engagement of any Third Party to conduct work in the Research Program or the Additional Research Program or in connection with the Targacept Development Activities **[********]**.

1.126 **"FDA"** means the United States Food and Drug Administration or any successor agency or authority thereto.

1.127 **"FDCA"** means the United States Federal Food, Drug, and Cosmetic Act, as amended.

1.128 **"Field"** means, subject to Section 8.9, the treatment, prevention or diagnosis of Primary Indications and Small Market Indications in humans or animals.

1.129 **"Final Option Compound Offer"** has the meaning set forth in Section 5.10.2(e)(1).

1.130 **"Final ROFN Offer"** has the meaning set forth in Section 5.10.3.

1.131 **"First Commercial Sale"** means, with respect to a Product, Other Licensed Product, Royalty-Bearing Terminated AZ Product or Royalty-Bearing Terminated Compound (or a Royalty-Bearing Product that contains such Royalty-Bearing Terminated Compound) in a country in the Territory, the first sale, transfer or disposition for value or for end use or consumption of such Product, Other Licensed Product, Royalty-Bearing Terminated AZ Product or Royalty-Bearing Terminated Compound (or a Royalty-Bearing Product that contains such

Royalty-Bearing Terminated Compound) in such country after Commercialization Regulatory Approval has been obtained therefor in such country; provided that any sale to an Affiliate or Sublicensee will not constitute a First Commercial Sale (unless the purchasing Affiliate or Sublicensee is the last entity in the distribution chain for the Product, Other Licensed Product, Royalty-Bearing Terminated AZ Product or Royalty-Bearing Terminated Compound (or a Royalty-Bearing Product that contains such Royalty-Bearing Terminated Compound) and is purchasing it for its own commercial use).

1.132 **"Follow-On Option Compound"** means, with respect to any Option Compound for a particular Primary Indication or for Schizophrenia, another Option Compound for such indication that possesses (a) a different Framework when compared with such first Option Compound and (b) at least as favorable an Option Compound Profile as such first Option Compound, but excluding any Excluded Zone Compound.

1.133 **"Force Majeure"** means any occurrence beyond the reasonable control of a Party that prevents or substantially interferes with the performance by such Party of any of its obligations hereunder including any act of God, flood, fire, explosion, earthquake, strike, lockout, labor dispute, casualty or accident, or war, revolution, civil commotion, act of terrorism, blockage or embargo, or any injunction, law, order, proclamation, regulation, ordinance, demand or requirement of any government or of any subdivision, authority or representative of any such government.

1.134 **"Framework"** means the structural framework of an Option Compound determined in accordance with the guidelines set forth in Schedule 1.134.

1.135 **"FTE"** means **[********]** hours of work devoted to or in support of the Research Program, the Additional Research Program or the Targacept Development Activities that is carried out by employees, contract personnel or consultants of Targacept, measured in accordance with Targacept's standard time allocation practices as disclosed by Targacept in writing as of the Execution Date, consistently applied, from time to time; provided that, upon advance written notice to AstraZeneca, Targacept's standard time allocation practices may change from time to time during the Term.

1.136 **"FTE Cost"** means, for any period, the FTE Rate multiplied by the applicable number of FTEs in such period.

1.137 **"FTE Rate"** means **[********]** Dollars (US $**[********]**); provided that on January 1 of each Calendar Year in the Term, commencing with January 1, 2007, the FTE Rate will be increased by multiplying the FTE Rate applicable on December 31 of the immediately preceding Calendar Year by 1 + [(CPIx - CPIy) / CPIy], where CPIx is the United States Consumer Price Index for All Urban Consumers published by the Bureau of Labor Statistics of the United States Department of Labor for December in the immediately preceding Calendar Year and CPIy is the United States Consumer Price Index for All Urban Consumers published by the Bureau of Labor Statistics of the United States Department of Labor for the month immediately preceding the Effective Date. Any such increase shall be rounded to the nearest one hundred US Dollars ($100).

1.138 **"Fully-Screened Collaboration Candidate"** means each Collaboration Candidate for which, as of a particular date, each of (a) the screening set forth in the Research Plan or an Additional Research Plan, as applicable, to enable the JRC or AstraZeneca to determine whether the Active+ Criteria are satisfied has been completed, (b) the data and analyses from such screening has been provided to the JRC and AstraZeneca, and (c) the JRC has met, having received such data and analyses at least thirty (30) days prior to such meeting, or has determined whether such Collaboration Candidate satisfies the Active+ Criteria.

1.139 **"GAAP"** means International Accounting Standards, except for purposes of any Co-Promotion Agreement, in which case it shall mean United States generally accepted accounting principles, consistently applied, in each case as amended from time to time.

1.140 **"GLP"** means the then-current standards for laboratory activities for pharmaceuticals, as are required by the Regulatory Authorities of Europe, the United States and Japan, including 21 C.F.R. part 58 and EC Directives 87/18/EEC, 88/320/EEC and 1999/11/EC, in each case, as amended from time to time.

1.141 **"GLP Toxicology Studies"** means, with respect to a compound or product, animal studies conducted in accordance with GLP and intended to support an IND for such compound or product.

1.142 **"Good Clinical Practices"** means international ethical, scientific, and quality standards for designing, conducting, recording, and reporting trials that involve the participation of human subjects, as set forth by the International Conference on Harmonization (**"ICH"**) E6: Good Clinical Practices Consolidated Guideline, as amended from time to time, or as otherwise required by Applicable Laws.

1.143 **"Good Manufacturing Practices"** means current good manufacturing practices for biological and other pharmaceutical products (and components thereof) as described in regulations promulgated by the FDA, or an analogous Regulatory Authority outside of the United States, in each case as amended from time to time.

1.144 **"Hatch-Waxman Act"** means the Drug Price Competition and Patent Term Restoration Act of 1984, as amended.

1.145 **"HSR Act"** means the Hart-Scott-Rodino Antitrust Improvements Act of 1976, as amended.

1.146 **"ICD-10"** means the International Statistical Classification of Diseases and Related Health Problems, Tenth Edition, published by the World Health Organization, as amended and as supplemented or superseded by subsequent editions published from time to time during the Term (*e.g.*, ICD-11).

1.147 **"IND"** means: (a) an Investigational New Drug Application as defined in the FDCA and regulations promulgated thereunder or any successor application or procedure required to initiate clinical testing of a Candidate Drug in humans in the United States; (b) a counterpart of an Investigational New Drug Application that is required in any other country or region in the Territory before beginning clinical testing of a Candidate Drug in humans in such country or region; and (c) all supplements and amendments to any of the foregoing.

1.148 **"IND-Ready"** means, with respect to an Option Compound, the completion of such studies and assessments as set forth in Schedule 1.148 to support the filing of an IND covering such Option Compound.

1.149 **"IND-Ready Notice"** has the meaning set forth in Section 5.10.2(b).

1.150 **"IND-Ready Option"** has the meaning set forth in Section 5.10.2(b).

1.151 **"IND-Ready Option Candidate Drug"** means an Option Compound (a) for which AstraZeneca exercises an IND-Ready Option or (b) that Achieves Proof of Concept under an Option Compound Development Plan assumed and completed by AstraZeneca pursuant to Section 5.10.2(b)(5). For purposes of clarity, an IND-Ready Option Candidate Drug is also a Candidate Drug.

1.152 **"IND-Ready Option Period"** has the meaning set forth in Section 5.10.2(b).

1.153 **"IND-Ready Option Product"** means a Product that contains an IND-Ready Option Candidate Drug as an active ingredient. For purposes of clarity, an IND-Ready Option Product is also a Product.

1.154 **"Indemnification Claim Notice"** has the meaning set forth in Section 13.3.1.

1.155 **"Indemnified Party"** has the meaning set forth in Section 13.3.1.

1.156 **"Indemnifying Party"** has the meaning set forth in Section 13.3.1.

1.157 **"Indemnitees"** has the meaning set forth in Section 13.3.1.

1.158 **"Indirect Taxes"** means value added taxes, sales taxes, consumption taxes and other similar taxes.

1.159 **"Infringement"** has the meaning set forth in Section 10.2.1(a).

1.160 **"Infringement Notice"** has the meaning set forth in Section 10.2.1(a).

1.161 **"Initiation"** means, with respect to a Clinical Trial, the first date that a properly enrolled subject is dosed in such Clinical Trial in accordance with the applicable protocol. "Initiate" shall be interpreted accordingly.

1.162 **"In-License Agreements"** has the meaning set forth in Section 12.2.1.

1.163 **"In-Licensed Patent Rights"** has the meaning set forth in Section 12.2.1.

1.164 **"Ispronicline"** means (2S)-(4E)-N-methyl-5-(5-isopropoxy-3-pyridyl)-4-pentene-2-amine, identified by the compound structure set forth in Schedule 1.164 and also identified as TC-1734 in **[********]**, including any salt form, polymorph, crystalline form, hydrate, solvate or formulation thereof.

1.165 **"Ispronicline Product"** means any Product that contains Ispronicline as an active ingredient. For purposes of clarity, an Ispronicline Product is also a Product.

1.166 **"Joint Development Committee" or "JDC"** means the committee comprised of Targacept and AstraZeneca representatives established pursuant to Section 2.3.

1.167 **"Joint Patent Rights"** has the meaning set forth in Section 9.1.3.

1.168 **"Joint Research Committee" or "JRC"** means the committee comprised of Targacept and AstraZeneca representatives established pursuant to Section 2.2.

1.169 **"Joint Technology"** has the meaning set forth in Section 9.1.3.

1.170 **"Joint Terminated Compound Patent Rights"** means any Joint Patent Rights that contain one or more claims Known by the Parties to solely cover one or more Terminated Compounds, or the Exploitation thereof.

1.171 **"Knowledge"** means, with respect to a Party, the good faith understanding of the facts and information in the possession of an officer of such Party or any of its Affiliates, or any in-house legal counsel of, or in-house Patent agents employed by, such Party or any of its Affiliates, without any duty to conduct any additional investigation with respect to such facts and information by reason of the execution of this Agreement. For purposes of this definition, an

"officer" means any person in the position of vice president, senior vice president, president or chief executive officer, or any person having similar responsibilities, of a Party or any of its Affiliates. "Known" shall be interpreted accordingly.

1.172 **"Label Expansion"** means, with respect to each Product for which Regulatory Approval for a Primary Indication or Schizophrenia is obtained in a particular country or region in the Territory, Regulatory Approval for a change or supplement to such Product's approved labeling in such country or region (a) to reflect **[********]** of, or **[********]** for, such Product or to reflect that such Product is **[********]** or for **[********]** and (b) that does not result in such approved labeling, as changed or supplemented, constituting (i) a separate Primary Indication or Small Market Indication or (ii) if the Regulatory Approval was for an indication other than Schizophrenia, Schizophrenia.

1.173 **"Lead Collaboration Compound"** means each Active+ Compound that is selected by the JRC or AstraZeneca as a Lead Collaboration Compound during the Research Program Term or the Tail Period, including any salt form, polymorph, crystalline form, hydrate, solvate or formulation thereof. Notwithstanding anything in this Agreement to the contrary, in no event shall a Licensed Derivative with respect to Ispronicline be a Lead Collaboration Compound unless AstraZeneca designates it as a Lead Collaboration Compound pursuant to Section 4.3.3. For purposes of clarity, Ispronicline is not a Lead Collaboration Compound and, except as provided in the preceding sentence, Licensed Derivatives with respect to Ispronicline, even if Derived during the Research Program Term or the Tail Period, are not Lead Collaboration Compounds.

1.174 **"Lead Collaboration Compound Designation"** has the meaning set forth in Section 4.7.1.

1.175 **"Licensed Derivative"** means (a) with respect to Ispronicline, a Lead Collaboration Compound, a Related Collaboration Compound, an IND-Ready Option Candidate Drug or a POC Option Candidate Drug or a Product or Option Compound Product that contains any of the foregoing, any compound Derived therefrom by or on behalf of AstraZeneca with the use of any AstraZeneca Research Program Technology or Targacept Technology that is either:

(1) an Additional Compound with respect to such Collaboration Compound, Candidate Drug or Product; or

(2) a compound that would be an Additional Compound with respect to such Collaboration Compound, Candidate Drug or Product if it met the criteria set forth in Section 1.9(a)(ii), Section 1.9(b)(ii), Section 1.9(c)(ii), or Section 1.9(d)(ii), as applicable, unless: (x) the failure to meet such criteria is a result of **[********]** where an objective thereof, in whole or in part, was to **[********]** (A) **[********]**, if such Collaboration Compound, Candidate Drug or Product is an Alpha4Beta2 Agonist, (B) the Alpha7 NNR, if such Collaboration Compound, Candidate Drug or Product is a Selective Alpha7 Compound, (C) the Alpha4Beta2 NNR or the Alpha7 NNR, if such Collaboration Compound, Candidate Drug or Product is a Dual Pharmacology Compound or (D) the NNR (other than the Alpha4Beta2 NNR and the Alpha7 NNR) that is principally responsible for the cholinergic activity of such Collaboration Compound, Candidate Drug or Product, if such Collaboration Compound, Candidate Drug or Product is an Other NNR Compound; or (y) Targacept exclusively Controls a Patent Right that specifically sets forth the **[********]** in a claim covering the **[********]** of such compound or a **[********]** comprising such compound (each, a "**Species Claim**"), with an earlier priority date than any Patent Right with a Species Claim with respect to such compound that is Controlled by AstraZeneca; provided that, for purposes of the foregoing, if in an interference proceeding in the United States between patents or patent applications of Targacept and AstraZeneca or their respective Affiliates, a Party or any of its Affiliates is determined to be the first to invent such compound individually (and not solely **[********]**), then such Party shall be deemed to have the earlier priority date;

or (b) any enantiomer, metabolite or Prodrug of any Collaboration Compound, Candidate Drug or Product. For purposes of clarity, and notwithstanding anything to the contrary herein, with respect to each Collaboration Compound that becomes a Terminated Compound prior to the end of the Tail Period (or, if later, the resolution of any dispute pursuant to Section 4.3.2 or as provided in Section 4.9), all Licensed Derivatives thereof shall, as of the date on which such Collaboration Compound becomes a Terminated Compound, be Terminated Compounds (unless, with respect to any such Licensed Derivative, such Licensed Derivative is also a Lead

Collaboration Compound or is a Related Collaboration Compound with respect to a Lead Collaboration Compound that has not been terminated).

1.176 **"Losses"** has the meaning set forth in Section 13.1.

1.177 **"Major Market Country"** means each of the United States, the United Kingdom, Germany, Spain, France, Italy and Japan.

1.178 **"Major Market European Country"** each of the United Kingdom, Germany, Spain, France and Italy.

1.179 **"Major Metabolite"** means, with respect to any compound, a metabolite of such compound that: (a) is identified using the metabolic profiling procedures set forth below in **[********]**; and (b) accounts for **[********]** or more of such compound administered to either of the **[********]** using such metabolic profiling procedures on a **[********]** basis. For purposes of this definition, metabolic profiling procedures shall, unless otherwise agreed by the Parties, mean **[********]** performed in approximately **[********]** with the **[********]** by adding **[********]**. [********]** shall be used as **[********]** for **[********]** to assess the **[********]**. Test compound will be tested at **[********]** final concentration and samples will be stored below approximately **[********]** until analyzed.

1.180 **"Material Unexpected Technical Development Problem"** has the meaning set forth in Section 5.5.2.

1.181 **"Material Unexpected Technical Research Problem"** has the meaning set forth in Section 4.4.1.

1.182 **"MCI"** means (a) mild cognitive impairment, a condition in which persons experience memory impairment as compared with persons of substantially the same age and education that is not accompanied by substantial impairment in normal activities of daily living or in thinking or reasoning skills and is not otherwise part of a pathological illness or other separately defined medical condition (such as, by way of example only, Dementia, delirium, stroke, inflammatory brain disease, depression or a history of alcohol or psychotropic drug use) unless and until (b) mild cognitive impairment becomes included in DSM-IV, ICD-10 or any

other Diagnostic Manual in any country in the Territory or becomes recognized as a distinct diagnosable condition by general consensus in the applicable medical community in any country in the Territory, or a product receives Product Regulatory Approval from the applicable Regulatory Authority in any country for MCI, in each case after the Execution Date, in which case, a condition with the diagnostic characteristics included in DSM-IV, ICD-10 or any other Diagnostic Manual or as recognized by the medical community in such country or such Regulatory Authority, as applicable, from time to time. For purposes of clarity, in the event that, notwithstanding the foregoing, the condition known as mild cognitive impairment on the Execution Date becomes included in DSM-IV, ICD-10 or any other Diagnostic Manual in any country in the Territory or becomes recognized as a distinct diagnosable condition by general consensus in the applicable medical community in any country in the Territory, or a product receives Product Regulatory Approval from the applicable Regulatory Authority in any country for mild cognitive impairment after the Execution Date by another name (including mild or early AD), then, for purposes of this Agreement, MCI shall mean such named condition.

1.183 **"Milestone-Bearing Licensed Derivative"** has the meaning set forth in Section 6.5.1(a).

1.184 **"Minimum Binding Affinity"** means, with respect to any compound, (a) binding affinity (Ki) for (i) the Alpha4Beta2 NNR that is **[********]** and (ii) the **[********]** that is **[********]**, and (b) **[********]**, in each case within the margins of error for the applicable assays, as such criteria may be amended from time to time in any Annual Research Plan.

1.185 **"NDA"** means a New Drug Application as defined in the FDCA and regulations promulgated thereunder or any successor application or procedure required to sell a Product in the United States.

1.186 **"Net Sales"** means the gross invoiced amount on sales of Products or Other Licensed Products by AstraZeneca or any of its Affiliates or Sublicensees (or sales of Royalty-Bearing Products or Royalty-Bearing Terminated AZ Products by Targacept or any of its Affiliates or Sublicensees) to Third Parties (including Distributors) after deduction of (a) normal and customary trade, quantity or prompt settlement discounts (including chargebacks and allowances) actually allowed; (b) amounts repaid or credited by reason of rejection, returns or

recalls of goods, rebates or bona fide price reductions determined by AstraZeneca or its Affiliates (or, in the case of Royalty-Bearing Products or Royalty-Bearing Terminated AZ Products, by Targacept or its Affiliates) in good faith; (c) rebates and similar payments made with respect to sales paid for by any governmental or regulatory authority such as, by way of illustration and not in limitation of the Parties' rights hereunder, federal or state Medicaid, Medicare or similar state program in the United States or equivalent governmental program in any other country; (d) **[********]**; (e) **[********]**; and (f) **[********]**.

AstraZeneca Net Sales shall be calculated using AstraZeneca's internal audited systems used to report such sales as adjusted for any of items (a) to (f) (inclusive) above not taken into account in such systems. Deductions pursuant to clause (d) in the preceding paragraph shall **[********]**.

In the case of pharmacy incentive programs, hospital performance incentive program chargebacks, disease management programs, similar programs or discounts on "bundles" of products, all discounts and the like shall be allocated among products on the basis on which such discounts and the like were actually granted or, if such basis cannot be determined, in proportion to the respective list prices of such products.

In the event that a Product (or, with respect to Targacept, a Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product or, with respect to AstraZeneca, an Other Licensed Product) is sold in any country in the form of a Combination Product, Net Sales of such Combination Product shall be adjusted by multiplying actual Net Sales of such Combination Product in such country calculated pursuant to the first paragraph of this Section by the fraction A/(A+B), where A is the average invoice price in such country of the Product(s) that contains only the Candidate Drug(s) that is contained in the Combination Product (or, with respect to Targacept, the Royalty-Bearing Product(s) that contains only the Royalty-Bearing Terminated Compound(s) that is contained in the Combination Product or the Royalty-Bearing Terminated AZ Product(s) that contains only the Terminated AZ Compound(s) that is contained in the Combination Product or, with respect to AstraZeneca, the Other Licensed Product(s) that contains only the Other Licensed Compound(s) that is contained in the Combination Product), if sold separately in such country, and B is the average invoice price in such country of product(s) that contains solely each other active ingredient in the Combination Product. If any of such Product(s) (or Royalty-Bearing

Product(s), Terminated AZ Product(s) or Other Licensed Product(s)) or product containing other active ingredients in the Combination Product are not sold separately in a particular country, the Parties shall negotiate in good faith a reasonable adjustment to Net Sales in such country that takes into account the medical contribution to the Combination Product of, and all other factors reasonably relevant to the relative value of, the Candidate Drug(s) (or the Royalty-Bearing Terminated Compound(s), Terminated AZ Compound(s) or Other Licensed Compound(s)), on the one hand, and all of the other active ingredients, collectively, on the other hand; provided that **[********]**.

For purposes of the preceding paragraph, the invoice price in a country for each Product (and Royalty-Bearing Product, Royalty-Bearing Terminated AZ Product or Other Licensed Product) and each product that contains solely active ingredients other than the Candidate Drug (or Royalty-Bearing Terminated Compound, Royalty-Bearing Terminated AZ Compound or Other Licensed Compound) included in the Combination Product shall be for a quantity comparable to that used in such Combination Product and of substantially the same class, purity and potency.

If a product (including a Product or an Other Licensed Product) sold by AstraZeneca or its Affiliates or Sublicensees contains more than one Candidate Drug or Other Licensed Compound (where such Candidate Drugs and Other Licensed Compounds are **[********]** (*e.g.*, a product that contains more than one of Ispronicline, a Collaboration Compound, an Option Compound Candidate Drug, a Licensed Derivative with respect to any of the foregoing or an Other Licensed Compound)), then **[********]**.

For purposes of clarity, none of (i) use of any Product, Other Licensed Product or Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product in Clinical Trials, pre-clinical studies or other research or development activities, or disposal or transfer of Products for purposes of sampling programs or for charitable, manufacturing, testing or qualification, regulatory or governmental purposes, (ii) sales of Product or Other Licensed Product (or Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product) that is (A) **[********]** and (B) **[********]**, (iii) sales on a treatment IND, named patient or compassionate use or other similar basis or (iv) sales between or among a Party or its Affiliates or Sublicensees (unless the purchasing Affiliate or Sublicensee is the last entity in the distribution chain for the Product or

Other Licensed Product and is purchasing it for its own commercial use), shall give rise to any Net Sales.

1.187 **"Newly-Defined Cognitive Disorder"** means any indication or condition: (a) that is not a Primary Indication, Schizophrenia or Small Market Indication on the Execution Date; (b) that is not an Associated Cognitive Impairment; (c) that is, as of the Execution Date, neither included in DSM-IV or ICD-10 nor recognized as a distinct diagnosable condition by general consensus in the medical community in the United States or Europe, and for which no product has received Product Regulatory Approval from the FDA in the United States or the EMEA in Europe prior to the Execution Date; (d) that either becomes included in DSM-IV, ICD-10 or any other Diagnostic Manual in a Major Market Country during the Term, becomes recognized as a distinct diagnosable condition by general consensus in the applicable medical community in a Major Market Country during the Term or for which a product receives Product Regulatory Approval from the applicable Regulatory Authority in a Major Market Country during the Term; (e) for which the diagnosis requires a finding of Cognitive Impairment; and (f) that **[********]**, as a Newly-Defined Cognitive Disorder. For purposes of clarity, a Newly-Defined Cognitive Disorder **[********]** shall apply throughout the Territory, even if such Newly-Defined Cognitive Disorder is not included in DSM-IV, ICD-10 or any other Diagnostic Manual in all Major Market Countries, is not recognized as a distinct diagnosable condition by general consensus in the applicable medical community in all Major Market Countries or a product has not received Product Regulatory Approval for Associated Cognitive Impairment from the applicable Regulatory Authority in all Major Market Countries.

1.188 **"Next Clinical Trial"** means the first Phase II Clinical Trial or Phase III Clinical Trial for a compound or product for an indication Initiated after the Achievement of Proof of Concept for such compound or product for such indication, except that, if Achievement of Proof of Concept for a compound or product for an indication is demonstrated by the **[********]** Clinical Trial (and not by achievement of **[********]** in a **[********]** Clinical Trial), "Next Clinical Trial" shall instead mean that Phase III Clinical Trial.

1.189 **"NNR"** means a neuronal nicotinic (acetylcholine) receptor subtype.

1.190 **"Non-Defaulting Party"** has the meaning set forth in Section 11.2.4.

1.191 **"Notice Date"** has the meaning set forth in Section 3.3.2.

1.192 **[********]**

1.193 "**Obligation Expiration Date**" means the date, after the expiration of the last royalty obligation pursuant to Section 6.6.1 with respect to the first Product (other than an Option Compound Product that contains an Option Compound Candidate Drug, unless pursuant to Section 5.5.1(c) such Option Compound Candidate Drug is sufficient to satisfy AstraZeneca's diligence obligation set forth in Section 5.5.1(b)) for which the First Commercial Sale occurs (or, if earlier, another Product for which the First Commercial Sale occurs), on which AstraZeneca is no longer using Commercially Reasonable Efforts to conduct research, development or commercialization activities with respect to at least one (1) Candidate Drug or Product for at least one (1) indication in the Field or in Schizophrenia.

1.194 **"Ongoing Ispronicline Trial"** means the Phase II Clinical Trial of Ispronicline in AAMI sponsored by Targacept that is ongoing as of the Execution Date (Protocol TC-1734-112-CRD-004).

1.195 **"Option"** means, with respect to each Option Compound, the IND-Ready Option or the POC Option.

1.196 **"Option Compound"** means during the Option Term (and, if an IND-Ready Option Period or POC Option Period begins during the Option Term and has not expired as of the last day of the Option Term, thereafter until the last day of such IND-Ready Option Period or POC Option Period), any Secondary Pharmacology Compound or Other NNR Compound on which Targacept conducts research or development activities specifically for use in the Territory in the Field or, prior to the Schizophrenia Expiration Date, Schizophrenia and elects, in its sole discretion, to designate as an Option Compound. For purposes of clarity, (a) an Alpha4Beta2 Agonist shall not be an Option Compound, (b) an Unexercised Option Compound shall, upon becoming an Unexercised Option Compound, cease to be an Option Compound, (c) a Terminated Compound that was previously an Option Compound shall, upon becoming a Terminated Compound, cease to be an Option Compound and (d) an Excluded Zone Compound shall not be an Option Compound.

1.197 **"Option Compound Candidate Drug"** means each (a) IND-Ready Option Candidate Drug, (b) POC Option Candidate Drug and (c) each Licensed Derivative with respect to any such IND-Ready Option Candidate Drug or POC Option Candidate Drug made by or on behalf of AstraZeneca or any of its Affiliates or Sublicensees and (d) in each case ((a) through (c)), any salt form, polymorph, crystalline form, hydrate, solvate or formulation thereof.

1.198 **"Option Compound Development Plan"** means, with respect to each Option Compound for which AstraZeneca pays the Option Maintenance Fee set forth in Section 6.3, the written plan prepared jointly by Targacept and AstraZeneca pursuant to Section 5.10.2(b)(3) that describes in detail the development activities to be carried out by Targacept with respect to such Option Compound, as may be amended from time to time by mutual written agreement of the Parties in accordance with the terms hereof. For purposes of clarity, a Targacept Option Compound Development Plan is not an Option Compound Development Plan.

1.199 **"Option Compound Development Plan Period"** has the meaning set forth in Section 5.10.2(b)(3).

1.200 **"Option Compound Product"** means any Product that contains an Option Compound Candidate Drug as an active ingredient.

1.201 **"Option Compound Profile"** means, with respect to any Option Compound for a particular Primary Indication or for Schizophrenia, the characteristics of such Option Compound that, when considered in the aggregate, would reasonably be considered predictive of the likelihood of the potential success or failure of such Option Compound as a pharmaceutical product for such Primary Indication or for Schizophrenia. For the avoidance of doubt, such characteristics may include safety, efficacy, potency, bioavailability, ease or cost of manufacture, and intellectual property protection.

1.202 **"Option Compound Proof of Concept"** means, with respect to an Option Compound, (a) the achievement of the standards or criteria identified as such in the Option Compound Development Plan (or in the Targacept Option Compound Development Plan) for such Option Compound at a dose range that is shown to be safe and tolerable in the patient group of interest and that is acceptable from each of a scientific, statistical, medical, regulatory and

commercial perspective for the Option Indication specified (i) with respect to each Targacept Option Compound Development Plan, in the applicable IND-Ready Option Notice and (ii) with respect to each Option Compound Development Plan, in such plan; or (b) if Section 5.10.2(b)(5) applies, Achievement of Proof of Concept for such Option Compound.

1.203 **"Option Compound ROFN Notice"** has the meaning set forth in Section 5.10.2(e).

1.204 **"Option Compound ROFN Period"** has the meaning set forth in Section 5.10.2(e).

1.205 **"Option Exercise Fee"** has the meaning set forth in Section 6.2.

1.206 **"Option Indication"** means any Primary Indication or, prior to the Schizophrenia Expiration Date, Schizophrenia; provided, however, that in no event shall AAMI or MCI be an Option Indication until such time as AAMI or MCI, respectively, is included in DSM-IV, becomes recognized as a distinct diagnosable condition by general consensus in the medical community in the United States, or a product receives Product Regulatory Approval from the FDA in the United States for AAMI or MCI (as applicable).

1.207 **"Option Maintenance Notice"** has the meaning set forth in Section 5.10.2(b)(3).

1.208 **"Option Term"** means the period commencing on the Effective Date and ending on the earliest of: (i) date on which AstraZeneca Initiates a Clinical Trial for (a) any Alpha4Beta2 Agonist other than a Collaboration Compound, Candidate Drug, Product or Licensed Derivative with respect to any of the foregoing, (b) any Other NNR Compound that is not (i) a Candidate Drug, Product or Licensed Derivative with respect to any of the foregoing or (ii) an Option Compound for which AstraZeneca elects to assume and complete an Option Compound Development Plan pursuant to Section 5.10.2(b)(5) or (c) if AstraZeneca does not terminate this Agreement pursuant to Section 11.2.3, a product or compound that is the subject of a Competitive Program that AstraZeneca does not cease, or cause its relevant Affiliate to cease or divest, or cause its relevant Affiliate to divest (whether by license or otherwise) in accordance with Section 15.2.2 subsequent to a merger, consolidation or acquisition (including through a Change of Control), in each case ((a) through (c)) in the Field or, prior to the Schizophrenia

Expiration Date, in Schizophrenia; (ii) the expiration of the Term; (iii) the effective date of termination of this Agreement in its entirety pursuant to Article 11; or (iv) the effective date of termination by Targacept pursuant to Section 11.2.5(a)(2). For purposes of clarity, Initiation of a Clinical Trial for a Secondary Pharmacology Compound shall not trigger the termination of the Option Term.

1.209 **"Other Licensed Compound"** means each (a) Licensed Derivative with respect to a Collaboration Compound, Candidate Drug or Product made after the applicable Restricted Derivative Period and (b) Additional Compound with respect to a Collaboration Compound, Candidate Drug or Product that is not a Licensed Derivative.

1.210 **"Other Licensed Product"** has the meaning set forth in Section 6.6.1(a)(3).

1.211 **"Other Licensed Product Royalty-Bearing Claim"** has the meaning set forth in Section 6.6.1(b)(2).

1.212 **"Other NNR Compound"** means any compound that acts through any Exclusivity Mechanism other than (a) an Alpha4Beta2 Agonist or (b) a Secondary Pharmacology Compound. For purposes of clarity, an Other NNR Compound may be (i) a Collaboration Candidate that does not meet Minimum Binding Affinity or a Licensed Derivative of any Collaboration Compound, Candidate Drug (other than an Option Compound Candidate Drug) or Product (other than an Option Compound Product) that is not itself an Alpha4Beta2 Agonist or (ii) an Option Compound Candidate Drug (or Option Compound Product) that is not itself a Selective Alpha7 Compound or a Dual Pharmacology Compound but was Derived from an Option Compound Candidate Drug (or Option Compound Product) that was a Selective Alpha7 Compound or a Dual Pharmacology Compound or (iii) an Option Compound that acts through any Exclusivity Mechanism other than the Alpha4Beta2 NNR or the Alpha7 NNR, in each case ((i), (ii) and (iii)) to the extent such compound is not an Alpha4Beta2 Agonist or Secondary Pharmacology Compound.

1.213 **"Owned Patent Rights"** has the meaning set forth in Section 12.2.1.

1.214 **"Partially-Terminated Product"** means any Candidate Drug or Product (but for clarity, not an Other Licensed Compound or an Other Licensed Product) that is terminated by

Targacept pursuant to Section 11.2.5(b) or Section 11.2.5(c) in one or more Major Market Countries in the Territory, but as to which AstraZeneca retains rights in other countries in the Territory.

1.215 **"Partially-Terminated Product Territory"** means, with respect to each Partially-Terminated Product, the Territory, but excluding all Major Market Countries in which such Partially-Terminated Product becomes terminated pursuant to Section 11.2.5(b) or Section 11.2.5(c).

1.216 **"Party"** or **"Parties"** has the meaning set forth in the preamble.

1.217 **"Patent Coordinator"** has the meaning set forth in Section 9.2.

1.218 **"Patent Rights"** means the rights and interests in and to issued patents and pending patent applications (which, for purposes of this Agreement, include certificates of invention, applications for certificates of invention and priority rights) in any country, including all provisional applications, substitutions, continuations, continuations-in-part, divisions, renewals, all letters patent granted thereon, and all reissues, reexaminations and extensions thereof, and all foreign counterparts of any of the foregoing.

1.219 **"Payments"** has the meaning set forth in Section 6.6.4.

1.220 **"Pentad Technology"** means proprietary know-how of Targacept or any of its Affiliates concerning structure activity relationships of compounds and NNRs (generally and without regard to a specific Collaboration Candidate, Active+ Compound, Collaboration Compound, Candidate Drug, Product or Additional Compound (or any Additional Product) with respect to any of the foregoing), pharmacophore mapping of NNRs and computational and quantum mechanical methods for use in the design, synthesis and evaluation of compounds.

1.221 **"Person"** means an individual, sole proprietorship, partnership, limited partnership, limited liability partnership, corporation, limited liability company, business trust, joint stock company, trust, incorporated association, joint venture or similar entity or organization, including a government or political subdivision, department or agency of a government.

1.222 **"Phase I Clinical Trial"** means a human clinical trial conducted in accordance with Applicable Laws in any country or countries that is designed, either alone or together with one or more other human clinical trials conducted in any country or countries, to obtain sufficient data of safety, metabolism and pharmacokinetic properties and clinical pharmacology to permit Initiation of a Phase II Clinical Trial, as described in or contemplated by 21 C.F.R. § 312.21(a), as may be amended from time to time, or other Applicable Laws.

1.223 **"Phase II Clinical Trial"** means a human clinical trial conducted in accordance with Applicable Laws in any country or countries in subjects with a particular disease or condition for which a primary endpoint is a preliminary determination of efficacy or dose ranges in patients with the disease target being studied, as described in or contemplated by 21 C.F.R. §312.21(b), as may be amended from time to time, or other Applicable Laws.

1.224 **"Phase III Clinical Trial"** means a human clinical trial conducted in accordance with Applicable Laws in any country or countries in subjects with a particular disease or condition the principal purpose of which is to establish safety and efficacy in patients with the disease target being studied as described in or contemplated by 21 C.F.R. §312.21(c), as may be amended from time to time, or other Applicable Laws, that is designed to obtain sufficient data to support the filing of an approvable Drug Approval Application in a Major Market Country.

1.225 **"POC Notice"** has the meaning set forth in Section 5.10.2(d).

1.226 **"POC Option"** has the meaning set forth in Section 5.10.2(d).

1.227 **"POC Option Candidate Drug"** means an Option Compound for which AstraZeneca exercises a POC Option. For purposes of clarity, a POC Option Candidate Drug is also a Candidate Drug.

1.228 **"POC Option Period"** has the meaning set forth in Section 5.10.2(d).

1.229 **"POC Option Product"** means a Product that contains a POC Option Candidate Drug as an active ingredient. For purposes of clarity, a POC Option Product is also a Product.

1.230 **"Potential Option Compound"** has the meaning set forth in Section 5.10.2(a).

1.231 **"Potential Option Indication"** has the meaning set forth in Section 5.10.2(a).

1.232 **"Pre-IND Studies"** has the meaning set forth in Section 5.10.2(a).

1.233 **"Preliminary IND Notice"** has the meaning set forth in Section 5.10.2(a).

1.234 **"Pre-Phase IIb Period"** means the period commencing on the Effective Date and ending on (a) the Commencement Date or (b) if there is no Commencement Date, the Sunset Date or if, subject to Section 3.3.2(b), neither Party terminates this Agreement in accordance with Section 11.2.1, the first date on which neither Party has the right to terminate this Agreement pursuant to Section 11.2.1, whichever is later.

1.235 **"Pre-Phase IIb Plan"** means the written plan agreed upon as such by the Parties as of the Execution Date.

1.236 **"Pre-Phase IIb Program"** means the non-clinical and clinical development program as set forth in the Pre-Phase IIb Plan.

1.237 **"Pre-Phase IIb Program Technology"** means, collectively, Targacept Pre-Phase IIb Program Technology (if any), AstraZeneca Pre-Phase IIb Program Technology and, if made, developed or conceived in the conduct of the Pre-Phase IIb Program, Joint Technology.

1.238 **"Primary Indication"** means each of AD, MCI, AAMI, CDS, ADHD, each Newly-Defined Cognitive Disorder that is not a Small Market Indication, each Associated Cognitive Impairment that is not a Small Market Indication, each Additional Primary Indication, and each of (a) Dementia due to general medical conditions (including Dementia with Lewy Bodies), (b) substance induced Dementia and (c) Dementia due to multiple etiologies, in each case ((a), (b) and (c)) if not a Small Market Indication. For purposes of clarity, Schizophrenia is not a Primary Indication.

1.239 **"Principal Indication"** means with respect to (a) any IND-Ready Option Candidate Drug or IND-Ready Option Product, the Option Indication specified by AstraZeneca in the Product Development Plan for such Option Compound, and (b) any POC Option Candidate Drug or POC Option Product, the Option Indication specified in the Option

Compound Development Plan, or if no such plan is agreed to by the Parties, the Targacept Option Compound Development Plan.

1.240 **"Prodrug"** means, with respect to a compound, a composition of matter that is designed to have such compound as its only primary Major Metabolite.

1.241 **"Product"** means a product that consists of or contains a Candidate Drug as an active ingredient.

1.242 **"Product Commercialization Plan"** means, with respect to a Product, the written plan for the Commercialization of such Product in the Territory (including expected manufacturing scale-up, manufacture, formulation and filling requirements for such Product and the overall strategy for Commercializing such Product), as such plan may be amended or updated from time to time in accordance with the terms of this Agreement.

1.243 **"Product Development Plan"** means, with respect to a Candidate Drug, the written plan for such Candidate Drug that describes (a) the overall strategy for Development of such Candidate Drug including the expected Regulatory Filings and Drug Approval Applications to be required and prepared and the expected timetable for completing such Development activities and making such Regulatory Filings and Drug Approval Applications, and (b) in reasonable detail any Targacept Development Activities to be carried out with respect to such Candidate Drug as such plan may be amended from time to time in accordance with the terms of this Agreement.

1.244 **"Product Regulatory Approval"** means, with respect to any product for an indication, the granting or approval of a Drug Approval Application by the applicable Regulatory Authority to market and sell such product for use in such indication in a country or region. For purposes of clarity, a Product Regulatory Approval shall not include pricing or reimbursement authority or approval.

1.245 **"Product Trademark"** means any Trademark, whether or not registered, or any trademark application or renewal, extension or modification thereof, in the Territory, including any trade dress and packaging, in each case (a) that are applied to or used solely in connection with one or more Candidate Drugs or Products by AstraZeneca and (b) together with all goodwill

associated therewith and promotional materials relating thereto. For purposes of clarity, Product Trademarks shall not include any name or logo used by AstraZeneca or its Affiliates that is not product specific.

1.246 **"Proprietary Materials"** means tangible chemical, biological or physical materials that are furnished by or on behalf of one Party to the other Party in connection with this Agreement that are not generally available or accessible from other sources, whether or not specifically designated as proprietary by the transferring Party.

1.247 **"Regulatory Action Plan"** means the written plan to explore the feasibility of obtaining Regulatory Approval of Products to treat MCI and AAMI in the United States developed by AstraZeneca in consultation with Targacept pursuant to Section 5.8, as such plan may be amended by AstraZeneca in consultation with Targacept from time to time.

1.248 **"Regulatory Approval"** means, with respect to any country or region in the Territory, (a) any approval, product and establishment license, registration or authorization of any Regulatory Authority required for the manufacture, use, storage, importation, exportation, transport or sale of a product and (b) any pricing or reimbursement approval or authorization that is necessary or reasonably useful to sell such product, in each case ((a) and (b)), for use in an indication in such country or region. For purposes of clarity, "Regulatory Approval" for a product for an indication in a country or region shall include Commercialization Regulatory Approval for such product for such indication in such country or region.

1.249 **"Regulatory Authority"** means the FDA or any counterpart of the FDA outside the United States, or other national, supra-national, regional, state or local regulatory agency, department, bureau, commission, council or other governmental entity with authority over the distribution, importation, exportation, manufacture, production, use, storage, transport, clinical testing or sale of a product.

1.250 **"Regulatory Filings"** means (a) all applications, registrations, licenses, authorizations and approvals, including all Drug Approval Applications and Regulatory Approvals, INDs, establishment license applications, drug master files, applications for designation as an "Orphan Product(s)" under the Orphan Drug Act, for "Fast Track" status under

Section 506 of the FDCA (21 U.S.C. § 356) or for a Special Protocol Assessment under Section 505(b)(4)(B) and (C) of the FDCA (21 U.S.C. § 355(b)(4)(B)) and all other similar filings (including counterparts of any of the foregoing in any country or region in the Territory); and (b) all supplements and amendments to any of the foregoing.

1.251 **"Related Collaboration Compound"** means, with respect to each Lead Collaboration Compound, any Collaboration Candidate that is an Additional Compound with respect to such Lead Collaboration Compound, including any salt form, polymorph, crystalline form, hydrate, solvate or formulation thereof.

1.252 **"Replacement Assay"** has the meaning set forth in Section 4.11.3.

1.253 **"Replacement Compound Designation"** has the meaning set forth in Section 4.7.1.

1.254 **"Replacement Expiration Date"** has the meaning set forth in Section 4.7.1.

1.255 **"Research Plan"** means the written plan agreed upon as such by the Parties as of the Execution Date that describes the research activities to be carried out in, and the objectives for, the research program to be conducted by the Parties during the Research Program Term, as may be amended from time to time in accordance with the terms of this Agreement.

1.256 **"Research Program"** means the research program to be conducted by the Parties during the Research Program Term pursuant to the Research Plan and the Annual Research Plans.

1.257 **"Research Program Tail Period"** means the eighteen (18)-month period beginning on the day after the last day of the Research Program Term; provided that, if and only if the entire Agreement is terminated by either Party pursuant to Section 11.2.1, by AstraZeneca pursuant to Section 11.2.3 or by Targacept pursuant to Section 11.2.4, or if the Research Program is terminated by AstraZeneca pursuant to Section 11.2.2(a) (and not Section 11.2.2(b)), the effective date of such termination shall be the last day of the Research Program Tail Period. For purposes of clarity, if the Research Program or this Agreement is terminated for any other reason, the Research Program Tail Period shall survive.

1.258 **"Research Program Technology"** means, collectively, Targacept Research Program Technology, AstraZeneca Research Program Technology and, if made, developed or conceived in the conduct of the Research Program, Joint Technology.

1.259 **"Research Program Term"** has the meaning set forth in Section 4.1.2.

1.260 **"Research Project Team"** means a team established by the JRC pursuant to Section 2.2.5.

1.261 **"Research Workaround"** has the meaning set forth in Section 4.4.1.

1.262 **"Restricted Derivative Period"** means the period beginning as of the Effective Date and ending on (a) with respect to Ispronicline, the **[********]** of the **[********]**, (b) with respect to each Collaboration Compound, the **[********]** of the last day of **[********]**, (c) with respect each IND-Ready Option Candidate Drug, the **[********]** of the **[********]** for such Option Compound Candidate Drug and (d) with respect to each POC Option Candidate Drug, the **[********]** of the date **[********]** for such Option Compound Candidate Drug.

1.263 **"ROFN Collaboration"** means any transaction between Targacept or any of its Affiliates and a Third Party for the purpose of collaborating, or licensing such Third Party, to research, develop, commercialize or otherwise Exploit compounds or products for one or more ROFN Indications in the Territory, but excluding any transaction with (a) a Third Party involving (i) an agreement or arrangement (A) with a contract manufacturer solely to manufacture or (B) with a contract sales organization solely to promote products, (ii) any fee-for-service or sponsored research agreement or arrangement where Targacept retains rights to any resulting Technology or Patent Rights, or (iii) any other agreement or arrangement involving the payment to Targacept or any of its Affiliates of governmental research or grant funding or research or grant funding from a non-profit organization or (b)The Stanley Medical Research Institute.

1.264 **"ROFN Indication Opportunity"** has the meaning set forth in Section 5.10.3.

1.265 **"ROFN Indication Opportunity Notice"** has the meaning set forth in Section 5.10.3.

1.266 **"ROFN Indications"** means the prevention or treatment in humans of: (a) any major depressive disorder or dysthymic disorder; (b) any of (i) generalized anxiety disorder, (ii) obsessive-compulsive disorder, (iii) panic disorder, (iv) post-traumatic stress disorder or (v) social phobia; or (c) any bipolar disorder, in each case based on diagnostic criteria included in DSM-IV, ICD-10 or any other Diagnostic Manual in a Major Market Country.

1.267 **"ROFN Notice"** has the meaning set forth in Section 5.10.3.

1.268 **"ROFN Notice Period"** has the meaning set forth in Section 5.10.3.

1.269 **"Royalty-Bearing Claim"** has the meaning set forth in Section 6.6.1(b)(1).

1.270 **"Royalty-Bearing Product"** has the meaning set forth in Section 11.4.1(a).

1.271 **"Royalty-Bearing Terminated Compound"** has the meaning set forth in Section 11.4.1(a).

1.272 **"Royalty-Bearing Terminated AZ Product"** has the meaning set forth in Section 11.4.1(b).

1.273 **"Sales -Based Milestones"** has the meaning set forth in Section 6.6.1(c).

1.274 **"Schizophrenia"** means a condition having the diagnostic criteria for schizophrenia identified in DSM-IV, ICD-10 or any other Diagnostic Manual, but excluding CDS. When used as reference to a field (as distinguished from an indication), Schizophrenia means the treatment, prevention or diagnosis of such a condition.

1.275 **"Schizophrenia Expiration Date"** means the date, if any, from and after which Schizophrenia is no longer eligible to be an Option Indication or Principal Indication as determined in accordance with Sections 5.10.2(b)(2) or 5.10.2(d)(2).

1.276 **"Secondary Pharmacology Compound"** means any Selective Alpha7 Compound or Dual Pharmacology Compound. For purposes of clarity, any compound or product Derived from a Secondary Pharmacology Compound is also a Secondary Pharmacology Compound.

1.277 **"Selective Alpha7 Compound"** means a compound that **[********]** for the Alpha7 NNR that is at least **[********]**, including any salt form, polymorph, crystalline form, hydrate, solvate or formulation thereof.

1.278 **"Small Market Indication"** means each of the following: (a) Vascular Dementia; (b) Dementia due to HIV; (c) Dementia due to head trauma; (d) Dementia due to Parkinson's disease; (e) Dementia due to Huntington's disease; (f) Dementia due to Pick's disease; and (g) Dementia due to Creutzfeldt-Jakob disease; (h) Dementia due to other general medical conditions (including Dementia with Lewy Bodies); (i) substance induced Dementia; (j) Dementia due to multiple etiologies; in each case ((a) through (j)) based on diagnostic criteria included in DSM-IV, ICD-10 or any other Diagnostic Manual; (k) any Newly-Defined Cognitive Disorder or Associated Cognitive Impairment; provided that, in the case of (h) through (k), only if such Dementia, Newly-Defined Cognitive Disorder or Associated Cognitive Impairment has a patient population in the United States of **[********]** based on the findings of such pharmaceutical market research organization(s) as AstraZeneca may designate from time to time with Targacept's consent, not to be unreasonably withheld, conditioned or delayed; and (l) any Additional Small Market Indication. For purposes of clarity, Schizophrenia is not a Small Market Indication.

1.279 **"SMRI Agreement"** has the meaning set forth in Section 5.10.4.

1.280 **"sNDA"** means a Supplemental New Drug Application, as defined in the FDCA and applicable regulations promulgated thereunder.

1.281 **"Specified Personnel"** has the meaning set forth in Section 4.4.2.

1.282 **[********]**

1.283 **"Sublicensee"** means (a) with respect to AstraZeneca, any Third Party (other than an Affiliate or a Distributor) to which AstraZeneca grants a sublicense under the licenses granted under Section 8.1 in accordance with Section 8.3 or as otherwise permitted hereunder and (b) with respect to Targacept, any Third Party (other than an Affiliate) to which Targacept grants a sublicense under the licenses granted under Section 8.2.3 or as otherwise permitted hereunder.

1.284 **"Sunset Date"** means the later of (a) fifteen (15) months after the Effective Date and (b) if any meeting(s) are requested by Targacept pursuant to Section 3.3.2, the Notice Date (as such term in defined in Section 3.3.2), or such later date as the Parties may agree in writing.

1.285 **"Tail Period"** means the period beginning on the last day of the Research Program Term and ending on (a) the last day of the Research Program Tail Period, (b) with respect to a Collaboration Candidate that is not a Fully Screened Collaboration Candidate as of the last day of the Research Program Tail Period because it fails to meet clause (b) or clause (c) of Section 1.138, the date on which such Collaboration Candidate becomes a Fully Screened Collaboration Candidate (if clause (c) of this Section 1.285 does not apply) or (c) with respect to any Collaboration Candidate or Active+ Compound that is (i) the subject of an Additional Research Program that continues after the Research Program Tail Period during the remainder of the Tail Period, or (ii) selected by AstraZeneca prior to the end of the Research Program Tail Period (or, in the case of a Collaboration Candidate that becomes a Fully Screened Collaboration Candidate or that is generated or identified in an Additional Research Program after the end of the Research Program Tail Period, prior to the end of the Tail Period) for additional research activities pursuant to Section 4.8 during the remainder of the Tail Period, in each case ((i) and (ii)) the ARP Selection Date, whichever is later; provided that if and only if the entire Agreement is terminated by either Party pursuant to Section 11.2.1, by AstraZeneca pursuant to Section 11.2.3 or by Targacept pursuant to Section 11.2.4, or if the Research Program is terminated by AstraZeneca pursuant to Section 11.2.2(a) (and not Section 11.2.2(b)), the effective date of such termination shall be the last day of the Tail Period. For purposes of clarity, if the Research Program or this Agreement is terminated for any other reason, the Tail Period shall survive.

1.286 **"Targacept"** has the meaning set forth in the preamble.

1.287 **"Targacept Change of Control Notice"** has the meaning set forth in Section 15.1.1.

1.288 **"Targacept Cure Period"** has the meaning set forth in Section 5.10.2(b)(4).

1.289 **"Targacept Development Activities"** means, collectively, (a) during the Research Program Term and any Additional Research Program Term only, **[**********]** if, with

respect to any of the foregoing, such activity is set forth in the Research Plan or an Annual Research Plan or Additional Research Plan and (b) such Development activities as may be specified to be conducted by Targacept in any Product Development Plan (or amendment thereto) approved by Targacept's representatives and AstraZeneca's representatives on the JDC or ESC (without resort to the dispute resolution procedures set forth in Section 2.1.5). For purposes of clarity, in no event shall any activity be a Targacept Development Activity unless Targacept's representatives on the applicable Committee have approved the Targacept Development Budget for such activity.

1.290 **"Targacept Development Budget"** has the meaning set forth in Section 5.3.

1.291 **"Targacept Development Program Technology"** means any Technology made, developed or conceived by employees or consultants of Targacept, alone or jointly with Third Parties, in the conduct of any Development Program.

1.292 **"Targacept Excluded Patent Rights"** means, collectively, all Targacept Patent Rights that would not be infringed (and, with respect to any applications included in the Patent Rights, that if issued would not be infringed) by the Exploitation of any Collaboration Candidate, Active+ Compound, Collaboration Compound, Candidate Drug or Product or any Additional Compound (or Additional Product) with respect to any of the foregoing in the Field or in Schizophrenia by a Third Party in the absence of a license.

1.293 **"Targacept Indemnitees"** has the meaning set forth in Section 13.2.

1.294 **"Targacept Net Sales"** means Net Sales by Targacept and its Affiliates and Sublicensees.

1.295 **"Targacept Option Compound Development Plan"** means a written plan prepared by Targacept in accordance with Section 5.10.2(b)(6) that describes in detail the development activities that Targacept may, in its sole election, carry out in an effort to establish Option Compound Proof of Concept for an Option Compound for which the Parties did not agree to an Option Compound Development Plan.

1.296 **"Targacept Other Technology"** means any Technology Controlled by Targacept that is necessary or reasonably useful for (a) the conduct of the Research Program or any Additional Research Program by the Parties and (b) AstraZeneca to Exploit any Collaboration Compound, Candidate Drug or Product, or any Additional Compound or Additional Product with respect to any of the foregoing, including Ispronicline or any Ispronicline Product; provided that Targacept Other Technology excludes Targacept Pre-Phase IIb Program Technology, Targacept Research Program Technology, Targacept Development Program Technology and AstraZeneca Assigned Technology.

1.297 **"Targacept Patent Rights"** means any Patent Rights Controlled by Targacept or its Affiliates that contain one or more claims that cover (a) Targacept Technology, (b) any (i) Collaboration Candidate, Active+ Compound, Collaboration Compound, Candidate Drug or Product, (ii) Additional Compound or Derivative with respect to any of the foregoing, or (iii) product that contains any of the foregoing (including any Additional Product) or (c) the Exploitation of any of the foregoing ((a) and (b)) in the Field or in Schizophrenia.

1.298 **"Targacept Plan POC Notice"** has the meaning set forth in Section 5.10.2(f).

1.299 **"Targacept Pre-Phase IIb Program Technology"** means any Technology made, developed or conceived by employees or consultants of Targacept, alone or jointly with Third Parties, in the conduct of the Pre-Phase IIb Program.

1.300 **"Targacept Product Patent Rights"** means any Targacept Patent Rights that (a) contain one or more claims that cover one or more Collaboration Compounds, Candidate Drugs or Products (including Option Compound Candidate Drugs and Option Compound Products) or Additional Compounds or Additional Products with respect to any of the foregoing, or the Exploitation of one or more Collaboration Compounds, Candidate Drugs or Products (including Option Compound Candidate Drugs and Option Compound Products) or Additional Compounds or Additional Products with respect to any of the foregoing, and (b) do not contain any claims that cover any Compound, or the Exploitation of any Compound, that is Known by Targacept not to be a Collaboration Compound, Candidate Drug or Product (including any Option Compound Candidate Drug and Option Compound Product) or an Additional Compound or Additional Product with respect to any of the foregoing.

1.301 **"Targacept Proposal"** has the meaning set forth in Section 5.10.2(e)(3).

1.302 **"Targacept Proprietary Materials"** means any Proprietary Materials Controlled by Targacept and used by Targacept, or provided by Targacept for use, in the Pre-Phase IIb Program, the Research Program, any Additional Research Program or any Development Program.

1.303 **"Targacept Research Budget"** has the meaning set forth in Section 4.2.

1.304 **"Targacept Research Program Technology"** means any Technology made, developed or conceived by employees or consultants of Targacept, alone or jointly with Third Parties, in the conduct of the Research Program or any Additional Research Program.

1.305 **"Targacept Technology"** means, collectively, Targacept Pre-Phase IIb Program Technology, Targacept Research Program Technology, Targacept Development Program Technology, Targacept Other Technology and AstraZeneca Assigned Technology.

1.306 **"Technology"** means, collectively, inventions, discoveries, improvements, trade secrets and proprietary methods, whether or not patentable (including: (a) methods of production or use of, and structural and functional information pertaining to, compounds and (b) data, formulations, processes, techniques, know-how and results (including any negative results)) that are not generally known; provided that Pentad Technology shall not be Technology.

1.307 **"Term"** has the meaning set forth in Section 11.1.

1.308 **"Terminated AZ Compound"** means each of (a) Ispronicline, if Ispronicline becomes a Terminated Compound other than pursuant to Section 3.3.2(b)(2) or Section 11.2.1 (provided that, if Ispronicline becomes a Terminated Compound pursuant to Section 3.3.2(b)(2) or Section 11.2.1, it shall, notwithstanding the foregoing, be treated as a Terminated AZ Compound for purposes of Section 11.3.6(c)(i)), (b) any Option Compound Candidate Drug or Option Compound Product (other than an Other Licensed Compound or a product that contains an Other Licensed Compound) that becomes a Terminated Compound at any time (other than pursuant to Section 5.10.2(b)(4), 5.10.2(b)(5), 5.10.2(b)(6), 5.10.2(e)(2) or 5.10.2(f)), and (c) any other Candidate Drug or Product (other than an Other Licensed Compound or a product that

contains an Other Licensed Compound) that becomes a Terminated Compound (i) after the end of the Research Program and the Tail Period or (ii) earlier pursuant to Section 11.2.4 (solely if Targacept terminates this Agreement pursuant thereto), 11.2.5(a) and 11.2.6 (solely if Targacept terminates this Agreement pursuant thereto). For purposes of clarity, each Terminated AZ Compound is also a Terminated Compound, and any Candidate Drug (other than Ispronicline or an Option Compound Candidate Drug), or Product that contains any such Candidate Drug (other than an Ispronicline Product or an Option Compound Product), that becomes a Terminated Compound during the Research Program Term or the Tail Period (other than pursuant to Section 11.2.4 (solely if Targacept terminates this Agreement pursuant thereto), 11.2.5(a) and 11.2.6 (solely if Targacept terminates this Agreement pursuant thereto) shall be a Terminated Compound but not a Terminated AZ Compound. For purposes of clarity, a Partially-Terminated Product shall not be a Terminated AZ Compound.

1.309 **"Terminated Compounds"** means, subject to Section 4.9, collectively:

(a) (i) all Collaboration Candidates that during the Research Program Term are classified as Terminated Compounds by the JRC, (ii) all Fully Screened Collaboration Candidates that as of the end of the Research Program Term are not determined by the JRC or AstraZeneca to be Active+ Compounds, and (iii) each Unscreened Collaboration Candidate that, as of the later of the end of the Research Program Term and the **[********]** after the date that AstraZeneca has received all screening data and analyses generated in the Research Program for such Unscreened Collaboration Candidate, is not selected by AstraZeneca for additional research activities pursuant to Section 4.8;

(b) all (i) Collaboration Candidates that, during the Research Program Tail Period, are classified as Terminated Compounds by the JRC, and (ii) Fully Screened Collaboration Candidates that within **[********]** after the applicable meeting of the JRC (A) are not determined by the JRC or AstraZeneca to be Active+ Compounds and (B) are not selected by AstraZeneca for additional research activities pursuant to Section 4.8 during the remainder of the Tail Period;

(c) all Active+ Compounds and other Collaboration Candidates that, as of the end of the Research Program Tail Period, are not (i) designated as Lead Collaboration

Compounds (and are not Related Collaboration Compounds with respect to a Lead Collaboration Compound), (ii) the subject of an Additional Research Program that continues after the Research Program Tail Period during the remainder of the Tail Period, or (iii) selected by AstraZeneca prior to the end of the Research Program Tail Period (or, in the case of a Collaboration Candidate that becomes a Fully Screened Collaboration Candidate or that is generated or identified in an Additional Research Program after the end of the Research Program Tail Period, prior to the end of the Tail Period) for additional research activities pursuant to Section 4.8 during the remainder of the Tail Period;

(d) all Active+ Compounds and other Collaboration Candidates that are not designated as Lead Collaboration Compounds (and are not Related Collaboration Compounds with respect to a Lead Collaboration Compound) as of the end of the Tail Period (or, if later, the resolution of any dispute pursuant to Section 4.3.2 or as provided in Section 4.9);

(e) all Lead Collaboration Compounds that are replaced in the Collaboration Compound Pool pursuant to Section 4.7.1 after the end of the Research Program Tail Period, unless any such replaced Lead Collaboration Compound (or any Related Collaboration Compound with respect thereto) is a Related Collaboration Compound with respect to another Lead Collaboration Compound, in which case such compound shall be or remain a Related Collaboration Compound;

(f) all Option Compounds that become Terminated Compounds pursuant to Section 5.10.2;

(g) each Excluded Derivative as of the date it is determined to be an Excluded Derivative; and

(h) all other compounds or products expressly identified as a Terminated Compound pursuant to Section 2.2.4(l), 2.2.4(n), 3.3.2(b)(2), 4.3.2, 11.2.2(a), 11.3.1(a), 11.3.1(g), 11.3.2(a) and 11.3.3(a) of this Agreement;

including in each case ((a) through (h)), any salt form, polymorph, crystalline form, hydrate, solvate or formulation thereof.

Notwithstanding anything in this Agreement to the contrary, in no event shall (i) a Collaboration Candidate, Active+ Compound, Collaboration Compound, Candidate Drug or Product that would not be a Terminated AZ Compound (or a product that contains a Terminated AZ Compound) be or remain a Terminated Compound if it is or becomes (as a result of a subsequent designation of a Collaboration Compound or Candidate Drug) an Additional Compound with respect to a Collaboration Compound, Candidate Drug or Product that is not a Terminated Compound, (ii) an Excluded Zone Compound be or remain a Terminated Compound, unless such Excluded Zone Compound is or would be a Terminated AZ Compound or (iii) a Licensed Derivative with respect to Ispronicline become a Terminated Compound pursuant to clauses (a) through (e) of this Section 1.309.

For purposes of clarity, a Partially-Terminated Product is not a Terminated Compound.

1.310 **"Terminated Efforts Test"** has the meaning set forth in Section 11.2.7(a).

1.311 **"Territory"** means all countries of the world, but excluding, solely with respect to each Partially-Terminated Product, those Major Market Countries in which such Partially-Terminated Product becomes terminated, if any, pursuant to Section 11.2.5(b) or 11.2.5(c).

1.312 **"Third Party"** means a Person other than AstraZeneca and Targacept and their respective Affiliates.

1.313 **"Third Party Claim"** has the meaning set forth in Section 13.3.2.

1.314 **"Total Research Budget"** has the meaning set forth in Section 2.1.5(a).

1.315 **"Trademark"** means any trademark, trade dress, brand mark, trade name, brand name, logo or business symbol.

1.316 **"Triggering Event"** has the meaning set forth in Section 10.2.6.

1.317 **"Unexercised Option Compound"** means any Option Compound that is not a Terminated Compound and that Targacept has the right to Exploit outside the Collaboration pursuant to Section 5.10.2(b)(2) or 5.10.2(d)(2), including any salt form, polymorph, crystalline form, Prodrug (other than any such Prodrug that is an Excluded Zone Compound), metabolite

(other than any such metabolite that is an Excluded Zone Compound), hydrate, solvate or formulation thereof; provided that each Unexercised Option Compound, upon becoming an Unexercised Option Compound, shall cease to be an Option Compound.

1.318 **"Unscreened Collaboration Candidate"** means each Collaboration Candidate for which the screening set forth in the Research Plan to enable the JRC or AstraZeneca, as applicable, to determine whether the Active+ Criteria are satisfied has not been completed or for which such screening has been completed but the results have not been delivered to the JRC and AstraZeneca, in each case, as of the last day of the Research Program Term.

1.319 **"Valid Claim"** means any claim of (a) an issued unexpired patent that (i) has not been finally canceled, withdrawn, abandoned or rejected by any administrative agency or other body of competent jurisdiction, (ii) has not been permanently revoked, held invalid, or declared unpatentable or unenforceable in a decision of a court or other body of competent jurisdiction that is unappealable or unappealed within the time allowed for appeal, (iii) has not been rendered unenforceable through disclaimer or otherwise, and (iv) is not lost through an interference proceeding, or (b) a pending patent application, provided that (i) the application was filed and is being prosecuted in good faith and has not been abandoned or finally disallowed without the possibility of appeal or re-filing of the application and (ii) **[********]**.

1.320 **"Working Licensed Derivatives"** means, with respect to any particular Collaboration Compound, Candidate Drug (including Ispronicline and Option Compound Candidate Drugs) or Product (including Ispronicline Products and Option Compound Products) as of a particular date, (a) all Licensed Derivatives with respect thereto as of such date, other than Other Licensed Compounds, (i) on which, as of such date, AstraZeneca is using Commercially Reasonable Efforts to research, develop or commercialize anywhere in the Territory or (ii) that are Additional Compounds with respect to any such Licensed Derivative in clause (i) and (b) all Other Licensed Compounds with respect thereto as of such date.

2. ADMINISTRATION OF THE COLLABORATION

2.1 **Executive Steering Committee**.

2.1.1 **Establishment**. Targacept and AstraZeneca hereby establish the Executive Steering Committee. The ESC shall have and perform the responsibilities set forth in Section 2.1.4.

2.1.2 **Membership**. Each Party shall designate, in its sole discretion, **[********]** members to the ESC, who shall be members of its senior management. Unless otherwise agreed by the Parties, **[********]**. Each Party shall have the right at any time to substitute individuals, on a permanent or temporary basis, for any of its previously designated representatives to the ESC, by giving written notice to the other Party. Initial designees of the Parties to the ESC shall be as follows:

For Targacept: **[********]**

For AstraZeneca: **[********]**

2.1.3 **Meetings**.

(a) Schedule of Meetings; Agenda. The ESC shall establish a schedule of times for regular meetings, taking into account the planning needs of the Collaboration and its responsibilities. In addition, special meetings of the ESC may be convened by any member upon thirty (30) days (or, if such meeting is proposed to be conducted by teleconference, upon ten (10) days) written notice to the other members; provided that (i) notice of any such special meeting may be waived in writing at any time, either before, during or after such meeting, and such waiver shall be the equivalent to the giving of a valid notice hereunder, and (ii) attendance of any member at a special meeting shall constitute a valid waiver of notice from such member, unless such member attends the meeting for the express purpose of objecting to its conduct for failure to provide valid notice. In no event shall the ESC meet less frequently than **[********]** in each Calendar Year during the Term. Regular and special meetings of the ESC may be held in person or by teleconference or videoconference; provided that meetings held in person shall alternate between the respective offices of the Parties. Without expanding the foregoing, and where practicable, the ESC shall schedule its meetings so that they fall within three (3) weeks after meetings of the JRC and the JDC to enable efficient resolution of any matter for ESC consideration arising from such JRC and JDC meetings. The Chairman shall prepare and circulate to each ESC member an agenda for each ESC meeting not later than one (1) week prior to such meeting.

(b) Quorum; Voting; Decisions. At each ESC meeting (i) the participation of at least **[********]** members designated by each Party shall constitute a quorum and (ii) all members designated by each Party who are participating shall **[********]** vote on all matters before the ESC at such meeting. All decisions of the ESC shall be made by **[********]** vote. Alternatively, the ESC may act by written consent signed by at least **[********]** members designated by each Party. Whenever any action by the ESC is called for hereunder during a time period in which the ESC is not scheduled to meet, the Chairman shall cause the ESC to take the action in the requested time period by calling a special meeting to be conducted in person or by teleconference on not less than five (5) Business Days notice or by circulating a written consent. Representatives of each Party or of its Affiliates who are not members of the ESC may attend ESC meetings as non-voting observers with the consent of the other Party, which shall not be unreasonably withheld, conditioned or delayed.

(c) Minutes. The ESC shall keep minutes of its meetings that record in reasonable detail all decisions and all actions recommended or taken. Drafts of the minutes shall be prepared and circulated to the members of the ESC during the meeting, and the Parties shall alternate responsibility for the preparation and circulation of draft minutes. Each member of the ESC shall have the opportunity to provide comments on the draft minutes. The minutes shall be approved, disapproved and revised as necessary prior to the end of the applicable ESC meeting, provided that any member of the ESC shall have the right to withhold his or her consent with respect to any issue discussed during the meeting (*e.g.*, in the event the proper expertise or level of information for a decision was not available), and the minutes for such meeting may reflect a lack of consensus on an issue-by-issue basis, the person(s) responsible for resolving such matter and by what date such matter shall be resolved. Upon approval, final minutes of each meeting shall be circulated to the members of the ESC by the Chairman.

(d) Expenses. Targacept and AstraZeneca shall each bear all expenses of their respective ESC members related to their participation on the ESC and attendance at ESC meetings.

2.1.4 **Responsibilities**. The ESC shall be responsible for overseeing the conduct and progress of the Research Program and the Development of Candidate Drugs. Without limiting the generality of the foregoing, the ESC shall have the following responsibilities:

(a) overseeing the JRC's performance of its responsibilities and the JDC's performance of its responsibilities;

(b) resolving any disputes regarding (i) any amendment to the Research Plan, (ii) the formulation or amendment of any Annual Research Plan or, if applicable, Additional Research Plan, or the formulation, amendment of or update to any Product Development Plan, including in each case with respect to any budget contained in any such plan (or amendment or update), or (iii) whether a particular Collaboration Candidate satisfies the Active+ Criteria;

(c) reviewing data, reports or other information submitted to it by the JRC or JDC from time to time;

(d) resolving all JRC or JDC matters that are in dispute;

(e) resolving any dispute as to whether a milestone event under Section 6.5 has occurred;

(f) resolving any dispute as to whether, for a particular Option Compound, Option Compound Proof of Concept has been achieved;

(g) approving any Newly-Defined Cognitive Impairment or Associated Cognitive Impairment;

(h) providing a forum for coordinating the Parties' activities with respect to Partially-Terminated Products; and

(i) making such other decisions as may be delegated to the ESC pursuant to this Agreement or by mutual written agreement of the Parties after the Effective Date.

2.1.5 **Dispute Resolution**. The ESC members shall use reasonable efforts to reach agreement on any and all matters. In the event that, despite such reasonable efforts, agreement on a particular matter cannot be reached by the ESC within **[********]** (**[********]** in the case of Section 2.1.5(e)) after the ESC first meets to consider such matter (each such matter, a "**Disputed Matter**"), then **[********]** shall have the right to make the final decision with regard to such Disputed Matter except that **[********]** with regard to the following Disputed Matters (each an "**Excepted Decision**") which shall be resolved as set out below:

(a) a proposal, or a series of proposals, the cumulative effect of which would be, to (i) amend the Research Plan to reduce the aggregate FTE Costs and External Targacept R&D Costs as detailed in the Research Plan (the "**Total Research Budget**") by more than ten percent (10%); or (ii) adopt an Annual Research Plan that, or amend an Annual Research Plan so that it (A) provides for **[********]** the FTE Costs and External Targacept R&D Costs budgeted for that Contract Year in the Research Plan or (B) amends **[********]**. Any such Disputed Matter shall be referred to **[********]**, who shall promptly initiate discussions in good faith to resolve such Disputed Matter. If such Disputed Matter is not resolved by such individuals within **[********]** of the date that the ESC first met to consider such Disputed Matter, the proposal will be rejected and, in the case of any Disputed Matter with respect to the proposal(s) referenced in clause (ii)(A) above, the proposed Annual Research Plan or amendment thereto shall promptly be modified to provide for **[********]** the FTE Costs and External Targacept R&D Costs budgeted for that Contract Year in the Research Plan. For purposes of clarity, no such proposal shall be implemented without the prior written approval of both Parties. Notwithstanding anything in this Agreement to the contrary, in no event shall the Total Research Budget, or the sum of the aggregate Targacept Research Budgets, exceed Twenty-Six Million, Four Hundred Thousand Dollars (US $26,400,000) without AstraZeneca's prior written consent, or be less than Twenty-Three Million, Seven Hundred Sixty Thousand Dollars (US $23,760,000) without Targacept's prior written consent.

(b) any decision that would constitute a deviation from any of the terms of, or would require an amendment to, this Agreement (including any schedule hereto but excluding the Exhibit hereto). For purposes of clarity, the Agreement may be amended only in accordance with Section 17.6.

(c) a disagreement as to whether (i) a particular **[********]**; (ii) for a particular **[********]**; or (iii) a particular Collaboration Candidate **[********]**. Any such Disputed Matter shall be resolved in accordance with Section 14.3 (accelerated arbitration).

(d) a disagreement as to whether a particular condition meets the requirements set forth in any of clauses (a) through (e) of Section 1.187 or clauses (a) through (d) of Section 1.28, as applicable, to be approved by **[********]** as a Newly-Defined Cognitive Impairment or an Associated Cognitive Impairment (but for clarity, not to otherwise challenge any such approval or designation). Any such Disputed Matter shall be resolved in accordance with Section 14.3 (accelerated arbitration).

(e) a disagreement as to whether the activities proposed for any Product Development Plan, or any update or amendment thereto, **[********]** hereunder. If the ESC is unable to resolve any such Disputed Matter, such matter shall be resolved in accordance with Section 14.3 (accelerated arbitration); provided that, if Targacept maintains that the activities allocated to AstraZeneca under a Product Development Plan (or under such plan as updated or amended) **[********]** Targacept shall submit such Disputed Matter to accelerated arbitration in accordance with Section 14.3 within fifty-five (55) days after the date that the ESC first met to consider such Disputed Matter. In the event that Targacept (i) approves a Product Development Plan (or, as applicable, an update or amendment thereto) in the JDC or the ESC, or (ii) does not approve a Product Development Plan (or, as applicable, an update or amendment thereto or, upon the occurrence of a tollgate, disputes any failure by AstraZeneca to update or amend the applicable Product Development Plan) but fails to submit such Disputed Matter to accelerated arbitration in accordance with Section 14.3 within such fifty-five (55)-day period, **[********]** with respect thereto (but, for purposes of clarity, **[********]** any such Product Development Plan (or such plan as updated or amended) and shall not **[********]**; provided that, with respect to any such Product Development Plan (or any such update or amendment thereto), **[********]** such Product Development Plan (or, if earlier, any update or amendment to such Product Development Plan), whereupon the procedures set forth in this Section shall be repeated. References in this Agreement to AstraZeneca development tollgates mean development tollgates that apply across its internal development programs and not solely to Development Programs hereunder. In the event this Section applies, AstraZeneca shall be entitled to either (A) **[********]** under a Product Development Plan or any amendment thereto

approved by the ESC whether or not such plan or such amendment [********] or (B) if [********] applicable fifty-five (55)-day period [********], except where such Disputed Matter relates to the Product Development Plan for [********] or any amendment thereto, in which case [********]. For purposes of clarity, during any such suspension with respect to a Collaboration Compound, Candidate Drug (including Ispronicline) or Product (including an Ispronicline Product), AstraZeneca shall [********] such Collaboration Compound, Candidate Drug or Product for purposes of Section 5.5.1 and such period of [********] shall not count against the twelve (12)-month period set forth in Section 11.2.7.

(f) a disagreement as to whether a particular [********]. Any such Disputed Matter shall be resolved in accordance with Section 14.3 (accelerated arbitration).

2.2 **Joint Research Committee**.

2.2.1 **Establishment**. Targacept and AstraZeneca hereby establish the Joint Research Committee. The JRC shall have and perform the responsibilities set forth in Section 2.2.4.

2.2.2 **Membership**. Each Party shall designate, in its sole discretion, **[********]**members to the JRC (which members shall be employees of such Party). Unless otherwise agreed by the Parties,**[********]**. Each Party shall have the right at any time to substitute individuals, on a permanent or temporary basis, for any of its previously designated representatives to the JRC, by giving written notice to the other Party; provided that, with respect to each representative designated by Targacept, Targacept shall not, during the Research Program Term or the Tail Period, substitute for such representative, an individual who does not hold a substantially similar position within Targacept or, for so long as such representative is employed by Targacept, who does not have substantially similar or greater experience with respect to NNRs as such representative. Initial designees of the Parties to the JRC shall be as follows:

For Targacept: **[********]**

For AstraZeneca: **[********]**

2.2.3 **Meetings**.

(a) Schedule of Meetings; Agenda. The JRC shall establish a schedule of times for regular meetings, taking into account the planning needs of the Research Program and its responsibilities. In addition, special meetings may be convened by any member upon thirty (30) days (or, if such meeting is proposed to be conducted by teleconference, upon ten (10) days) written notice to the other members; provided that (i) notice of any such special meeting may be waived at any time, either before or after such meeting, and such waiver shall be the equivalent to the giving of a valid notice hereunder, and (ii) attendance of any member at a special meeting shall constitute a valid waiver of notice from such member, unless such member attends the meeting for the express purpose of objecting to its conduct for failure to provide valid notice. In no event shall the JRC meet less frequently than **[********]** times in each Calendar Year during the Research Program Term and any Additional Research Program Term. Regular and special meetings of the JRC may be held in person or by teleconference or videoconference; provided that, unless otherwise agreed by the JRC, meetings held in person shall alternate between the respective offices of the Parties. The Chairman shall prepare and circulate to each JRC member an agenda for each JRC meeting not later than one (1) week prior to such meeting.

(b) Quorum; Voting; Decisions. At each JRC meeting, (i) the participation of at least **[********]** members designated by each Party shall constitute a quorum and (ii) all members designated by each Party who participate shall **[********]** vote on all matters before the JRC at such meeting. All decisions of the JRC shall be made by **[********]** vote. Alternatively, the JRC may act by written consent signed by at least **[********]** members designated by each Party. Whenever any action by the JRC is called for hereunder during a time period in which the JRC is not scheduled to meet, the Chairman shall cause the JRC to take the action in the requested time period by calling a special meeting or by circulating a written consent. Representatives of each Party or of its Affiliates who are not members of the JRC (including the Patent Coordinators) may attend JRC meetings as non-voting observers with the consent of the other Party, which shall not be unreasonably withheld, conditioned or delayed. The Parties shall use reasonable efforts to reach consensus on matters properly before the JRC but, to the extent that that the JRC is unable to resolve any such matter, unless otherwise provided in this Agreement, such matter shall be referred to the ESC to be resolved in accordance with Section 2.1.5.

(c) Minutes. The JRC shall keep minutes of its meetings that record all decisions and all actions recommended or taken in reasonable detail. Drafts of the minutes shall be prepared and circulated to the members of the JRC during the meeting, and the Parties shall alternate responsibility for the preparation and circulation of draft minutes. Each member of the JRC shall have the opportunity to provide comments on the draft minutes. The minutes shall be approved, disapproved and revised as necessary prior to the end of the applicable JRC meeting, provided that any member of the JRC shall have the right to withhold his or her consent with respect to any issue discussed during the meeting (*e.g.*, in the event the proper expertise or level of information for a decision was not available), and the minutes for such meeting may reflect a lack of consensus on an issue-by-issue basis, the person(s) responsible for resolving such matter and by what date such matter shall be resolved. Upon approval, final minutes of each meeting shall be circulated to the members of the JRC by the Chairman.

(d) Expenses. Targacept and AstraZeneca shall each bear all expenses of their respective JRC members related to their participation on the JRC and attendance at JRC meetings.

2.2.4 **Responsibilities**. The JRC shall be responsible for overseeing the conduct and progress of the Research Program. Without limiting the generality of the foregoing, the JRC shall have the following responsibilities:

(a) preparing or directing the preparation of and approving all Annual Research Plans, including the Targacept Research Budget;

(b) subject to Section 4.2, preparing, or directing the preparation of, and approving amendments to the Research Plan or any Annual Research Plans as it deems appropriate in furtherance of the objectives of the Research Program as set forth in Section 4.1.1 and the Research Plan;

(c) subject to Section 4.8.2, preparing, or directing the preparation of, and approving any Additional Research Plan or amendment thereto, including the applicable ARP Budget;

(d) determining the steps to be taken in accordance with Section 4.4.1 upon the occurrence of a Material Unexpected Technical Research Problem;

(e) monitoring the progress of each Annual Research Plan and of each Party's activities thereunder, including performance against the relevant Targacept Research Budget, identifying potential overruns and, subject to Section 4.2, where appropriate approving changes to such Targacept Research Budget;

(f) monitoring the progress of each Additional Research Plan and of each Party's activities thereunder, including performance against the relevant ARP Budget, identifying potential overruns and, subject to Section 4.8.2, where appropriate approving changes to such ARP Budget;

(g) providing a forum for consensual decision making with respect to the Research Program;

(h) appointing a Research Project Team (or, if it deems appropriate, multiple Research Project Teams), and overseeing the activities of, advising and considering recommendations from each such Research Project Team;

(i) reviewing data, reports or other information submitted by either Party with respect to work conducted in the Research Program;

(j) preparing for the ESC on at least a quarterly basis a progress report for the Research Program in reasonable detail and providing to the ESC such additional information as it may request;

(k) subject to Section 2.1.5(a), approving amendments to the Active+ Criteria as it deems appropriate in furtherance of the objectives of the Research Program;

(l) without limiting AstraZeneca's rights under Article 4, determining whether any Collaboration Candidate satisfies the Active+ Criteria; provided that the JRC shall, promptly (and in any event not later than its next regularly scheduled meeting) following any failure by a Collaboration Candidate to meet any of the Active+ Criteria required to be met for such compound to be an Active+ Compound, classify such Collaboration Candidate as a

Terminated Compound unless the JRC specifically elects to conduct further research on such Collaboration Candidate on a priority basis in furtherance of the objectives of the Research Program;

(m) without limiting AstraZeneca's rights under Article 4, determining the order in which Collaboration Candidates and Active+ Compounds shall progress through additional screens under the Research Program or any Additional Research Program;

(n) evaluating the continued screening or advancement of Collaboration Candidates in the Collaboration and classifying as a Terminated Compound each Collaboration Candidate (including each Unscreened Collaboration Candidate) for which it considers continued screening or advancement in the Collaboration impractical or inadvisable because of failure of such Collaboration Candidate to meet standards or criteria (other than Minimum Binding Affinity or Active+ Criteria) set forth in the Research Plan or any Annual Research Plan or Additional Research Plan (including, by way of example only, DMPK, preliminary drug safety, chemical stability) or for any other reason; provided, however, that, notwithstanding anything in this Agreement to the contrary, AstraZeneca shall have the right, in its sole discretion, to resolve any dispute with respect to any such evaluation or classification in the JRC without escalation to the ESC pursuant to Section 2.2.3(b) or resort to the dispute resolution procedures set forth in Section 2.1.5 or Article 14;

(o) reviewing publications and presentations with respect to any Research Program, Additional Research Program, Development Program or any Collaboration Compound, Candidate Drug or Product;

(p) without limiting AstraZeneca's rights under Article 4 or 5, nominating Collaboration Compounds for further Development by AstraZeneca as Candidate Drugs;

(q) maintaining an updated list of Terminated Compounds during the Research Program Term and Tail Period, based on information provided by the Parties; and

(r) making any other decisions as may be delegated to the JRC pursuant to this Agreement or by mutual written agreement of the Parties after the Effective Date.

2.2.5 **Research Project Teams**. The JRC shall establish a Research Project Team (and may, from time to time during the Research Program Term as it deems appropriate, establish multiple Research Project Teams) to conduct various aspects of the Annual Research Plans and the Additional Research Plans. Each Party shall have such representation on each such Research Project Team as is appropriate to the responsibilities of such Research Project Team as assigned by the JRC and consistent with the terms of this Agreement; provided that **[********]**. Each Party shall make its initial designation of its representatives not later than thirty (30) days after such JRC determination; provided that any such designation by Targacept shall include the Specified Personnel, consistent with their experience and expertise as well as the job descriptions set out in Schedule 4.4.2 hereto. Either Party may change its designees on any Research Project Team at any time on written notice to the other Party; provided that, if any of the Specified Personnel is a Targacept representative on a Research Project Team, Targacept shall not, during the Research Program Term, substitute or reduce his or her participation in a Research Project Team, or in the conduct of the Research Program, except as provided in Section 4.4.2. Each Research Project Team shall have such responsibilities as may be assigned to it by the JRC and shall report to the JRC.

2.3 **Joint Development Committee**.

2.3.1 **Establishment**. Targacept and AstraZeneca hereby establish the Joint Development Committee. The JDC shall have and perform the responsibilities set forth in Section 2.3.4.

2.3.2 **Membership**. Each Party shall designate, in its sole discretion, **[********]** members to the JDC (which members shall be employees of such Party). Unless otherwise agreed by the Parties, **[********]**. Each Party shall have the right at any time to substitute individuals, on a permanent or temporary basis, for any of its previously designated representatives to the JDC by giving written notice to the other Party. Initial designees of the Parties to the JDC shall be as follows:

For Targacept: **[********]**

For AstraZeneca: **[********]**

2.3.3 **Meetings**.

(a) Schedule of Meetings. The JDC shall establish a schedule of times for regular meetings, taking into account the planning needs of each Development Program and its responsibilities. In addition, special meetings may be convened by any member in good faith and for good cause or by the Chairman for any reason upon thirty (30) days (or, if such meeting is proposed to be conducted by teleconference, upon ten (10) days) written notice to the other members; provided that (i) notice of any such special meeting may be waived at any time, either before or after such meeting, and such waiver shall be the equivalent to the giving of a valid notice hereunder, and (ii) attendance of any member at a special meeting shall constitute a valid waiver of notice from such member, unless such member attends the meeting for the express purpose of objecting to its conduct for failure to provide valid notice. In no event shall the JDC meet less frequently than **[********]** times in each Calendar Year during the Term. Regular and special meetings of the JDC may be held in person or by teleconference or videoconference; provided that meetings held in person shall alternate between the respective offices of the Parties. The Chairman shall prepare and circulate to each JDC member an agenda for each JDC meeting at least one (1) week prior to such meeting.

(b) Quorum; Voting; Decisions. At each JDC meeting, (i) the participation of at least two (2) members designated by each Party shall constitute a quorum and (ii) all members designated by each Party who are participating shall **[********]** vote on all matters before the JDC at such meeting. All decisions of the JDC shall be made by **[********]** vote. Alternatively, the JDC may act by written consent signed by at least **[********]**members designated by each Party. Whenever any action by the JDC is called for hereunder during a time period in which the JDC is not scheduled to meet, the Chairman shall cause the JDC to take the action in the requested time period by calling a special meeting or by circulating a written consent. Representatives of each Party or of its Affiliates who are not members of the JDC (including the Patent Coordinators) may attend JDC meetings as non-voting observers with the consent of the other Party, which shall not be unreasonably withheld, conditioned or delayed. The Parties shall use reasonable efforts to reach consensus on matters properly before the JDC

but to the extent that the JDC is unable to resolve any matter before it, such matter shall be referred to the ESC to be resolved in accordance with Section 2.1.5.

(c) Minutes. The JDC shall keep minutes of its meetings that record all decisions and all actions recommended or taken in reasonable detail. Drafts of the minutes shall be prepared and circulated to the members of the JDC during the meeting, and the Parties shall alternate responsibility for the preparation and circulation of draft minutes. Each member of the JDC shall have the opportunity to provide comments on the draft minutes. The minutes shall be approved, disapproved and revised as necessary prior to the end of the applicable JDC meeting, provided that any member of the JDC shall have the right to withhold its consent with respect to any issue discussed during the meeting (*e.g.*, in the event the proper expertise or level of information for a decision was not available), and the minutes for such meeting may reflect a lack of consensus on an issue-by-issue basis, the person(s) responsible for resolving such matter and by what date such matter shall be resolved. Upon approval, final minutes of each meeting shall be circulated to the members of the JDC by the Chairman.

(d) Expenses. Targacept and AstraZeneca shall each bear all expenses of their respective JDC members related to their participation on the JDC and attendance at JDC meetings.

2.3.4 **Responsibilities**. The JDC shall be responsible for overseeing the Development of Candidate Drugs and the conduct and progress of each Development Program (but not, for purposes of clarity, the Pre-Phase IIb Program). Without limiting the generality of the foregoing, the JDC shall have the following responsibilities:

(a) preparing, or directing the preparation of, and approving all Product Development Plans, including any Targacept Development Budgets;

(b) preparing, or directing the preparation of, and approving updates or amendments to any Product Development Plan (including any Targacept Development Budget) as it deems appropriate in furtherance of the Development of Candidate Drugs and the Commercialization of Products;

(c) monitoring the progress of the Development of each Candidate Drug in accordance with, and of each Party's activities under, such Candidate Drug's Product Development Plan;

(d) determining the steps to be taken in accordance with Section 5.5.2 upon the occurrence of a Material Unexpected Technical Development Problem;

(e) overseeing the activities of, advising and considering recommendations from, any Development Project Team;

(f) reviewing data, reports or other information submitted by either Party with respect to work conducted in any Development Program;

(g) when requested by the ESC, preparing for the ESC a progress report for a Development Program in reasonable detail and providing to the ESC such additional information with respect thereto as it may request;

(h) without limiting AstraZeneca's rights under Article 4 or 5, determining whether and when to (A) commence further Development of a Collaboration Compound as a Candidate Drug, (B) commence or continue Development of an Option Compound Candidate Drug or (C) discontinue any such Development, in each case ((A) through (C), subject to Section 5.5.1;

(i) reviewing publications and presentations with respect to any Research Program, Additional Research Program, Development Program or any Collaboration Compound, Candidate Drug or Product; and

(j) making such other decisions as may be delegated to the JDC pursuant to this Agreement or by mutual written agreement of the Parties after the Effective Date.

2.3.5 **Development Project Teams**. For each Development Program, AstraZeneca may, from time to time during the Term as it deems appropriate, establish one or more Development Project Teams to coordinate Targacept Development Activities, if any, pursuant to the applicable Product Development Plan. Each Party shall have representation on each such Development Project Team as is appropriate to the responsibilities of such

Development Project Team as assigned by AstraZeneca and consistent with the terms of this Agreement; provided that **[********]**. Each Party shall make its initial designation of its representatives not later than thirty (30) days after such determination. Either Party may change its designees to any Development Project Team at any time upon written notice to the other Party. Each Development Project Team shall have such responsibilities as may be assigned to it by AstraZeneca and shall report to the JDC.

2.4 **Establishment and Function of CCC**.

2.4.1 **Establishment**. If Targacept exercises a Co-Promotion Option, Targacept and AstraZeneca shall establish the Commercial Coordination Committee as soon as practicable, and in any event within**[********]**, following the exercise by Targacept of such Co-Promotion Option. The CCC shall have and perform the responsibilities set forth in Section 2.4.4.

2.4.2 **Membership**. Each Party shall designate, in its sole discretion, **[********]** members to the CCC (which members shall be employees of such Party). Unless otherwise agreed by the Parties, **[********]**. Each Party shall have the right at any time to substitute individuals, on a permanent or temporary basis, for any of its previously designated representatives to the CCC by giving written notice to the other Party.

2.4.3 **Meetings**.

(a) Schedule of Meetings; Agenda. The CCC shall establish a schedule of times for regular meetings, taking into account the planning needs for the Co-Promotion of Co-Promoted Products and its responsibilities. In addition, special meetings may be convened by any member of the CCC in good faith and for good cause or by the Chairman for any reason upon thirty (30) days (or, if such meeting is proposed to be conducted by teleconference, upon ten (10) days) written notice to the other members; provided that (i) notice of any such special meeting may be waived at any time, either before or after such meeting, and such waiver shall be the equivalent to the giving of a valid notice hereunder, and (ii) attendance of any member at a special meeting shall constitute a valid waiver of notice from such member, unless such member attends the meeting for the express purpose of objecting to its conduct for failure to provide valid notice. If formed, in no event shall the CCC meet less frequently than **[********]** times per Calendar Year. Regular and special meetings of the CCC may be held in

person or by teleconference or videoconference. The Chairman shall prepare and circulate to each CCC member an agenda for each CCC meeting not later than one (1) week prior to such meeting.

(b) Quorum; Voting; Decisions. At each CCC meeting, (i) the participation of at least **[********]** members designated by each Party shall constitute a quorum and (ii) all members designated by each Party who are participating shall **[********]** vote on all matters before the CCC at such meeting. Alternatively, the CCC may act by written consent signed by at least **[********]** members designated by each Party. The Parties shall use reasonable efforts to ensure that consensus is reached on matters before the CCC but, to the extent that the CCC is unable to resolve any matter before it, such matter shall be resolved by AstraZeneca's members on the CCC; provided that **[********]**, such unresolved matter shall be referred to the Vice President, Business and Commercial Development of Targacept (or such other officer with comparable seniority and responsibility with respect to Targacept's promotional activities as Targacept may designate in writing to AstraZeneca from time to time), and the U.S. Vice President, Commercial Operations of AstraZeneca Pharmaceuticals, LP (or such other officer with comparable seniority and responsibility with respect to AstraZeneca's promotional activities as AstraZeneca may designate in writing to Targacept from time to time), who shall promptly initiate discussions in good faith to resolve such unresolved matter. If such unresolved matter is not resolved by such individuals within **[********]** of the date that the CCC first met to consider such unresolved matter, **[********]**; and provided further that neither the CCC nor AstraZeneca shall have the authority to determine the resolution of a dispute arising in connection with a Party's breach under a Co-Promotion Agreement, which shall be governed by the dispute resolution process set forth therein. Whenever any action by the CCC is called for hereunder during a time period in which the CCC is not scheduled to meet and is not able to meet in a timely manner, the Chairman shall, in consultation with the Vice President, Business and Commercial Development of Targacept (or such other officer with comparable seniority and responsibility with respect to Targacept's promotional activities as Targacept may designate in writing to AstraZeneca from time to time), take the action in the requested time period. Representatives of each Party or of its Affiliates who are not members of the CCC may attend CCC meetings as non-voting observers with the consent of the other Party, which shall not be unreasonably withheld, conditioned or delayed.

(c) Minutes. The CCC shall keep minutes of its meetings that record all decisions and all actions recommended or taken in reasonable detail. Drafts of the minutes shall be prepared and circulated to the members of the CCC during the meeting, and the Parties shall alternate responsibility for the preparation and circulation of draft minutes. Each member of the CCC shall have the opportunity to provide comments on the draft minutes. The minutes shall be approved, disapproved and revised as necessary prior to the end of the applicable CCC meeting, provided that any member of the CCC shall have the right to withhold its consent with respect to any issue discussed during the meeting (*e.g.*, in the event the proper expertise or level of information for a decision was not available), and the minutes for such meeting may reflect a lack of consensus on an issue-by-issue basis, the person(s) responsible for resolving such matter and by what date such matter shall be resolved. Upon approval, final minutes of each meeting shall be circulated to the members of the CCC by the Chairman.

(d) Expenses. Targacept and AstraZeneca shall each bear all expenses of their respective CCC members related to their participation on the CCC and attendance at CCC meetings.

2.4.4 **Responsibilities**. The CCC shall be responsible for overseeing Co-Promotion Activities. Without limiting the generality of the foregoing and except as otherwise specified in a Co-Promotion Agreement, the CCC shall have the following responsibilities:

(a) the development and discussion of strategies for the promotion and marketing of each Co-Promoted Product to the Co-Promotion Target Audience in the Co-Promotion Territory, including allocation of responsibilities for Co-Promotion Activities;

(b) implementing the Product Commercialization Plan with respect to the Co-Promotion Activities for the Co-Promoted Product in the Co-Promotion Territory;

(c) the preparation of short-term and long-term sales forecasts for Co-Promoted Products in the Co-Promotion Territory;

(d) presenting sales forecasts and the results of all Commercialization efforts for Co-Promoted Products in the Co-Promotion Territory to the Parties as needed, but no less often than four (4) times per Calendar Year;

(e) coordinating the Detailing efforts of both Parties with respect to the Co-Promotion Target Audience in the Co-Promotion Territory with respect to Co-Promoted Products;

(f) providing a forum for discussing all recalls, market withdrawals and any other corrective actions related to Co-Promoted Products in the Co-Promotion Territory;

(g) receiving and providing to the Parties sales reports with respect to the Co-Promotion Target Audience pertaining to Co-Promoted Products in the Co-Promotion Territory; and

(h) performing such activities as may be delegated to the CCC pursuant to this Agreement, in any Co-Promotion Agreement or by mutual written agreement of the Parties after the Effective Date.

2.5 **Alliance Management**.

2.5.1 **Collaboration Managers**. Each Party shall appoint a person(s) who shall oversee contact between the Parties for all matters related to the Collaboration between meetings of the ESC, JRC, JDC or CCC and shall have such other responsibilities as the Parties may agree in writing after the Effective Date (each, a "**Collaboration Manager**"). Each Party may replace its Collaboration Manager at any time by notice in writing to the other Party. The initial Collaboration Managers shall be:

For Targacept: **[********]**

For AstraZeneca: **[********]**

2.5.2 **Executive Review**. The Chief Executive Officer of Targacept and the Vice President of the Neuroscience Therapeutic Area and the Vice President of the CNS and Pain Control Research Area of AstraZeneca shall meet at least **[********]** to review and discuss generally the status of the Research Program, any Additional Research Programs and each Development Program.

2.5.3 **Interactions Between Committees and Internal Teams**. The Parties recognize that AstraZeneca possesses an internal structure (including various committees, teams

and review boards) that will be involved in administering AstraZeneca's activities under this Agreement. Nothing contained in this Article 2 shall prevent a Party from making routine day-to-day decisions relating to the conduct of those activities for which it has a performance or other obligations hereunder, in each case in a manner consistent with the then-current applicable plans and budgets and the terms and conditions of this Agreement. Each committee shall establish procedures to facilitate communications between such committee and the relevant internal committee, team or board of AstraZeneca in order to maximize the efficiency of the committees and the performance AstraZeneca of its obligations and the exercise of its rights under this Agreement, including by requiring appropriate members of such committee to be available at mutually convenient times and places and upon reasonable prior notice for making appropriate oral reports to, and responding to reasonable inquiries from, the relevant internal committee, team or board.

3. PRE-PHASE IIb PROGRAM

3.1 **Implementation of the Pre-Phase IIb Program**. AstraZeneca shall use Commercially Reasonable Efforts to perform the non-clinical and clinical studies and other activities with respect to Ispronicline set forth in the Pre-Phase IIb Plan prior to the Sunset Date. Except for activities expressly assigned to Targacept in the Pre-Phase IIb Plan (if any) and such other activities as Targacept may agree to undertake, in its sole discretion, at AstraZeneca's reasonable request in support of the Pre-Phase IIb Program, AstraZeneca shall have the sole right and responsibility to conduct the Pre-Phase IIb Program at its sole expense.

3.2 **Cooperation and Reporting**. Scientists at Targacept shall reasonably cooperate in the performance of the Pre-Phase IIb Program and, subject to the terms of this Agreement and any confidentiality obligations to Third Parties, shall, if reasonably requested by AstraZeneca, and at Targacept's cost, furnish AstraZeneca with such data, information and materials (including Proprietary Materials) in Targacept's possession or control as are reasonably necessary for AstraZeneca to perform its obligations under the Pre-Phase IIb Plan. During the Pre-Phase IIb Period, AstraZeneca shall (a) keep Targacept reasonably informed regarding the progress of the Pre-Phase IIb Program (including by providing updates (which may be by telephone) to Targacept at least quarterly and, with respect to any particular activity conducted in

the Pre-Phase IIb Program, promptly after AstraZeneca determines the results achieved for such activity), (b) respond (which response may be by telephone) in a reasonable manner to all reasonable queries raised by Targacept in connection with the Pre-Phase IIb Program and (c) upon completion of each of the studies to be conducted in the Pre-Phase IIb Program, prepare and deliver to Targacept a final written report of the results of each such study.

3.3 **Conclusion of Pre-Phase IIb Program**.

3.3.1 **Election to Commence Development of Ispronicline**. If AstraZeneca determines, in its sole discretion, to proceed with further Development of Ispronicline (including any Ispronicline Product) pursuant to the Product Development Plan for Ispronicline (as the same may have been amended prior to such notification in accordance with Section 2.3.4), AstraZeneca shall, on or prior to the Sunset Date, provide Targacept with written notice of such determination and AstraZeneca shall (a) within twenty (20) days of such notice, pay Targacept the milestone in Section 6.5.1(a)(3) in the amount of Twenty Million Dollars (US $20,000,000), (b) from the date of such notice (the "**Commencement Date**"), use Commercially Reasonable Efforts to Develop and Commercialize Ispronicline in accordance with Section 5.5.1(a), (c) as provided in Section 6.4.1, pay (to the extent not already paid), all of the aggregate FTE Costs for all FTEs and External Targacept R&D Costs relating to the Research Program incurred in accordance with the Targacept Research Budget during the Pre-Phase IIb Period, such amount to be paid in accordance with Section 6.4.3.

3.3.2 **Election to Not Commence Development of Ispronicline**. If AstraZeneca determines, in its sole discretion based on the results of the Pre-Phase IIb Program and all other available information with respect to Ispronicline, to not proceed with the further Development of Ispronicline, AstraZeneca shall, on or prior to the Sunset Date, and in any event promptly following its determination, provide Targacept with written notice of such determination and, if so requested by Targacept, shall participate in a meeting, to include senior executives from both Targacept and AstraZeneca, to discuss such termination and the reasons therefor. AstraZeneca shall have the right, on written notice to Targacept within **[********]** following the end of such meeting, or such longer period as the Parties may agree in writing (the last day of such period, or, if earlier, the date of such notice, the "**Notice Date**"), to elect, (x)

notwithstanding its earlier notice, to proceed with further Development of Ispronicline pursuant to the Product Development Plan for Ispronicline (as the same may have been amended prior to such notification in accordance with Section 2.3.4), in which event Section 3.3.1 shall apply, with the date of such notice being the Commencement Date, or (y) to not proceed with the further Development of Ispronicline, in which event, (i) AstraZeneca may elect to terminate this Agreement in accordance with Section 11.2.1(a) or (ii) subject to Targacept's right to terminate this Agreement in accordance with Section 11.2.1(b), AstraZeneca may indicate to Targacept its desire to proceed with the conduct of the Research Program and continue this Agreement, in which event Section 3.3.2(b) applies.

(a) Termination of this Agreement. If (i) AstraZeneca elects to terminate this Agreement in accordance with Section 11.2.1(a) or (ii) Targacept elects to terminate this Agreement in accordance with Section 11.2.1(b), then, notwithstanding anything in this Agreement to the contrary, (A) AstraZeneca shall not be required to pay (1) the milestone in Section 6.5.1(a)(3) in the amount of Twenty Million Dollars (US $20,000,000) or any other milestone payments under Section 6.5, or (2) any of the aggregate FTE Costs for all FTEs and External Targacept R&D Costs relating to the Research Program incurred by or on behalf of Targacept in connection with the Research Program, (B) to the extent any such milestone payments or FTE Costs have been paid, such amounts shall be refunded to AstraZeneca in accordance with Section 11.3.1, (C) as consideration for the assignment of rights in and to the AstraZeneca Pre-Phase IIb Program Technology and AstraZeneca Pre-Phase IIb Program Patent Rights under Section 11.3.1(c), Targacept shall pay to AstraZeneca Five Million Dollars (US $5,000,000) in accordance with 11.3.1 and (D) the other consequences of such termination set forth in Sections 11.3.1 and 11.3.6 shall apply.

(b) Continuation of Research Program. If (x) AstraZeneca elects to not proceed with the Development of Ispronicline but to continue this Agreement as set forth in Section 3.3.2(y)(ii) and (y) Targacept does not elect to terminate this Agreement in accordance with Section 11.2.1(b), Targacept shall have the right, at its sole election, to either: (A) terminate all specific diligence obligations with respect to Ispronicline under this Agreement (including Section 5.5.1(a)) such that Ispronicline becomes a Collaboration Compound hereunder, or (B) terminate this Agreement with respect to Ispronicline such that Ispronicline becomes a

Terminated Compound (but, for purposes of clarity, not a Terminated AZ Compound), provided that upon either election ((A) or (B)), AstraZeneca shall have the right to terminate this Agreement within ten (10) Business Days of delivery of notice of such election by Targacept in accordance with Section 11.2.1(a). If AstraZeneca does not elect to terminate this Agreement pursuant to Section 11.2.1(a), the conduct of the Research Program and all other activities under this Agreement shall continue except with respect to Ispronicline as set forth in this Section 3.3.2(b).

(1) If Targacept elects, pursuant to Section 3.3.2(b)(y)(A), to terminate all specific diligence obligations with respect to Ispronicline under this Agreement, (A) Ispronicline shall become a Collaboration Compound (and, if subsequently Exploited by or on behalf of AstraZeneca, subject to payment of royalties and milestones as Ispronicline, but otherwise to be treated in all respects under this Agreement as a Collaboration Compound), (B) AstraZeneca shall not be required to pay the milestone in Section 6.5.1(a)(3) in the amount of Twenty Million Dollars (US $20,000,000) or any other milestone payments under Section 6.5 with respect to Ispronicline or any Ispronicline Products, and (C) AstraZeneca shall pay (to the extent not already paid), all of the aggregate FTE Costs for all FTEs and External Targacept R&D Costs relating to the Research Program incurred in accordance with the Targacept Research Budget during the Pre-Phase IIb Period, such amount to be paid in accordance with Section 6.4.3.

(2) If Targacept elects, pursuant to Section 3.3.2(b)(y)(B), to terminate this Agreement with respect to Ispronicline, and AstraZeneca does not elect to terminate this Agreement pursuant to Section 11.2.1(a), (A) Ispronicline shall become a Terminated Compound (but not a Terminated AZ Compound), Targacept shall have the right to Exploit Ispronicline outside the Field and Sections 11.3.1(c), 11.3.1(d), and 11.3.6(c)(1) shall apply with respect to Ispronicline, (B) AstraZeneca shall not be required to pay the milestone in Section 6.5.1(a)(3) in the amount of Twenty Million Dollars (US $20,000,000) or any other milestone payments under Section 6.5 with respect to Ispronicline or any Ispronicline Products, (C) as consideration for the assignment of rights in and to the AstraZeneca Pre-Phase IIb Program Technology and

AstraZeneca Pre-Phase IIb Program Patent Rights granted under this Agreement, Targacept shall pay to AstraZeneca Five Million Dollars (US $5,000,000), and (D) AstraZeneca shall pay (to the extent not already paid), all of the aggregate FTE Costs for all FTEs and External Targacept R&D Costs relating to the Research Program incurred in accordance with the Targacept Research Budget during the Pre-Phase IIb Period, such amount to be paid in accordance with Section 6.4.3, provided that AstraZeneca shall have the right to offset the Targacept payment set forth in clause (C), if not already paid to AstraZeneca, against AstraZeneca's payment under this clause (D).

4. RESEARCH PROGRAM

4.1 **Implementation of the Research Program**.

4.1.1 **Objectives of the Research Program**. The objectives of the Research Program shall be the discovery and development of Active+ Compounds for consideration by AstraZeneca so as to permit AstraZeneca to select **[********]**Collaboration Compounds suitable for further scientific evaluation as provided in the Research Plan. Except for the AstraZeneca Research Activities, which activities AstraZeneca shall (x) have the sole right and responsibility to conduct at its sole expense and (y) coordinate through the JRC with Targacept's activities in the Research Program, Targacept shall have the sole right and responsibility to conduct the Research Program. Targacept shall have the right to contract with Third Parties for the conduct of any activities under the Research Plan, an Annual Research Plan or an Additional Research Plan, subject to the prior approval of AstraZeneca, not to be unreasonably withheld, conditioned or delayed; provided that Targacept shall (a) before engaging any contractor to perform such activities, **[********]** in good faith **[********]** perform such activities, (b) not unreasonably select a Third Party to conduct such activities **[********]**, and (c) remain responsible for the performance of its obligations hereunder with respect to such activities (unless conducted by AstraZeneca). For purposes of clarity, it would not be reasonable for AstraZeneca to withhold its consent to Targacept's contracting certain activities to a particular contractor solely because AstraZeneca wishes to perform such activities. In the event that Targacept selects AstraZeneca to conduct any activity that was originally assigned to Targacept (or a Third Party engaged by Targacept) in the Research Plan, an Annual Research Plan or an Additional Research Plan, and

for which the corresponding expense was included in the applicable Targacept Research Budget, such Targacept Research Budget shall be reduced by the amount budgeted for such activity in the applicable plan. For purposes of clarity, in addition to AstraZeneca Research Activities, AstraZeneca shall have the right, in its sole discretion, to conduct research and development activities other than AstraZeneca Research Activities with respect to Collaboration Compounds, Candidate Drugs and Products during the Term, including by generating Derivatives with respect thereto. Any Derivatization of Ispronicline during the Research Program Term shall be subject to the notice to, coordination by and oversight of the JRC.

4.1.2 **Research Program Term**. The Research Program shall commence on the Effective Date and, unless terminated earlier in accordance with Section 11.2.2, shall continue until the earlier of (a) the fourth anniversary of the Effective Date, or such later date as the Parties may agree in writing, and (b) the end of the Term (the "**Research Program Term**"); provided that, for purposes of clarity, if the Research Program is terminated pursuant to Section 11.2.2, the effective date of such termination shall be the last day of the Research Program Term.

4.2 **Research Plan; Annual Research Plans**. The Research Plan and the Annual Research Plan for the first Contract Year shall be agreed upon by the Parties as of the Execution Date. For each Contract Year during the Research Program Term commencing with the second Contract Year, an Annual Research Plan shall be prepared by or at the direction of, and shall be approved by, the JRC, with any disputes with respect to it being submitted to the ESC for resolution in accordance with Section 2.1.5. The Parties shall manage the preparation of each Annual Research Plan in a manner designed to obtain approval no later than thirty (30) days prior to the end of the then-current Contract Year. Each Annual Research Plan shall: (a) set forth (i) the research objectives and activities to be performed for the Contract Year covered by the Annual Research Plan with reasonable specificity, (ii) the Party that shall be responsible for performing such activities, (iii) a timeline for such activities, and (iv) with respect to those activities for which Targacept is responsible, the number of FTEs estimated to be required to perform such activities, the corresponding FTE Cost for such activities, and the estimated External Targacept R&D Costs for such activities (if any), broken down on a Contract Quarter basis (collectively, a "**Targacept Research Budget**"); and (b) be consistent with the Research Plan and the terms of this Agreement. Without limiting the generality of the foregoing, the

objectives of each Annual Research Plan shall include, as appropriate from time to time during the Research Program Term and consistent with the Research Plan, conducting the necessary research activities to identify or generate Collaboration Candidates that show promise to be Active+ Compounds, to identify or generate Active+ Compounds, and select Collaboration Compounds, that show promise for Development as Candidate Drugs and Commercialization as Products, and to recommend Collaboration Compounds for Development as Candidate Drugs. The Research Plan and any Annual Research Plan may be amended from time to time by the JRC pursuant to Section 2.2.4; provided, however, that in the event that such an amendment would change or otherwise increase Targacept's activities under the applicable plan (as distinguished from an amendment that modifies the objectives of a plan but not Targacept's activities), resulting in an expense to Targacept not contemplated in the then-current Total Research Budget or applicable then-current Targacept Research Budget, which additional expense is **[********]**, Targacept shall advise AstraZeneca in good faith of the aggregate additional cost of such activities and the Parties through the JRC shall agree on a corresponding amendment to the Total Research Budget or applicable Targacept Research Budget to reflect the commercially reasonable costs of such activities **[********]**, such matter shall promptly be referred to an Expert in accordance with Section 14.4 (expedited arbitration).

4.3 **Screening and Designation of Compounds**.

4.3.1 **Screening and Prioritization of Compounds**. During the Research Program Term, Targacept shall use good faith and Commercially Reasonable Efforts to identify and screen for Minimum Binding Affinity all Compounds that show promise to be potential Collaboration Candidates. For the avoidance of doubt, any compounds that both (a) are Derived from a Collaboration Candidate, Active+ Compound, Collaboration Compound or Candidate Drug (other than Ispronicline (or any Licensed Derivatives with respect thereto) after the end of the Research Program Term or the Restricted Derivative Period for Ispronicline, whichever occurs first (for purposes of clarity, any Licensed Derivatives with respect to Ispronicline (or any Licensed Derivatives with respect thereto) shall be included in this Section 4.3.1 solely for screening purposes and not for purposes of expanding the definition of Collaboration Candidate), and other than any Option Compound Candidate Drug) by or on behalf of a Party during the Research Program Term or the Tail Period and (b) either have Minimum Binding Affinity or are

not the **[********]** where an objective of the **[********]**, in whole or in part, was **[********]** shall be Collaboration Candidates, subject to screening under the Research Program or an Additional Research Program. The JRC shall prioritize for each Contract Quarter the order in which Collaboration Candidates and Active+ Compounds shall progress through additional screens and activities under the Research Program or any Additional Research Program, provided that the JRC shall prioritize the screening of any Derivatives of a Collaboration Candidate that do not satisfy clause (b) of the definition of Minimum Binding Affinity in Section 1.184 so as to enable the JRC to determine whether each such Derivative is an Active+ Compound promptly following the determination that such Derivative does not satisfy clause (b) of such definition. For the avoidance of doubt, with respect to any Compounds in the Research Program or any Additional Research Program, Targacept shall have the right, in any Contract Quarter, to screen and conduct research activities under the Research Program or any Additional Research Program with respect to Collaboration Candidates and Active+ Compounds that are not scheduled for screening in such Contract Quarter under the applicable Annual Research Plan or Additional Research Plan at its own cost and expense; provided that Targacept shall provide AstraZeneca with advance written notice of any such activities, which notice shall specify those Collaboration Candidates and Active+ Compounds with respect to which Targacept plans to screen and conduct research activities, and the specific screening and research activities to be performed, during such Calendar Quarter; and provided further that such activities shall not derogate from or otherwise adversely affect Targacept's conduct of activities under the Research Program during such Contract Quarter with respect to such Collaboration Candidates or Active+ Compounds, or screening or other activities that are scheduled for such Contract Quarter. For purposes of clarity, all Technology resulting from such additional research activities shall be Targacept Research Technology or Joint Technology, as applicable, and all Compounds that are subject to, or generated or identified under, such additional research activities, shall remain subject to this Article 4 and the other terms and conditions of this Agreement. Notwithstanding the foregoing, neither Party shall, in connection with the Research Program, make any Derivatives (including by conducting further optimization) of a Collaboration Candidate that that does not satisfy clause (b) of the definition of Minimum Binding Affinity in Section 1.184 unless such Collaboration Candidate is an Active+ Compound.

4.3.2 **Designation of Active+ Compounds**. The JRC or, on written notice to Targacept, AstraZeneca, shall have the right at any time during the Research Program Term or the Tail Period to determine that a Collaboration Candidate that is not a Terminated Compound satisfies the Active+ Criteria, whereupon such Collaboration Candidate shall become an Active+ Compound; provided, however, that Targacept shall have the right, for a period of **[********]** after such determination, to challenge such determination by referring its dispute with respect to such determination to the ESC pursuant to Section 2.1.5(c), and then, if applicable, to an Expert for resolution in accordance with Section 14.3 (accelerated arbitration); provided further that, for clarity, such Collaboration Candidate shall continue to be an Active+ Compound unless and until Targacept challenges such determination within such **[********]** period and such Collaboration Candidate is finally determined by the ESC (in accordance with Section 2.1.5(c)) or an Expert (in accordance with Section 14.3) to not satisfy the Active+ Criteria, in which event, if such putative Active+ Compound had been designated a Lead Collaboration Compound, (i) it and all Related Collaboration Compounds with respect to it shall be Terminated Compounds (unless, with respect to any such Related Collaboration Compound, such Related Collaboration Compound is a Related Collaboration Compound to another Lead Collaboration Compound that has not been terminated) and (ii) AstraZeneca shall have the right to designate a replacement Lead Collaboration Compound pursuant to Section 4.7.1.

4.3.3 **Designation of Lead and Related Collaboration Compounds**. Subject to Section 4.7.1, the JRC or AstraZeneca may at any time during the Research Program Term or the Tail Period designate any Active+ Compound that is not a Terminated Compound as a Lead Collaboration Compound. With respect to each such designated Lead Collaboration Compound, any Related Collaboration Compounds with respect thereto shall be automatically deemed to be designated as a Collaboration Compound. Upon each designation of a Lead Collaboration Compound by AstraZeneca, the Parties shall cooperate to prepare a list of all Related Collaboration Compounds with respect thereto. For purposes of clarity, all Licensed Derivatives with respect to Ispronicline shall be Candidate Drugs and not Collaboration Compounds, unless AstraZeneca, in its sole discretion, elects to designate such a Licensed Derivative as a Lead Collaboration Compound.

4.4 **Conduct of Research Program**.

4.4.1 **Targacept Diligence**. Targacept shall use Commercially Reasonable Efforts to conduct the Research Program in accordance with the Research Plan and to achieve the objectives set forth therein and in Section 4.1.1 and to do so in accordance with the Total Research Budget and each Targacept Research Budget, including by committing such resources, including FTEs, as are specified in each Annual Research Plan to conduct its activities set forth therein; provided that Targacept shall have the right to notify the JRC promptly upon becoming aware of a scientific or technical problem outside of its reasonable control (which, for purposes of clarity, shall not include issues arising from [********]) that is likely, notwithstanding Targacept's exercise of Commercially Reasonable Efforts, to preclude Targacept from completing any activity or meeting any objective set forth in an Annual Research Plan with the estimated FTEs (or 110% of the FTEs) (a "**Material Unexpected Technical Research Problem**"). As part of such notification, Targacept shall provide the JRC with a reasonably detailed description of such Material Unexpected Technical Research Problem, together with its good faith belief as to the steps necessary to complete such activity or meet such objective, if practicable at all, in light of such Material Unexpected Technical Research Problem. Upon receipt of such notification, the JRC shall then meet [********] to determine whether to modify the Annual Research Plan as it applies to such activity or objective to: [********] take such other action as may be mutually acceptable to the Parties (each a "**Research Workaround**"); provided that, following notification of a Material Unexpected Technical Research Problem with respect to an activity or objective, Targacept shall not be required to perform such activity or seek to achieve any such objective unless and until the JRC acts to address such Material Unexpected Technical Research Problem. Except as otherwise provided in a Research Workaround or in Section 6.4.3, Targacept shall be solely responsible for any FTE Costs or External Targacept R&D Costs for an activity that exceed the amount set forth in the Targacept Research Budget for such activity or the Total Research Budget in the aggregate. For purposes of clarity, subject to Targacept's rights to conduct additional activities under the Research Program as provided in Section 4.3.1, no modification to the Annual Research Plan (or Targacept Research Budget with respect thereto) will be implemented unless agreed by the JRC pursuant to Section 2.2.4, in accordance with the proviso set forth in Section 4.2.

4.4.2 **Specified Personnel**. The scientific and technical personnel of Targacept considered by AstraZeneca to be important for the conduct of the Research Program (the

"**Specified Personnel**") are listed on Schedule 4.4.2, **[********]**. Without limiting the foregoing, Targacept shall, consistent with **[********]** Schedule 4.4.2 and their experience and expertise, assign each Specified Personnel (or, in the event any Specified Personnel is no longer employed by Targacept, an individual who holds a substantially similar position within Targacept and who has substantially similar or greater expertise with respect to NNRs generally) to conduct those activities under the Research Program (including service on a Research Project Team) that are relevant to his or her area(s) of expertise without regard to other projects that Targacept may be conducting itself or with or for a Third Party. For so long as each of the Specified Personnel is employed by Targacept, as and to the extent the Research Plan requires, **[********]**, and Targacept shall not materially reduce the responsibilities or activities of any Specified Personnel with respect to the Research Program without the prior written approval of AstraZeneca, which approval shall not be unreasonably withheld, conditioned or delayed. In the event that any Specified Personnel is no longer employed by Targacept or is otherwise incapable of helping Targacept perform its obligations under this Agreement (e.g., becomes disabled), the Parties shall meet and discuss in good faith how best to proceed, provided in no event shall this discontinuation of employment or incapacity of any Specified Personnel with Targacept in and of itself be deemed a breach by Targacept of this Agreement or a basis for termination by AstraZeneca pursuant to Section 11.2.4. In any event, Targacept shall continue to be responsible for performing the Research Program in accordance with this Agreement, and any consent or agreement by AstraZeneca pursuant to this Section 4.4.2 shall not be deemed to be a waiver of any failure of Targacept to conduct the Research Program under this Agreement.

4.4.3 **AstraZeneca Diligence**. AstraZeneca shall use Commercially Reasonable Efforts to conduct the AstraZeneca Research Activities set forth in each Annual Research Plan, if any.

4.4.4 **Compliance and Funding**. Each Party shall perform its obligations under each Annual Research Plan in good scientific manner and in compliance with all Applicable Laws. For purposes of clarity, with respect to each activity performed under an Annual Research Plan that will or would reasonably be expected to be submitted to a Regulatory Authority in support of a Regulatory Filing or Drug Approval Application, the Party performing such activity shall comply in all material respects with the regulations and guidance of the FDA that constitute

Good Laboratory Practice or Good Manufacturing Practices (or, if and as appropriate under the circumstances, International Conference on Harmonization (ICH) guidance or other comparable regulation and guidance of any Regulatory Authority in any country or region in the Territory). Subject to Targacept's right to receive the funding described in Section 6.4, each Party shall be solely responsible for paying the salaries, benefits and all other costs and expenses of its employees and the fees and all other costs and expenses payable to any consultants or Third Party contractors, in each case conducting its activities under Annual Research Plans or Additional Research Plans.

4.4.5 **Cooperation**. Scientists at Targacept and AstraZeneca shall cooperate in the performance of the Research Program and, subject to the terms of this Agreement and any confidentiality obligations to Third Parties, shall, if requested by the other Party and at its own cost, exchange such data, information and materials as are reasonably necessary for the other Party to perform its obligations under any Annual Research Plan.

4.5 **Records**.

4.5.1 **Record Keeping**.

(a) Research Program Records. Each Party shall maintain records of its activities in the Research Program in sufficient detail, in good scientific manner and otherwise in a manner that reflects all work done and results achieved. Subject to Article 7, each Party shall provide the other Party with access during normal business hours and upon reasonable advance notice to inspect and copy such records to the extent reasonably required for the performance of the requesting Party's obligations under this Agreement.

(b) Record Keeping Policies. Without limiting the generality of Section 4.5.1(a), each Party agrees to maintain a policy that requires its employees and consultants to record and maintain all data and information developed during the Research Program in a manner designed to establish the earliest date of invention or diligence to reduction to practice. At a minimum, the policy shall require such individuals to record such data and information by them in standard laboratory notebooks that are dated and corroborated by non-inventors on a regular, contemporaneous basis.

4.6 **Reports**. Each Party shall keep the JRC regularly informed of the progress of its activities under the Research Program and any Additional Research Program. Without limiting the generality of the foregoing, Targacept shall, **[********]**, provide: (a) reports to the JRC and AstraZeneca in reasonable detail regarding the status of its activities under the Research Program and any Additional Research Program, **[********]**; (b) advise the JRC and AstraZeneca of its identification of Collaboration Candidates (and any Derivatives of Ispronicline); (c) provide the JRC and AstraZeneca with the results of activities conducted in the Research Program and any Additional Research Program with respect to each Collaboration Candidate (and any Derivative of Ispronicline) so as to enable AstraZeneca and the JRC to determine (i) whether such Collaboration Candidate (or such Derivative) is an Active+ Compound and (ii) **[********]**; (d) provide the JRC and AstraZeneca with a complete list of all Terminated Compounds of which it is aware as of such date; (e) **[********]** and AstraZeneca copies of any applications for Patent Rights, results of freedom to operate analyses and other information with respect to the intellectual property status of any Collaboration Candidates or Active+ Compounds (including a description of all license agreements regarding, and other agreements relating to Targacept's Control (including any financial or other obligations with respect thereto) of any such Collaboration Candidate or Active+ Compound, which agreements Targacept shall deliver to AstraZeneca (with financial terms redacted to the extent AstraZeneca has no responsibility therefor) upon request); provided that Targacept shall not be required to provide privileged information with respect to such intellectual property status unless and until procedures reasonably acceptable to Targacept are in place to protect such privilege; and (f) provide the JRC and AstraZeneca with such additional information with respect to the foregoing ((a) through (e)) known to Targacept as may be reasonably requested from time to time by the JRC or AstraZeneca. AstraZeneca shall provide the JRC and Targacept, **[********]**, with: (i) reports in reasonable detail regarding the status of all AstraZeneca Research Activities and such additional information with respect thereto known to AstraZeneca as may be reasonably requested from time to time by the JRC or Targacept; (ii) notice of all Collaboration Candidates and **[********]**; (iii) notice of all Derivatives with respect to Ispronicline Derived prior to the end of the Research Program Term or the Restricted Derivative Period for Ispronicline, whichever occurs first; (iv) the results of activities conducted in the Research Program and any Additional Research Program with respect to each Collaboration Candidate so as to enable the JRC to determine (A)

whether such Collaboration Candidate is an Active+ Compound, and (B) the order in which Active+ Compounds should progress through additional screens and the additional screens to be performed; and (v) a complete list of all Terminated Compounds of which it is aware as of such date. In addition, AstraZeneca shall provide Targacept with a copy of the final report (or if no final report is produced, the latest available report) for each AstraZeneca Research Activity; provided that, if such AstraZeneca Research Activity is a non-clinical study designed to be conducted in accordance with GLP, such copy shall be signed. For purposes of clarity, (x) if either Party is required pursuant to this Section 4.6 to provide a report, advisement, results or information to the JRC and provides such report, advisement, results or information to the representatives of the other Party on the JRC, such providing Party shall thereupon also be deemed to have provided such report, advisement, results or information to the other Party pursuant to this Section 4.6 or (y) all information provided by Targacept (including by its Patent Coordinator) to AstraZeneca's Patent Coordinator shall be deemed to have been provided to the JRC and AstraZeneca pursuant to clause (e) above.

4.7 **Collaboration Compound Pool**.

4.7.1 **Replacement of Lead Collaboration Compounds**. If, following the Collaboration Compound Pool Satisfaction Date but on or prior to the last day of the Tail Period (or, if later, resolution of any dispute pursuant to Section 4.3.2), the JRC or AstraZeneca designates an Active+ Compound as a Lead Collaboration Compound (a "**Lead Collaboration Compound Designation**"), AstraZeneca shall, not later than (i) thirty (30) days after the date on which Targacept delivers to AstraZeneca the written statement called for by Section 12.4 with respect to such Lead Collaboration Compound or (ii) such other date as the Parties may agree in writing (the "**Replacement Expiration Date**"), determine which existing Lead Collaboration Compound shall be replaced in the Collaboration Compound Pool with such Active+ Compound (each determination to replace an existing Lead Collaboration Compound, a "**Replacement Compound Designation**"). Each such Replacement Compound Designation shall be reflected in a written notice to Targacept on or before the applicable Replacement Expiration Date. Each Active+ Compound (and all Related Collaboration Compounds with respect thereto) that is the subject of a Lead Collaboration Compound Designation by AstraZeneca shall thereupon be included in the Collaboration Compound Pool as of the date of the applicable Lead Collaboration

Compound Designation, and each Lead Collaboration Compound (and all Related Collaboration Compounds with respect thereto) replaced in the Collaboration Compound Pool shall no longer be a Collaboration Compound on the date of the Replacement Compound Designation and, if such date is after the end of the Tail Period, such Lead Collaboration Compound shall become a Terminated Compound; provided that, notwithstanding the foregoing, if such replaced Lead Collaboration Compound or any Related Collaboration Compound with respect thereto is a Related Collaboration Compound with respect to another Lead Collaboration Compound, such compound shall be or remain a Related Collaboration Compound. If the JRC or AstraZeneca makes a Lead Collaboration Compound Designation under this Section 4.7.1 but a corresponding Replacement Compound Designation is not made on or prior to the Replacement Expiration Date, the Lead Collaboration Compound subject to the Lead Collaboration Compound Designation shall no longer be a Lead Collaboration Compound as of the Replacement Expiration Date and, if such date is after the end of the Research Program Tail Period, such Collaboration Compound shall become a Terminated Compound.

4.7.2 **Composition of Collaboration Compound Pool**. For purposes of clarity, (a) except as provided in Section 4.7.1 there can be no more than **[********]** Lead Collaboration Compounds in the Collaboration Compound Pool at any time (provided that, for purposes of clarity, AstraZeneca shall have the right to designate each such Lead Collaboration Compound and any or all Related Collaboration Compounds and Licensed Derivatives with respect thereto as Candidate Drugs under Article 5), (b) neither Ispronicline nor, except if designated by AstraZeneca pursuant to Section 4.3.3, any Licensed Derivative with respect thereto, shall count towards the Collaboration Compound Pool, (c) a Lead Collaboration Compound that is designated as a Candidate Drug other than Ispronicline shall continue to count towards the Collaboration Compound Pool, (d) no Terminated Compound or Option Compound (including any Option Compound Candidate Drug or any Option Compound Product) shall count towards the Collaboration Compound Pool and (e) until the Collaboration Compound Pool Satisfaction Date, all Collaboration Compounds so designated by the JRC or AstraZeneca shall be included in the Collaboration Compound Pool.

4.8 **Additional Research Program**.

4.8.1 **Scope of Additional Research Program**. Subject to Section 4.8.2, if requested by AstraZeneca: (a) prior to the later of the end of the Research Program Term and the **[********]** after the date that AstraZeneca has received all screening data and analyses generated in the Research Program for a particular Unscreened Collaboration Candidate, the Parties shall, during the Research Program Tail Period, undertake such additional research activities with respect to such Unscreened Collaboration Candidate selected prior to such date by AstraZeneca for such additional research activities and, in such event, the Parties shall use Commercially Reasonable Efforts to conduct such additional research activities so as to enable the JRC to determine whether such Unscreened Collaboration Candidate satisfies the Active+ Criteria promptly following the end of the Research Program Term; or (b) during the Research Program Term or the Tail Period, the Parties shall undertake such additional research activities with respect to any (i) Active+ Compound or (ii) any Collaboration Candidate that is Derived from an Active+ Compound, Collaboration Compound or Candidate Drug (other than any Option Compound Candidate Drug) during the Research Program or the Tail Period that are, in each case ((i) and (ii)), selected by AstraZeneca during the Research Program or the Tail Period for such additional research activities; in each case ((a) and (b)), as AstraZeneca reasonably determines are necessary or useful in connection with the selection of Collaboration Compounds or the designation of Candidate Drugs (each, an "**Additional Research Program**"); provided that, except as provided in Section 4.9 or as otherwise agreed in writing by the Parties, no Additional Research Program Term shall continue after **[********]** (such date, as may be extended pursuant to Section 4.9 or by the written agreement of the Parties, the "**ARP Selection Date**").

4.8.2 **Additional Research Plan**. Promptly following any request pursuant to Section 4.8.1, the JRC shall prepare a plan for such additional research activities, as may be amended from time to time in accordance with the terms hereof (each, an "**Additional Research Plan**"), which plan shall set forth (a) the research objectives for and activities to be performed in such period with reasonable specificity, (b) the Party that shall be responsible for performing each activity, (c) a timeline for each activity, and (d) with respect to those activities for which Targacept is responsible, the number of FTEs estimated to be required to perform such activities, the corresponding FTE Cost for such activities (provided that if such activities were performed under the Research Program, the FTE Cost for such activities under an Additional Research Plan

shall be substantially similar to the FTE Cost for such activities under the Research Program), and the estimated External Targacept R&D Costs for such activities, broken down on a Calendar Quarter basis (collectively the "**ARP Budget**"); provided that Targacept, without its consent, not to be unreasonably withheld, conditioned or delayed, shall not be required to undertake any activities that are materially different from those undertaken by Targacept in the course of the Research Program. Any Additional Research Plan (including any ARP Budget with respect thereto) may be amended (including, by the identification of additional compounds identified by AstraZeneca pursuant to Section 4.8.1) at any time by the JRC pursuant to Section 2.2.4; provided, however, that in the event that such an amendment would change or otherwise increase Targacept's activities under the applicable plan (as distinguished from an amendment that modifies the objectives of a plan but not Targacept's activities), resulting in an expense to Targacept not contemplated in the then-current ARP Budget, which additional expense is **[********]**, Targacept shall advise AstraZeneca in good faith of the aggregate additional cost of such activities and the Parties through the JRC shall agree on a corresponding amendment to the applicable ARP Budget to reflect the commercially reasonable costs of such activities **[********]**, such matter shall promptly be referred to an Expert in accordance with Section 14.4 (expedited arbitration).

4.8.3 **Implementation of an Additional Research Plan**. Each Additional Research Plan (and any amendment thereto) shall be implemented as if it were an Annual Research Plan and, with respect to all activities undertaken pursuant to such Additional Research Plan, Sections 4.4 to 4.7 (inclusive) shall apply and AstraZeneca shall reimburse Targacept for its FTE Costs and the External R&D Costs in accordance with ARP Budget, pursuant to Section 6.4.

4.9 **Disputes and Delays**. If (x) there is (a) any dispute as to **[********]**, (b) any delay in approving or dispute with respect to **[********]**, or (c) there is any delay **[********]**, and (y) AstraZeneca reasonably believes that such dispute or delay has, as a practical matter (*e.g.*, because AstraZeneca's access to data or results is delayed), shortened the period during which AstraZeneca is entitled to make a decision or election with respect to a particular compound, or otherwise exercise a right with respect to a particular compound, under this Agreement, AstraZeneca shall give written notice of its belief to Targacept. **[********]**. The

Parties shall thereafter negotiate in good faith an extension of the date on which AstraZeneca must make such decision or election or exercise such right with respect to such compound so that AstraZeneca shall have the full benefit of such period as though such dispute or delay had not occurred; provided that if, notwithstanding such good faith negotiation, the Parties are unable to agree on the terms of such extension within **[********]**, then AstraZeneca shall have the right, within **[********]**, to refer the matter to an Expert for resolution in accordance with Section 14.4 (expedited arbitration).

4.10 **Supply of Proprietary Materials**. From time to time during the Research Program Term and any Additional Research Program Term, either Party (the "**transferring Party**") may supply the other Party (the "**recipient Party**") with Proprietary Materials of the transferring Party for use in the Research Program or an Additional Research Program (as the case may be). In connection therewith, each recipient Party hereby agrees that (a) it shall not use such Proprietary Materials for any purpose other than exercising its rights or performing its obligations hereunder; (b) it shall use such Proprietary Materials only in compliance with all Applicable Laws; (c) it shall not transfer any such Proprietary Materials to any Third Party without the prior written consent of the transferring Party, except as expressly permitted hereby or, in the case of Targacept, except for any transfer to a Third Party engaged by a Party to perform services in the Research Program; provided that in no event shall such Proprietary Materials be transferred to a Third Party unless that Third Party has entered into a Confidentiality Agreement and a Material Transfer Agreement reasonably acceptable to the transferring Party; (d) the recipient Party shall not acquire any right, title or interest in or to such Proprietary Materials as a result of such supply by the transferring Party; and (e) upon the expiration or termination of the Research Program Term, or if there is an Additional Research Program, with respect to the Compound that is the subject thereof, upon the expiration or termination of the Tail Period, the recipient Party shall, if and as instructed by the Party, either destroy or return any such Proprietary Materials that are not the subject of the grant of a continuing license hereunder. For purposes of this Section 4.10, Proprietary Materials with respect to Collaboration Compounds and Candidate Drugs shall be deemed Proprietary Materials of AstraZeneca.

4.11 **Additional Compounds and Licensed Derivatives**.

4.11.1 **Disputes as to Designation of Additional Compounds or Licensed Derivatives**. In the event the Parties are unable to agree as to whether a compound or product is (a) an Additional Compound (including a Related Collaboration Compound) with respect to a Collaboration Compound, Candidate Drug or Product (or an Additional Product that contains such Additional Compound) or (b) a Licensed Derivative with respect to a Collaboration Compound, Candidate Drug or Product (or a Product that contains such Licensed Derivative), such matter shall be referred to an Expert for resolution in accordance with Section 14.3 (accelerated arbitration) and such compound or product shall **[********]**, as the case may be, unless and until such product or compound **[********]**; provided that **[********]**.

4.11.2 **Designation of Initial *in vivo* Assay for an Other NNR Compound**. If at any time, either Party believes in good faith, based on general consensus in the scientific community, that a certain validated assay is a predictor of therapeutic activity in the Field or Schizophrenia, as applicable, for an Other NNR Compound, such Party shall propose in writing to the other Party such assay, and the criteria (including the applicable dose) by which activity will be measured with respect to such assay. If the Parties are unable to agree as to (a) whether such assay is a predictor of therapeutic activity in the Field or Schizophrenia, as applicable, or (b) the activity criteria for such an assay, in each case ((a) and (b)), within sixty (60) days after such written proposal, such matter shall be referred to an Expert for resolution in accordance with Section 14.3 (accelerated arbitration). If any such assay is approved and designated, then from and after the date of such designation (which, for purposes of clarity, shall be the date the Parties agree on such assay or, in the event of a dispute, the date of the Expert's final decision pursuant to Section 14.3.2), such assay shall be employed for purposes of the definition of Additional Compound set forth in Section in Section 1.9(d)(iii). For each *in vivo* assay for an Other NNR Compound designated and approved pursuant to this Section 4.11.2 (i) during the Research Program Term or the Tail Period, the minutes of the next meeting of the JRC following such designation and approval shall identify such assay as having been designated and approved for such Other NNR Compound and the date of such designation and approval or (ii) after the end of the Tail Period, the minutes of the next meeting of the JDC following such designation and approval shall identify such assay as having been designated and approved for such Other NNR Compound and the date of such designation and approval.

4.11.3 **Disputes as to Replacement Assays**. In the event a Party desires to replace **[********]** with a different validated assay that (a) is **[********]**, than the existing assay or test with respect to the applicable NNR, based on general consensus in the scientific community, and (b) **[********]** such Party shall propose in writing to the other Party such replacement assay, and the criteria **[********]** with respect to such assay. If the Parties are unable to agree as to (i) whether any such proposed replacement assay (A) is **[********]** or (B) **[********]** or (ii) the **[********]**for such an assay, in each case ((i) and (ii)) **[********]**, such matter shall be referred to an Expert for resolution in accordance with Section 14.3 (accelerated arbitration). If any such replacement assay is approved and designated (such an approved replacement assay, a "**Replacement Assay**") for an existing assay, then from and after the date of such designation (which, for purposes of clarity, shall be the date the Parties agree on such Replacement Assay or, in the event of a dispute the date of the Expert's final decision pursuant to Section 14.3.2), such Replacement Assay shall **[********]**; provided that, with respect to any compound or product **[********]**, the then-existing assay shall **[********]**. For each Replacement Assay designated and approved pursuant to this Section 4.11.3 (A) during the Research Program Term or the Tail Period, the minutes of the next meeting of the JRC following such designation and approval shall identify such Replacement Assay as having been designated and approved and the applicable NNR and the date of such designation and approval or (B) after the end of the Tail Period, the minutes of the next meeting of the JDC following such designation and approval shall identify such Replacement Assay as having been designated and approved and the applicable NNR and the date of such designation and approval. For purposes of clarity, (x) **[********]** activity in the applicable Replacement Assay, and (y) **[********]** active in the applicable Replacement Assay.

5. DEVELOPMENT OF CANDIDATE DRUGS; COMMERCIALIZATION OF PRODUCTS

5.1 **Implementation of Development Programs**.

5.1.1 **Objectives of the Development Programs**. The objectives of the Development Programs, collectively, shall be the Development of Candidate Drugs in the Field and in Schizophrenia to enable the Commercialization of Products in the Field and in Schizophrenia in the Territory.

5.1.2 **Designation of Candidate Drugs**. Within **[********]** after the JRC nominates a Collaboration Compound as a Candidate Drug, the Chairman of the JRC shall cause the JRC to notify the JDC in writing and to provide to the JDC and AstraZeneca data, reports or other information in the JRC's or the Parties' possession that support its nomination. Thereafter, the Chairman of the JRC shall cause the JRC to provide the JDC and AstraZeneca with such additional data, other information and materials, including Proprietary Materials of the Parties as AstraZeneca may reasonably request; provided that for purposes of clarity, data, information and materials provided to the representatives of AstraZeneca on the JDC shall be deemed to have been provided to AstraZeneca pursuant to this Section 5.1.2. AstraZeneca shall have the right, in its sole discretion, at any time during the Term, to elect to further Develop any Collaboration Compound as a Candidate Drug based on such standards and criteria as it deems appropriate, irrespective of whether such Collaboration Compound was recommended by the JRC. If and when AstraZeneca decides to commence GLP Toxicology Studies for a Collaboration Compound, AstraZeneca shall notify Targacept in writing and the JDC shall prepare or direct the preparation of, and approve a Product Development Plan for such Collaboration Compound. For purposes of clarity, if AstraZeneca determines not to accept the JRC nomination of a Collaboration Compound as a Candidate Drug, or AstraZeneca otherwise does not elect to Develop a Collaboration Compound as a Candidate Drug (subject to AstraZeneca's diligence obligations pursuant to Section 5.5.1(b)), such Collaboration Compound shall continue to be a Collaboration Compound.

5.2 **Responsibility for Development and Commercialization of Candidate Drugs and Products**.

5.2.1 **In General**. Subject to Section 5.2.2 and except as provided in Section 3.1 with respect to the Pre-Phase IIb Program and Article 4 with respect to the Research Program and any Additional Research Program and except for the Targacept Development Activities, AstraZeneca shall have the sole right and responsibility, at its sole expense, for all aspects of the Development of Candidate Drugs (including Ispronicline and Option Compound Candidate Drugs) in accordance with the applicable Product Development Plans (as updated and amended

pursuant to Section 5.3), and all aspects of the Commercialization of Products (including Ispronicline Products and Option Compound Products) in accordance with the applicable Product Commercialization Plans, in the Field and in Schizophrenia in the Territory, including the conduct of: (a) all IND-enabling studies that are outside of the Research Program or any Additional Research Program or are not completed during the Research Program Term or the applicable Additional Research Program Term; (b) all activities related to studies and Clinical Trials (including Phase I Clinical Trials, Phase II Clinical Trials, Phase III Clinical Trials and any post-approval studies); (c) all activities relating to the manufacture and supply of Collaboration Compounds, Candidate Drugs and Products (including all required process development, formulation development and scale up work with respect thereto), in each case from and after the date a compound is designated as a Collaboration Compound; and (d) all pre-marketing, marketing, promotion, sales, distribution, import and export activities (including securing reimbursement, sales and marketing and conducting any post-marketing trials or databases and post-marketing safety surveillance) subject to Targacept's rights under Section 5.11.2 and, if such rights are exercised, the oversight of the CCC with respect to the Co-Promotion of Co-Promoted Products in the Co-Promotion Territory and the terms of each applicable Co-Promotion Agreement. Without limiting the generality of the foregoing, AstraZeneca shall have the sole right and responsibility, at its sole expense (except with respect to Co-Promotion Activities undertaken by Targacept, which shall be subject to Section 5.11.2), to (i) make all Regulatory Filings for Candidate Drugs and Products and file all Drug Approval Applications and otherwise seek all Regulatory Approvals for Products, as well as to conduct all correspondence and communications with Regulatory Authorities regarding such matters, and (ii) report all Adverse Events to Regulatory Authorities if and to the extent required by Applicable Laws, subject in each case to Section 5.9.3.

5.2.2 **Exceptions**. Notwithstanding Section 5.2.1, (a) Targacept shall (i) have the right, in its sole discretion and at its sole expense, to continue all or any portion of the Ongoing Ispronicline Trial in accordance with the protocol as it exists as of the Execution Date and (ii) complete the Clinical Trial ongoing as of the Execution Date designed to compare the bioavailability of the salt forms of Ispronicline known to Targacept as the 112 and 226 salts; provided that all data therefrom and results thereof shall be Targacept Other Technology and shall be delivered to AstraZeneca in such form and with such frequency as AstraZeneca may

reasonably request from time to time; and provided further that **[********]**, and (b) without limiting the foregoing, but except as provided in Section 16.17.3, AstraZeneca shall not be responsible for any costs or expenses incurred by Targacept with respect to the research and development of Ispronicline prior to the Effective Date.

5.3 **Product Development Plans**. A Product Development Plan for each Collaboration Compound for which AstraZeneca elects to commence GLP Toxicology Studies shall be prepared and approved as provided in Section 5.1.2. Each Product Development Plan shall: (a) set forth (i) the Development objectives and activities to be performed to progress to the next AstraZeneca development tollgate with reasonable specificity, (ii) a timeline for such activities, (iii) which activities, if any, are Targacept Development Activities, (iv) with respect to any such Targacept Development Activities, the number of FTEs estimated to be required to perform such activities, the corresponding FTE Cost, and the estimated External Targacept R&D Costs for such activities (if any), broken down on a Calendar Quarter basis (collectively, a "**Targacept Development Budget**"), and (v) the decision points and criteria required to pass the next AstraZeneca development tollgate; and (b) be consistent with the other terms of this Agreement. References in this Agreement to AstraZeneca development tollgates mean development tollgates that apply across its internal development programs and not solely to Development Programs hereunder. Each such Product Development Plan shall be reviewed from time to time by the JDC in accordance with AstraZeneca's internal milestones and tollgates and may be updated and amended from time to time by the JDC pursuant to Section 2.3.4, with any disputes with respect thereto submitted to the ESC for resolution in accordance with Section 2.1.5; provided, however, that in the event that such an update or amendment would change or otherwise increase Targacept's activities under the applicable plan (as distinguished from an update or amendment that modifies the objectives of a plan but not Targacept's activities), resulting in an expense to Targacept not contemplated in the applicable then-current Targacept Development Budget, which additional expense is **[********]**, Targacept shall advise AstraZeneca in good faith of the aggregate additional cost of such activities and the Parties through the JDC shall agree on a corresponding amendment to the applicable Targacept Development Budget to reflect the commercially reasonable costs of such activities, **[********]**, such matter shall promptly be referred to an Expert in accordance with Section 14.4 (expedited arbitration). Targacept shall have the right to contract with Third Parties for the conduct of any

Targacept Development Activities solely to the extent provided for in the applicable Product Development Plan and subject to the prior approval of AstraZeneca, not to be unreasonably withheld, conditioned or delayed.

5.4 **Product Commercialization Plans**. No later than **[********]** after the date of submission to the FDA of the first NDA for a Product, AstraZeneca shall prepare and provide to Targacept for its review and comment a Product Commercialization Plan for such Product, and thereafter AstraZeneca shall promptly provide Targacept with an update or amendment thereto **[********]** (which for clarity may be to simply continue with the then-current Product Commercialization Plan); provided that if such Product Commercialization Plan is for a Co-Promoted Product, such Product Commercialization Plan and each such update and amendment thereto, in each case solely relating to the Co-Promotion Territory, shall be submitted to the CCC. Within **[********]** after the delivery of any such Product Commercialization Plan (or update or amendment thereto, or if AstraZeneca does not elect to update or amend any such Product Commercialization Plan in a given year, written notice of such election) to Targacept, Targacept shall have the right to request a meeting with **[********]** for the applicable Product (or such other officer with comparable seniority and responsibility with respect to AstraZeneca's promotional activities as AstraZeneca may designate in writing to Targacept from time to time) to discuss such Product Commercialization Plan (or update or amendment thereto or, with respect to a given year, the lack thereof). **[********]**, AstraZeneca shall deliver written notice to Targacept as to whether AstraZeneca shall prepare and deliver, in AstraZeneca's sole discretion, a revised Product Commercialization Plan (or revised update or amendment thereto), which revised plan shall be delivered to Targacept no later than **[********]**. Targacept shall have ten (10) Business Days after delivery of (a) written notice that AstraZeneca elects not to prepare a revised Product Commercialization Plan (or revised update or amendment thereto) or (b) a revised Product Commercialization Plan (or revised update or amendment thereto), as applicable, to deliver written notice to AstraZeneca maintaining that the activities allocated to AstraZeneca under such Product Commercialization Plan (or update or amendment thereto) or revision of any of the foregoing, even if conducted diligently, would not satisfy AstraZeneca's diligence obligations under this Agreement with respect to the Commercialization of such Product, and thereupon Targacept shall have the right to refer such matter to **[********]**(or such other officer with comparable seniority and responsibility with respect to AstraZeneca's promotional activities

as AstraZeneca may designate in writing to Targacept from time to time) and **[********]** (or such other officer with comparable seniority and responsibility with respect to Targacept's promotional activities as Targacept may designate in writing to AstraZeneca from time to time) for resolution. If such matter remains unresolved by **[********]**, such dispute shall be referred to an Expert for resolution in accordance with Section 14.3 (accelerated arbitration). For purposes of clarity, during any such dispute period, AstraZeneca shall not be deemed to not be exercising Commercially Reasonable Efforts to Commercialize the Product to which the Product Commercialization Plan (or update or amendment thereto) in dispute applies for purposes of Section 5.5.1. In the event that Targacept fails to (x) request a meeting with **[********]** for the applicable Product within **[********]** after delivery of the relevant Product Commercialization Plan, (y) deliver written notice to AstraZeneca of its objection to such Product Commercialization Plan within **[********]** after delivery by AstraZeneca of written notice that there will not be a revised Product Commercialization Plan or of a revised Product Commercialization Plan, or (z) submit such matter to accelerated arbitration in accordance with Section 14.3 within **[********]**, Targacept shall **[********]** the exercise by AstraZeneca of Commercially Reasonable Efforts to perform its activities under such Product Commercialization Plan (or such plan as updated or amended)**[********]** with respect to the Commercialization of such Product and **[********]** with respect thereto (but, for purposes of clarity, Targacept **[********]** with respect to **[********]** under any such Product Commercialization Plan (or any such update or amendment thereto) and shall not thereafter be **[********]** to **[********]**; provided that, with respect to any such Product Commercialization Plan (or any such update or amendment thereto), the foregoing **[********]** Targacept shall apply only to **[********]** until the **[********]** on which **[********]**, whereupon the procedures set forth in this Section shall be repeated.

5.5 **Development and Commercialization Diligence**.

5.5.1 **AstraZeneca Diligence Obligations**.

(a) Diligence Obligation for Ispronicline. If the Commencement Date occurs, from and after the Commencement Date until (1) Ispronicline is terminated pursuant to Section 11.2.3 or Section 11.2.5 or (2) the First Commercial Sale of Ispronicline has occurred

and AstraZeneca has thereafter satisfied all of its royalty obligations to Targacept with respect to Ispronicline under Section 6.6.1, AstraZeneca shall use Commercially Reasonable Efforts to Develop Ispronicline and to Commercialize an Ispronicline Product for AD and CDS, and, if Achievement of Proof of Concept for Ispronicline in either AD or CDS has occurred, ADHD, in each case in at least one Major Market Country. For purposes of clarity, (x) in deciding whether to proceed with the Development of Ispronicline, or the Commercialization of an Ispronicline Product, in AD or CDS, AstraZeneca shall have the right to take into consideration the results of the Pre-Phase IIb Program, the results of the Ongoing Ispronicline Study conducted by Targacept and all other relevant factors (except for the **[********]** Developing Ispronicline **[********]** or **[********]** of AstraZeneca that is **[********]** (other than other Candidate Drug(s) or Product(s))) and (y) upon Achievement of Proof of Concept for Ispronicline for AD or CDS, AstraZeneca shall not be required to pursue the ongoing Development of Ispronicline for AD and CDS at the same time, unless the exercise of Commercially Reasonable Efforts would require that AstraZeneca do so. If Regulatory Approval is obtained for an Ispronicline Product **[********]** in a Major Market Country, AstraZeneca shall use Commercially Reasonable Efforts to (i) Commercialize such Ispronicline Product **[********]** in such Major Market Country and (ii) obtain Regulatory Approval for such Ispronicline Product **[********]** in each other Major Market Country. If such Regulatory Approval is obtained **[********]** in any such other Major Market Country, AstraZeneca shall use Commercially Reasonable Efforts to Commercialize such Ispronicline Product **[********]** in such other Major Market Country. For purposes of clarity, AstraZeneca shall have no obligation, if Ispronicline is Developed or an Ispronicline Product is Commercialized for: **[********]** in at least one Major Market Country, but the exercise of Commercially Reasonable Efforts would not require it to do so in one or more other Major Market Countries, to Develop Ispronicline or Commercialize any such Ispronicline Product in those other Major Market Countries; or **[********]** in a Major Market Country, to Develop Ispronicline or Commercialize any such Ispronicline Product for Schizophrenia in any other Major Market Country.

(b) Diligence Obligation for Other Candidate Drugs or Products. If (i) there is a Commencement Date and after the Commencement Date (A) AstraZeneca ceases to use Commercially Reasonable Efforts to Develop Ispronicline or Commercialize an Ispronicline Product for any reason, (B) in the exercise of Commercially Reasonable Efforts AstraZeneca

terminates both, as applicable at the time of such termination, the Development of Ispronicline and the Commercialization of an Ispronicline Product throughout the Territory or (C) Ispronicline and all Ispronicline Products, but not this Agreement, is terminated pursuant to Section 11.2.3 or Section 11.2.5, or (ii) pursuant to Section 3.3.2(b), either the Parties agree to (A) terminate all specific diligence obligations with respect to Ispronicline under this Agreement (including under Section 5.5.1(a)) such that Ispronicline becomes a Collaboration Compound hereunder or (B) terminate this Agreement with respect to Ispronicline such that Ispronicline becomes a Terminated Compound (but, for purposes of clarity, not a Terminated AZ Compound), but, in each case ((A) and (B)) neither Party terminates this Agreement pursuant to Section 11.2.1, AstraZeneca shall use Commercially Reasonable Efforts until the First Commercial Sale of the first Product (other than an Option Compound Product that contains an Option Compound Candidate Drug, unless pursuant to Section 5.5.1(c) such Option Compound Candidate Drug is sufficient to satisfy AstraZeneca's diligence obligation set forth in this Section 5.5.1(b)) has occurred and AstraZeneca has thereafter satisfied all of its royalty obligations to Targacept under Section 6.6.1 with respect to either such Product or, if earlier, another Product that has had its First Commercial Sale to either (x) Develop **[********]** (which, at any time at which there is no Candidate Drug (other than an Option Compound Candidate Drug, except as expressly provided in Section 5.5.1(c)) that has not become a Terminated Compound, shall be satisfied by funding the Research Program as required under Section 2.1.5(a) in accordance with the then-current Annual Research Plan or conducting or, if applicable, funding, any Additional Research Program in accordance with an Additional Research Plan, or, if after the Research Program Term, using Commercially Reasonable Efforts to conduct research or development in support of the selection or development of a Candidate Drug, but not including, except as expressly provided in Section 5.5.1(c), research or Development of an Option Compound Candidate Drug) or (y) Commercialize **[********]** (not including, except as expressly provided in Section 5.5.1(c), an Option Compound Product), in either case ((x) or (y)) for **[********]**. If Regulatory Approval is obtained for such a Product **[********]** in a Major Market Country, AstraZeneca shall use Commercially Reasonable Efforts to (1) Commercialize such Product **[********]** in such Major Market Country and (2) obtain Regulatory Approval for such Product **[********]** in each other Major Market Country. If such Regulatory Approval is obtained in any other Major Market Country, AstraZeneca shall use Commercially Reasonable Efforts to

Commercialize such Product **[********]** in such other Major Market Country. Notwithstanding anything in this Agreement to the contrary, AstraZeneca shall have no obligation: (i) (A) **[********]** (but not including, except as permitted in Section 5.5.1(c), an Option Compound Candidate Drug) is being Developed **[********]**, to Develop **[********]** (other than Ispronicline, to the extent required pursuant to Section 5.5.1(a), and in which case AstraZeneca shall have no diligence obligations under this Section 5.5.1(b), and Option Compound Candidate Drugs, to the extent required pursuant to Section 5.5.1(c)), or (B) **[********]** (but not including an Option Compound Product, except as permitted in Section 5.5.1(c)), is being Commercialized **[********]**, to Develop **[********]** (other than Ispronicline, to the extent required pursuant to Section 5.5.1(a), and in which case AstraZeneca shall have no diligence obligations under this Section 5.5.1(b), and Option Compound Candidate Drugs, to the extent required pursuant to Section 5.5.1(c)), or Commercialize **[********]** (other than an Ispronicline Product, to the extent required pursuant to Section 5.5.1(a), and in which case AstraZeneca shall have no diligence obligations under this Section 5.5.1(b), and Option Compound Products, to the extent required pursuant to Section 5.5.1(c)); (ii) to Develop a Candidate Drug or Commercialize a Product, in each case **[********]** (other than with respect to Ispronicline, to the extent required pursuant to Section 5.5.1(a)); or (iii) if a Candidate Drug is Developed or a Product Commercialized for (A) **[********]** in at least one Major Market Country, but the exercise of Commercially Reasonable Efforts would not require AstraZeneca to do so in one or more other Major Market Countries, to Develop any such Candidate Drug or Commercialize any such Product in those other Major Market Countries or (B) **[********]** in a Major Market Country, to Develop such Candidate Drug or Commercialize such Product for Schizophrenia in any other Major Market Country. For purposes of clarity, the diligence obligations in this Section 5.5.1(b) shall not apply to, and shall not be satisfied by, any Other Licensed Compound or Other Licensed Product.

(c) Diligence Obligations for Option Compounds. In addition to the foregoing, if AstraZeneca exercises an IND-Ready Option or a POC Option, AstraZeneca shall use Commercially Reasonable Efforts to Develop the Option Compound Candidate Drug subject to such Option and Commercialize one Option Compound Product that contains such Option Compound Candidate Drug in at least one Major Market Country for either (i) if AstraZeneca exercises the IND-Ready Option for such Option Compound Candidate Drug, either (A) the

Option Indication specified in the IND-Ready Notice or (B) any other Option Indication that **[********]** or (ii) if AstraZeneca exercises the POC Option for such Option Compound Candidate Drug, either (A) the Option Indication specified in the IND-Ready Notice or (B) any other Option Indication that **[********]**, the Option Indication for which Option Compound Proof of Concept was acheived. Notwithstanding anything in this Agreement to the contrary, if an IND-Ready Notice or POC Notice specifies, or Option Compound Proof of Concept is achieved, for two Option Indications, AstraZeneca shall only have a diligence obligation with respect to one Principal Indication. If Regulatory Approval is obtained for an Option Compound Product **[********]** in a Major Market Country, AstraZeneca shall use Commercially Reasonable Efforts to (1) Commercialize such Option Compound Product **[********]** in such Major Market Country and (2) obtain Regulatory Approval for such Option Compound Product **[********]** in each other Major Market Country. If such Regulatory Approval is obtained in any other Major Market Country, AstraZeneca shall use Commercially Reasonable Efforts to Commercialize such Option Compound Product **[********]** in such other Major Market Country. If, notwithstanding exercise by AstraZeneca of Commercially Reasonable Efforts, (x) an IND-Ready Option Candidate Drug fails to Achieve Proof of Concept **[********]** or (y) following the designation of an Option Compound as a POC Option Candidate Drug, the exercise of Commercially Reasonable Efforts would not require AstraZeneca to continue to Develop such POC Option Candidate Drug **[********]**, AstraZeneca shall have no further obligations pursuant to this Section 5.5.1(c) with respect to such Option Compound Candidate Drug or any Option Compound Product that contains such Option Compound Candidate Drug; provided that if AstraZeneca, in its sole discretion, elects to do so, the exercise by AstraZeneca of Commercially Reasonable Efforts to Develop such Option Compound Candidate Drug or Commercialize an Option Compound Product that contains such Option Compound Candidate Drug **[********]** shall, after such failure, be sufficient to satisfy AstraZeneca's diligence obligation set forth in Section 5.5.1(b). Notwithstanding anything in this Agreement to the contrary, AstraZeneca shall have no obligation (i) to Develop an Option Compound Candidate Drug or Commercialize an Option Compound Product **[********]**, or (ii) if such Option Compound Candidate Drug is Developed or such Option Compound Product is Commercialized for **[********]** in at least one Major Market Country, but the exercise of Commercially Reasonable Efforts would not require AstraZeneca to do so in one or more other Major Market

Countries, to Develop any such Option Compound Candidate Drug or Commercialize any such Option Compound Product in those Major Market Countries. For purposes of clarity, the diligence obligations in this Section 5.5.1(c) shall not apply to, and shall not be satisfied by, any Other Licensed Compound or Other Licensed Product.

(d) No Breach of Diligence Obligations. For purposes of clarity, in no event shall AstraZeneca be deemed in breach of its diligence obligations pursuant to this Section 5.5.1 solely because it elects not to Develop any Candidate Drug in a particular Major Market Country or to Commercialize any Product in a particular Major Market Country if such election is due to the failure by Targacept to perform its material obligations under this Agreement. Except with respect to the Pre-Phase IIb Program as provided in Article 3 and except as provided in Section 5.6, AstraZeneca shall have no other obligation, express or implied, to Exploit Collaboration Compounds, Candidate Drugs or Products, other than as set out in this Section 5.5.1. For purposes of clarity, in determining Commercially Reasonable Efforts with respect to the Development or Commercialization of a Candidate Drug or a Product (other than with respect to the Development of Ispronicline or an Ispronicline Product), other Candidate Drugs and Products that AstraZeneca is researching, Developing or Commercializing shall be taken into account.

(e) Effect of Breach of Diligence Obligations. If Targacept at any time believes that AstraZeneca is not meeting a diligence obligation pursuant to this Section 5.5.1, Targacept may give written notice to AstraZeneca specifying the basis for its belief, and the Parties shall meet within **[********]** after such notice to discuss in good faith Targacept's concerns and AstraZeneca's explanation supporting the proposition that AstraZeneca is meeting such diligence obligations. In the event that Targacept does not agree with AstraZeneca's explanation and considers AstraZeneca to be in material breach of its obligations under this Section 5.5.1, then Targacept shall have the right, in its sole discretion, to **[********]** in accordance with **[********]** and, if it is determined **[********]** that AstraZeneca failed to meet such diligence obligation, to exercise its rights under Section 11.2.5 or any or all other rights or remedies that it may have under this Agreement (other than Section 11.2.4), at law or in equity. For purposes of clarity, Targacept shall have no rights to terminate pursuant to Section 11.2.5 if, after having been determined to be in material breach in such arbitration, and following such

determination, Targacept having served notice of its intention to terminate this Agreement in accordance with Section 11.2.5, AstraZeneca cures such breach within the Cure Period or such longer period as provided for in Section 11.2.5.

(f) For purposes of clarity, AstraZeneca shall have the right to satisfy its diligence obligations under this Section 5.5.1 through one or more of its Affiliates, Sublicensees or Distributors.

5.5.2 **Targacept Diligence**. Targacept shall use Commercially Reasonable Efforts to conduct the Targacept Development Activities in accordance with each Product Development Plan and the applicable Targacept Development Budget, including by committing such resources, including FTEs, as are specified in each such Product Development Plan to conduct its activities set forth therein; provided that Targacept shall have the right to notify the JDC promptly upon becoming aware of a scientific or technical problem outside of its reasonable control **[********]** that is likely, notwithstanding Targacept's use of Commercially Reasonable Efforts, to preclude Targacept from completing any Targacept Development Activity set forth in a Product Development Plan with the estimated FTEs (or not more than 110% of such FTEs) (a "**Material Unexpected Technical Development Problem**"). As part of such notification, Targacept shall provide the JDC with a reasonably detailed description of such Material Unexpected Technical Development Problem, together with its good faith belief as to the steps necessary to complete such Targacept Development Activity, if practicable at all, in light of such Material Unexpected Technical Development Problem. Upon receipt of such notification, the JDC shall **[********]** take such other action as may be mutually acceptable to the Parties (each a "**Development Workaround**"); provided that, following notification of a Material Unexpected Technical Development Problem with respect to a Targacept Development Activity, Targacept shall not be required to perform such Targacept Development Activity (except with respect to a Clinical Trial, in which case if Targacept has already commenced an activity in connection therewith, it shall not terminate such activity unless and until agreed to by the JDC) unless and until the JDC acts to address such Material Unexpected Technical Development Problem. Except as otherwise provided in a Development Workaround or in Section 6.4.3, Targacept shall be solely responsible for any FTE Costs and External Targacept R&D Costs for an activity that exceed the amount set forth in the Targacept Development Budget for such activity and are not

otherwise approved in writing by the JDC. For purposes of clarity, no modification to a Product Development Plan (or budget with respect thereto) will be implemented unless agreed by the JDC pursuant to Section 3.2.4, in accordance with the proviso set forth in Section 5.3.

5.6 **Compliance**. Each Party shall perform its obligations under each Product Development Plan in good scientific manner and in compliance with all Applicable Laws. For purposes of clarity, with respect to each activity performed under a Product Development Plan that will or would reasonably be expected to be submitted to a Regulatory Authority in support of a Regulatory Filing or Drug Approval Application, the Party performing such activity shall comply in all material respects with, if and as applicable, the regulations and guidance of the FDA that constitute GLP, Good Manufacturing Practices or Good Clinical Practices (or, if and as appropriate under the circumstances, International Conference on Harmonization (ICH) guidance or other comparable regulation and guidance of any Regulatory Authority in any country or region in the Territory). Subject to Targacept's right to receive the funding described in Section 6.4, each Party shall be solely responsible for paying the salaries, benefits and all other costs and expenses of its employees and the fees and all other costs and expenses payable to any consultants or Third Party contractors, in each case conducting its activities under Product Development Plans.

5.7 **Cooperation**. Scientists at Targacept and AstraZeneca shall reasonably cooperate in the performance of each Development Program and, subject to Article 16 and the other terms of this Agreement and any confidentiality obligations to Third Parties, shall, if reasonably requested by the other Party and at its own cost, exchange such data, information and materials as are reasonably necessary for the other Party to perform its obligations under any Product Development Plan, or in the case of Targacept, such other assistance as AstraZeneca may reasonably request in connection with the research, manufacture, Development or Commercialization of any Collaboration Compound, Candidate Drug or Product, provided Targacept shall not be required to incur any out-of-pocket costs in connection with such other assistance unless AstraZeneca agrees to bear such costs.

5.8 **Regulatory Action Plan**. If AstraZeneca determines, in its sole discretion, that there are changes in the regulatory environment **[********]**, AstraZeneca shall prepare a

Regulatory Action Plan, which shall contain a strategy and, where appropriate, budget and estimated timelines for exploring, where appropriate, the feasibility of seeking Regulatory Approval **[********]**. The Regulatory Action Plan shall not assign any activities or expenses to Targacept unless approved by Targacept. Each Party shall commit such resources as are specified in the Regulatory Action Plan to conduct its activities set forth therein; provided that any failure by a Party to commit such resources or otherwise comply with this Section 5.8 shall not give rise to a right to terminate this Agreement. **[********]**.

5.9 **Exchange of Reports; Information; Updates**.

5.9.1 **Development Program Reports**. AstraZeneca shall keep the JDC regularly informed of the progress of its efforts to Develop Candidate Drugs in the Field and in Schizophrenia in the Territory. Without limiting the generality of the foregoing, AstraZeneca shall, on at least **[********]**, provide the JDC and Targacept with reports. Such reports shall include **[********]**; provided, however, that in no event shall AstraZeneca be required to include **[********]** in such reports **[********]**. Targacept shall, on at least **[********]**, or as may otherwise be provided in the applicable Product Development Plan, provide the JDC and AstraZeneca with reports in reasonable detail regarding the status of the Ongoing Ispronicline Trial and all Targacept Development Activities, including the rate of spending compared to the applicable budget for such Targacept Development Activities, and such additional information known to Targacept as may be reasonably requested from time to time by the JDC or AstraZeneca. For purposes of clarity, if either Party is required pursuant to this Section 5.9.1 to provide a report, summary, results or information to the other Party and provides such report, summary, results or information to the representatives of the other Party on the JDC, such providing Party shall thereupon also be deemed to have provided such report, results or information to the other Party pursuant to this Section 5.9.1. In addition, AstraZeneca shall provide Targacept with written notice of any Major Metabolites of any Collaboration Compound, Candidate Drug or Additional Compound that are Known to AstraZeneca.

5.9.2 **Commercialization Reports and Meetings**. AstraZeneca shall keep Targacept informed of the progress of AstraZeneca's efforts to Commercialize Products in the Field and, if applicable, in Schizophrenia in the Territory through **[********]** reports. Following

submission of the first Product Commercialization Plan for a Product or such later date as the Parties may agree in writing, AstraZeneca shall provide Targacept with **[********]** written updates to each Product Commercialization Plan for such Product, which shall **[********]**; provided, however, that in no event shall AstraZeneca be required to include **[********]** in such reports **[********]**. All such updates and reports shall be sent to the attention of Targacept's Vice President, Business and Commercial Development (or such other officer with comparable seniority and responsibility with respect to Targacept's promotional activities as Targacept may designate in writing to AstraZeneca from time to time).

5.9.3 **Adverse Event Reports; Review of Regulatory Filings and Correspondence**.

(a) Adverse Events. With respect to each Candidate Drug and Product (including Partially-Terminated Products), prior to Targacept's performance of any Targacept Development Activities for which Targacept has reporting obligations to any Regulatory Authority or execution of any Co-Promotion Agreement and, with respect to each Partially-Terminated Product, promptly after such Partially-Terminated Product becomes a Partially-Terminated Product, Targacept shall execute AstraZeneca's then-current safety agreement that is intended to cover the same types of regulatory activities as are covered by the safety agreement with respect to Ispronicline attached hereto as Exhibit A. Without limiting the foregoing, (i) AstraZeneca shall be responsible for Adverse Event and product complaint reporting to applicable Regulatory Authorities in the Territory, (ii) in addition to the updates described in Section 5.9.1 and 5.9.2, AstraZeneca shall, **[********]**, provide Targacept's Medical Director, or such other person as Targacept may designate in writing to AstraZeneca from time to time, with all unexpected or serious Adverse Event and product complaint information relating to Candidate Drugs or Products after such information is submitted to the FDA, and (iii) Targacept shall report and provide to AstraZeneca all Adverse Event and product complaint information relating to any Partially-Terminated Product that Targacept is Developing or Commercializing and any Co-Promoted Product in such a manner, time and format, and to such person(s) or department(s), as may be reasonably designated by AstraZeneca from time to time, so as to enable AstraZeneca to comply with all Applicable Laws.

(b) Preparation of Drug Approval Applications. Unless under the circumstances it would be impracticable to do so, AstraZeneca shall consult with Targacept in the preparation of all Drug Approval Applications for Products in the United States and each of the Major Market Countries in Europe.

(c) Regulatory Meetings with FDA; Review of Other Regulatory Filings and Correspondence. AstraZeneca shall use reasonable efforts to provide Targacept with at least **[********]** advance notice of any meeting with the FDA regarding a Drug Approval Application relating to, or Product Regulatory Approval for, any Candidate Drug or Product and Targacept may elect to send one person reasonably acceptable to AstraZeneca to attend such meeting as an observer (at Targacept's sole expense) unless **[********]**. In addition, subject to any Third Party confidentiality obligations, AstraZeneca shall provide Targacept with access to drafts of each Regulatory Filing (including all data and other information contained therein) or other material document or material correspondence pertaining to any Candidate Drug or Product and prepared for submission to the FDA or the EMEA, where practicable, in advance of submission thereof. In addition, AstraZeneca shall promptly provide Targacept with copies of any document or other correspondence received from the FDA or the EMEA pertaining to any Candidate Drug or Product.

5.10 **Development and Commercialization Rights and Restrictions**.

5.10.1 **Development and Commercialization Rights in the Field**. Except (a) in the conduct of the Research Program or any Additional Research Program as provided in Sections 4.1, 4.3, 4.4 and 4.8, (b) subject to Section 5.10.2(c)(1), for the identification, research and development of potential Back-Up Option Compounds (which, for purposes of clarity, are Additional Compounds with respect to the corresponding Option Compound Candidate Drugs) that have not yet themselves become Option Compound Candidate Drugs, (c) as provided in Section 5.2.2 and (d) for the Targacept Development Activities, notwithstanding anything else in this Agreement to the contrary, AstraZeneca shall have the sole and exclusive right during the Term to research, develop, manufacture, commercialize and otherwise Exploit all Collaboration Compounds, Candidate Drugs and Products (including to Develop Candidate Drugs and Commercialize Products) in the Territory for use in the Field and in Schizophrenia.

5.10.2 **AstraZeneca Options**.

(a) Progress Reports and Pre-IND Studies. Promptly after the Effective Date, the Parties shall meet to review and discuss generally (i) Targacept's Option Compound research strategy and **[********]** IND-Ready Option Compounds **[********]** in each case if any, including discussion of screening and pre-clinical development strategies, (ii) the expected target profile for each IND-Ready Option Compound for any such indication, taking into consideration scientific, clinical and commercial inputs if and as available, and (iii) **[********]** Option Compound updates, and thereafter shall meet **[********]** to discuss generally any updates with respect thereto; provided that, for purposes of clarity, it is not contemplated that the Parties will discuss chemical structures or structure-activity relationships at any such meeting (and that similarly no such information will be included in any Preliminary IND Notice or update thereto as provided below). With respect to each Compound in respect of which Targacept expects to submit an IND-Ready Notice (each, a "**Potential Option Compound**"), Targacept shall provide AstraZeneca a written notice (each, a "**Preliminary IND Notice**") at least **[********]** the date Targacept expects to provide AstraZeneca with an IND-Ready Notice therefor. Each Preliminary IND Notice shall identify the specific anticipated Option Indication (each, a "**Potential Option Indication**") for which Targacept intends to develop and commercialize such Potential Option Compound, include a summary of the results of the studies and assessments with respect to such Potential Option Compound completed by or on behalf of Targacept (which shall include, at a minimum, those studies and assessments identified as **[********]** studies on Schedule 1.148, as such Schedule may be amended by the Parties from time to time with respect to a particular Potential Option Compound) and specify the research and development activities to be conducted by or on behalf of Targacept with respect thereto, in each case with sufficient detail for AstraZeneca to interpret such results and **[********]** such tests or studies or expected research and development activities; provided, however, that Targacept shall not have any obligation to offer such Potential Option Compound for the Potential Option Indication identified in the Preliminary IND Notice or to offer such Potential Option Compound as an Option Compound at all. If AstraZeneca reasonably believes that additional data beyond what has been provided, or that will result from the activities to be conducted by or on behalf of Targacept as set forth in the Preliminary IND Notice with respect to a Potential Option Compound, would be required for AstraZeneca to make a determination as to

whether AstraZeneca would Initiate a Phase I Clinical Trial for such Potential Option Compound should it be offered as an Option Compound, AstraZeneca shall have the right to request, on written notice to Targacept, and Targacept shall,, at AstraZeneca's expense (for reasonable and verifiable expenses incurred in accordance with the applicable budget) and at Targacept's election, either perform or cooperate with AstraZeneca (or its designee) to enable AstraZeneca (or its designee) to perform, such additional tests, studies or other activities requested by AstraZeneca as are necessary to generate those data (the "**Pre-IND Studies**") in accordance with a plan and budget approved by the Parties; provided that (A) all such Pre-IND Studies, taken in the aggregate and using reasonable diligence, shall be able to be **[********]** and **[********]** such plan and budget are approved, **[********]**; (B) the subject matter of any such Pre-IND Studies shall, if targeted directly or indirectly to an indication, be reasonably targeted specifically to the Potential Option Indication identified in the Preliminary IND Notice; (C) the conduct of any such Pre-IND Studies shall not affect Targacept's right not to offer such Potential Option Compound for the Potential Option Indication identified in the Preliminary IND Notice or not to offer such Potential Option Compound as an Option Compound at all; provided, however, that in the event Targacept does not offer a Potential Option Compound that was the subject of any Pre-IND Studies as an Option Compound to AstraZeneca, and does not terminate the research and development of such Potential Option Compound, Targacept shall reimburse AstraZeneca for **[********]** percent (**[********]**%) of the reasonable and verifiable costs incurred by or on behalf of AstraZeneca (including any reimbursements or payments to Targacept) in connection with such Pre-IND Studies; and (D) if the Parties cannot agree on **[********]** such Pre-IND Studies, such matter shall promptly be referred to an Expert in accordance with Section 14.4 (expedited arbitration). After the Preliminary IND Notice for a particular Potential Option Compound and unless and until Targacept shall have determined, on written notice to AstraZeneca, not to offer such Potential Option Compound as an Option Compound, Targacept shall provide updates with respect to such Potential Option Compound to AstraZeneca **[********]**, which updates shall include a summary of the results of the material studies and assessments with respect to such Potential Option Compound completed by or on behalf of Targacept; provided that, for purposes of clarity, no such update shall give rise to any obligation of Targacept to offer such Potential Option Compound for the Potential Option Indication

identified in the Preliminary IND Notice or to offer such Potential Option Compound as an Option Compound at all.

(b) IND-Ready Option. If Targacept elects to provide AstraZeneca with an IND-Ready Option for an Option Compound, Targacept shall, subject to Section 5.10.2(c), provide AstraZeneca with written notice when and if such Option Compound becomes IND-Ready, which notice shall, at a minimum, (i) identify the Option Compound and describe Targacept's assessment of the Option Compound Profile at that time, (ii) include **[********]** studies and assessments on such Option Compound completed by or on behalf of Targacept, (iii) include a summary of the status of existing Patent Rights with respect to such Option Compound, whether Controlled by Targacept or controlled by a Third Party, Known to Targacept, (iv) include a description of all license agreements regarding, and other agreements relating to Targacept's Control of (including any financial or other obligations with respect thereto) such Option Compound and (v) specify the specific Option Indication for which Targacept then intends to develop and commercialize such Option Compound (the "**IND-Ready Notice**"). AstraZeneca shall thereafter have the option to designate such Option Compound as a Candidate Drug (the "**IND-Ready Option**"). AstraZeneca shall notify Targacept if it desires to conduct due diligence at Targacept's offices with respect to such Option Compound and, if so, the Business Day(s) on which it will do so during normal business hours; provided that such date(s) shall be at least three (3) Business Days following the date of Targacept's receipt of such notice from AstraZeneca. Each IND-Ready Option shall expire on the later of **[********]** following the date that the corresponding IND-Ready Notice is delivered to AstraZeneca and, if any Pre-IND Studies are conducted with respect to such Option Compound, **[********]** after the date that any such Pre-IND Studies are completed and the data and results thereof delivered to AstraZeneca, or such later date as the Parties may agree in writing (such period, the "**IND-Ready Option Period**"); provided if AstraZeneca requests further information relating to such Option Compound as permitted by the next sentence, and all such information is not provided within **[********]** of any such request, then the IND-Ready Option Period with respect to such Option Compound shall be extended for any such delay in responding to such request (for example, if AstraZeneca requests certain information and that information is not completely provided until **[********]** after the request, then the IND-Ready Option period would be extended by **[********]** to **[********]**). For a period of **[********]** days after the IND-Ready

Notice for an Option Compound, Targacept shall: (A) provide to AstraZeneca for review at Targacept's offices during normal business hours in a reasonable and prompt manner, such data, documentation and other information in Targacept's possession or control regarding such Option Compound, including its studies and assessments and any such Pre-IND Studies with respect to such Option Compound, as AstraZeneca reasonably requests for purposes of evaluating the IND-Ready Option for such Option Compound (including true, complete and correct copies of all license agreements (with financial terms redacted to the extent AstraZeneca has no responsibility therefor) regarding, and other agreements relating to Targacept's Control of (including any financial or other obligations with respect thereto), such Option Compound and applications for Patent Rights, results of freedom to operate analyses and other information with respect to the intellectual property status of such Option Compound; provided that Targacept shall not be required to provide privileged information with respect to such intellectual property status unless and until procedures reasonably acceptable to Targacept are in place to protect such privilege); and (B) respond in a prompt and reasonable manner to all reasonable queries raised by AstraZeneca in connection with its evaluation of such IND-Ready Option. For purposes of clarity, (x) AstraZeneca shall not have an IND-Ready Option for any Compound other than an Option Compound that becomes IND-Ready and for which Targacept delivers to AstraZeneca an IND-Ready Notice as provided above and (y) unless otherwise agreed in writing by the Parties, Targacept shall have no right to offer an IND-Ready Option for (i) any indication other than an Option Indication or (ii) any **[********]**.

(1) Exercise of IND-Ready Option. AstraZeneca shall exercise the IND-Ready Option for an Option Compound, if at all, by giving written notice of exercise to Targacept and paying the Option Exercise Fee for an IND-Ready Option set forth in Section 6.2 at any time during the IND-Ready Option Period; provided that AstraZeneca agrees that, if it determines not to exercise an IND-Ready Option prior to expiration of the IND-Ready Option Period, it shall in good faith provide written notice to Targacept promptly upon such determination and the date on which any such notice is given shall constitute the last day of the IND-Ready Option Period. Upon such exercise by AstraZeneca, such Option Compound shall become an IND-Ready Option Candidate Drug and subject to AstraZeneca's obligations pursuant to Section 5.5.1(c).

(2) Failure to Exercise IND-Ready Option. Unless AstraZeneca timely provides an Option Maintenance Notice pursuant to Section 5.10.2(b)(3), if AstraZeneca does not exercise the IND-Ready Option for an Option Compound within the IND-Ready Option Period, then, subject to Section 5.10.2(c), Targacept shall thereafter have the right in all respects, itself or with, for the benefit of or sponsored by any Third Party, to research, develop, commercialize and otherwise Exploit, or to grant a license or other rights to any Third Party to research, develop, commercialize and otherwise Exploit, such Option Compound either (A) if the Option Indication designated in the IND-Ready Notice is a Primary Indication, in or outside of the Field or (B) if (x) the Option Indication designated in the IND-Ready Notice is Schizophrenia, solely outside the Field, and (y) as of the last day of the IND-Ready Option Period for such Option Compound, (i) no Option Compound has or had become an Option Compound Candidate Drug for which the Principal Indication is Schizophrenia, (ii) there is no other Option Compound for which Targacept has delivered to AstraZeneca an IND-Ready Notice or a POC Notice or that otherwise is the subject of an Option Compound Development Plan or Targacept Option Compound Development Plan that specifies Schizophrenia as the Option Indication, and (iii) there is no other Option Compound Candidate Drug or Option Compound Product that AstraZeneca is otherwise Developing or Commercializing for Schizophrenia, the last day of the IND-Ready Option Period shall be the Schizophrenia Expiration Date. If (1) the last day of the IND-Ready Option Period is not the Schizophrenia Expiration Date because there is one or more Option Compound(s) for which Targacept has delivered to AstraZeneca an IND-Ready Notice or a POC Notice or that otherwise is the subject of an Option Compound Development Plan or Targacept Option Compound Development Plan that specifies Schizophrenia as the Option Indication or because AstraZeneca is Developing an Option Compound Candidate Drug for Schizophrenia (other than an Option Compound Candidate Drug for which the Principal Indication is Schizophrenia), (2) all such Option Compound(s) become Terminated Compound(s) or Unexercised Option Compound(s), (3) as of the date all such Option Compound(s) have become Terminated Compound(s) or Unexercised Option Compound(s), each of clauses (i), (ii) and (iii) above are true, (4) then, if not occurring earlier pursuant to Section 5.10.2(d)(2), the Schizophrenia Expiration Date shall be the date, if any, on which all

such Option Compound(s) have become Terminated Compound(s) or Unexercised Option Compound(s). For purposes of clarity, if prior to the Schizophrenia Expiration Date, AstraZeneca has exercised an Option for an Option Compound Candidate Drug for which Schizophrenia is a Principal Indication or AstraZeneca otherwise Commercializes an Option Compound Product for Schizophrenia there shall be no Schizophrenia Expiration Date. For purposes of clarity, Targacept shall have no right to Exploit any Compound under this Section for which it did not provide AstraZeneca with an IND-Ready Notice in material compliance with, and otherwise satisfy its material obligations with respect thereto under, this Section 5.10.2(b).

(3) Option Maintenance Fee and Option Compound Development Plan. If AstraZeneca does not wish to exercise the IND-Ready Option for an Option Compound but wishes potentially to obtain a POC Option for such Option Compound, AstraZeneca shall, at any time during the IND-Ready Option Period, provide written notice to Targacept (each, an "**Option Maintenance Notice**"). Thereafter, the Parties shall work in good faith and with sufficient diligence to prepare a mutually acceptable Option Compound Development Plan within [********] after AstraZeneca gives the Option Maintenance Notice or such longer period as the Parties may agree in writing (the "**Option Compound Development Plan Period**"). Each Option Compound Development Plan shall specify the standards or criteria that, if achieved, constitute Option Compound Proof of Concept for the Option Indication (i) specified in the applicable IND-Ready Option Notice or (ii) otherwise agreed to by the Parties. Each Option Compound Development Plan shall be commercially reasonable. An Option Compound Development Plan shall be commercially reasonable if it requires Targacept to use substantially similar efforts and resources as those typically used by companies in the research-based pharmaceutical industry with resources and expertise comparable to those of Targacept (or any successor thereto) at such time (or, **[********]** Targacept as of the Execution Date) in the development of products and product candidates of comparable market potential on their own behalf (and not as a contract research organization) without regard to any license or option rights of any Person with respect to such product or product candidate, to provide a **[********]** of **[********]** for the Option Indication (A) specified in the IND-Ready Option Notice or (B) otherwise agreed to in

writing by the Parties. If the Parties agree to an Option Compound Development Plan, (1) it shall be signed by an authorized officer of each Party and may be amended thereafter only by mutual written agreement of the Parties, (2) AstraZeneca shall pay the Option Maintenance Fee set forth in Section 6.3 within **[********]** of the date of signature, (3) Targacept shall use Commercially Reasonable Efforts to execute the Option Compound Development Plan and (4) Targacept shall provide AstraZeneca on at least **[********]** written progress reports for each Option Compound Development Plan, which shall summarize the status of all activities conducted and results achieved under each Option Compound Development Plan and such additional information in Targacept's possession or control as may be reasonably requested from time to time by AstraZeneca. If the Parties are unable to agree to an Option Compound Development Plan, Section 5.10.2(b)(6) shall apply.

(4) Breach of Option Compound Development Plan. If AstraZeneca at any time believes that Targacept is not using Commercially Reasonable Efforts to execute the Option Compound Development Plan in accordance with its terms, AstraZeneca may give written notice to Targacept specifying the basis for its belief, and the Parties shall meet within **[********]** after such notice to discuss in good faith AstraZeneca's concerns and Targacept's explanation supporting the proposition that Targacept is meeting such diligence obligations. In the event that AstraZeneca does not agree with Targacept's explanation and considers Targacept to be in material breach of its obligation to use Commercially Reasonable Efforts to execute the Option Compound Development Plan, then AstraZeneca shall have the right, in its sole discretion, to initiate arbitration in accordance with Section 14.3 (accelerated arbitration). If it is determined in such arbitration that Targacept has failed to meet such diligence obligation, AstraZeneca may serve notice on Targacept requiring Targacept to cure such breach within **[********]**, failing which (or, if such breach cannot be cured within such **[********]** period, if Targacept does not commence actions to cure such breach within such **[********]** period and thereafter diligently continue such actions) (such **[********]** period or such longer period during which Targacept is diligently seeking to cure such breach, the "**Targacept Cure Period**"), Targacept shall refund the applicable Option Maintenance Fee within **[********]** after the end of the Targacept Cure Period and

AstraZeneca shall have the right, but not the obligation, to complete the Option Compound Development Plan. If Targacept does not cure such breach by the end of the Targacept Cure Period and if requested by AstraZeneca within **[********]** after the end of the Targacept Cure Period, Targacept shall within an additional **[********]** provide to AstraZeneca at Targacept's cost such data, documentation and other information in Targacept's possession or control regarding its studies and assessments of such Option Compound as AstraZeneca reasonably requests for the purpose of evaluating whether it wishes to complete the Option Compound Development Plan (excluding any such information to the extent previously provided to AstraZeneca but including any information necessary to update or correct any information previously provided to AstraZeneca) and Targacept shall respond in a reasonable and prompt manner to all reasonable queries raised by AstraZeneca in connection with such evaluation. If AstraZeneca wishes to complete the Option Compound Development Plan, it shall notify Targacept of such decision in writing within **[********]** of receiving such information. If AstraZeneca serves such notice within such period, Section 5.10.2(b)(5) shall apply. If AstraZeneca does not serve such notice within such period the applicable Option Compound shall cease to be an Option Compound and shall become a Terminated Compound (but not a Terminated AZ Compound) and Targacept's rights thereto shall be subject to the restrictions applicable to Terminated Compounds (but not Terminated AZ Compounds) as set forth in Section 8.6. For purposes of clarity, a determination that Targacept has breached an Option Compound Development Plan shall not give rise to a right to terminate this Agreement, and AstraZeneca's sole and exclusive remedy therefor shall be as expressly prescribed in this Section 5.10.2(b)(4) and, if applicable, Section 5.10.2(b)(5).

(5) Assumption of Option Compound Development Plan by AstraZeneca. If AstraZeneca elects to complete the Option Compound Development Plan in accordance with Section 5.10.2(b)(4), Targacept shall, at the request and sole expense of AstraZeneca, provide AstraZeneca with such assistance as is reasonably necessary to effectuate a smooth and orderly transition of such Option Compound Development Plan so as to minimize any disruption of activities being conducted pursuant to such plan. In particular, Targacept shall transfer to AstraZeneca, in each case

as they relate directly to the Option Compound, (i) at AstraZeneca's written request, all of Targacept's and its Affiliates' right, title and interest in all INDs, (ii) all material aspects of Confidential Information Controlled by Targacept or its Affiliates as of the date of transfer, (iii) at AstraZeneca's written request, control of all Clinical Trials then being conducted and, if so requested, Targacept shall assign (or cause its Affiliates to assign) to AstraZeneca all agreements with any Third Party with respect to the conduct of such Clinical Trials, (iv) all supplies of such Option Compound in the possession of Targacept or any of its Affiliates or contractors pursuant to Article 16. Following such transfer AstraZeneca shall use Commercially Reasonable Efforts to complete the Option Compound Development Plan; provided that AstraZeneca shall have the right to amend the Option Compound Development Plan (including by winding down or varying one or more Clinical Trials or studies being conducted pursuant to the plan and undertaking additional or substitute Clinical Trials and studies). If completion of the Option Compound Development Plan demonstrates Option Compound Proof of Concept: (A) AstraZeneca shall promptly notify Targacept in writing thereof andthereupon shall be deemed to have exercised **[********]** with respect to such Option Compound; (B) within twenty (20) days after such notice, AstraZeneca shall pay to Targacept the sum of **[********]** being the Option Exercise Fee **[********]** AstraZeneca **[********]** for such Option Compound in accordance with **[********]** (and, if Option Compound Proof of Concept is demonstrated by **[********]** Clinical Trial (and not by achievement of **[********]** Clinical Trial), AstraZeneca shall also then pay to Targacept the sum of **[********]**, which amount represents **[********]** that would be then payable pursuant to clause (C)); and (C) such Option Compound shall become an **[********]** in respect of which milestones (for purposes of clarity, **[********]** shall be payable with respect to such Option Compound Candidate Drug) and royalties shall be paid thereafter in accordance with Sections 6.5 (column B) and 6.6.1(a)(1) (column B). If Option Compound Proof of Concept is not achieved, AstraZeneca shall promptly notify Targacept in writing thereof and Section 5.10.2(e) shall apply, except that if pursuant to that Section the applicable Option Compound does not become an Option Compound Candidate Drug for any reason, such Option Compound shall, notwithstanding Section 5.10.2(e)(4), become a Terminated Compound (but not a Terminated AZ Compound) and

and Targacept's rights thereto shall be subject to the restrictions applicable to Terminated Compounds (but not Terminated AZ Compounds) as set forth in Section 8.6. For purposes of clarity, an uncured breach by AstraZeneca of its obligations to use Commercially Reasonable Efforts to complete an Option Compound Development Plan for an Option Compound assumed and conducted by AstraZeneca pursuant to this Section 5.10.2(b)(5) shall not give rise to a right to terminate this Agreement, and Targacept's sole and exclusive remedy therefor shall be to terminate AstraZeneca's rights under this Section 5.10.2(b)(5) with respect to such Option Compound, whereupon such Option Compound shall become a Terminated Compound (but not a Terminated AZ Compound) as expressly prescribed in the foregoing sentence.

(6) No Agreement on Option Compound Development Plan. If, after diligent, good faith discussions, the Parties do not agree to an Option Compound Development Plan within the Option Compound Development Plan Period, Targacept shall either: (A) modify by written notice to AstraZeneca, the IND-Ready Option Notice to specify an Option Indication that was not specified in the original IND-Ready Option Notice, in which event (unless AstraZeneca withdraws its Option Maintenance Notice by written notice to Targacept) the date such notice is delivered to AstraZeneca shall re-start the Option Compound Development Plan Period and the Parties shall work in good faith and with sufficient diligence to prepare a mutually acceptable Option Compound Development Plan for such newly-specified Option Indication or such other Option Indication as the Parties may agree, (B) provide written notice to AstraZeneca that it withdraws the Option Compound from application of Section 5.10.2(b), in which event such Option Compound shall cease to be an Option Compound and shall become a Terminated Compound (but not a Terminated AZ Compound) and Targacept's rights with respect thereto shall be subject to the restrictions applicable to Terminated Compounds (but not Terminated AZ Compounds) as set forth in Section 8.6; or (C) provide a Targacept Option Compound Development Plan to AstraZeneca, in which event Section 5.10.2(f) shall apply.

(c) Restrictions on Targacept's Development and Commercialization of Option Compounds. Notwithstanding anything to the contrary in this Section 5.10.2,

AstraZeneca shall not be required to consider or take any further action with respect to, and Targacept shall have no right to develop, commercialize or otherwise Exploit (other than as expressly permitted under Section 8.6), with respect to any Option Compound in the event that:

(1) the IND-Ready Notice for such Option Compound specifies a Primary Indication (other than ADHD or any type of Dementia) or Schizophrenia and there is an Option Compound (i) for which an IND-Ready Notice has been served previously that specifies the same indication and in respect of which AstraZeneca has served the Option Maintenance Notice but it has not yet been determined whether such Option Compound shall be an Option Compound Candidate Drug, a Terminated Compound or an Unexercised Option Compound, or (ii) for which AstraZeneca exercised an IND-Ready Option or POC Option and for which the resulting Option Compound Candidate Drug is being Developed or the Option Compound Product is being (or has been) Commercialized, in each case, by AstraZeneca or any of its Affiliates or Sublicensees for a Principal Indication that is the same as such specified Option Indication, unless the second Option Compound **[********]** is **[********]** to that first Option Compound; provided that Targacept shall not provide the IND-Ready Notice for **[********]** to **[********]** Option Compound for that same indication until the earlier of (A) **[********]** of (1) AstraZeneca's exercise of the IND-Ready Option for such first Option Compound pursuant to Section 5.10.2(b)(1), (2) AstraZeneca's payment of the Option Maintenance Fee for such first Option Compound pursuant to Section 5.10.2(b)(3) or (3) in the event the Parties are unable to agree on an Option Compound Development Plan, Targacept's delivery to AstraZeneca of a Targacept Option Compound Development Plan, whichever is applicable, and (B) completion of **[********]** for such first Option Compound; and provided further that in the event of a dispute as to whether an Option Compound is **[********]**, such dispute shall be resolved by an Expert in accordance with Section 14.3 (accelerated arbitration);

(2) the IND-Ready Notice for such Option Compound specifies a Primary Indication and there are at that time **[********]** Option Compounds in respect of which (i) IND-Ready Notices have been served previously, the Principal Indication for each of which is a Primary Indication and in respect of which AstraZeneca

has served the Option Maintenance Notice but it has not yet been determined whether such Option Compound shall be an Option Compound Candidate Drug, a Terminated Compound or an Unexercised Option Compound, or (ii) AstraZeneca has exercised an IND-Ready Option or POC Option and for which the resulting Option Compound Candidate Drug is being Developed or the Option Compound Product is being (or has been) Commercialized, in each case, by AstraZeneca or any of its Sublicensees for a Principal Indication that is a Primary Indication;

(3) the IND-Ready Notice for such Option Compound specifies AD, MCI, AAMI or CDS and there are at that time **[********]** Option Compounds for which (i) IND-Ready Notices have been served previously, the Principal Indication for each of which is either AD, MCI, AAMI or CDS as specified in such IND-Ready Notice and in respect of which AstraZeneca has served the Option Maintenance Notice but it has not yet been determined whether such Option Compound shall be an Option Compound Candidate Drug, a Terminated Compound or an Unexercised Option Compound, or (ii) AstraZeneca has exercised an IND-Ready Option or POC Option and for which the resulting Option Compound Candidate Drug is being Developed or Option Compound Product is being (or has been) Commercialized, in each case, by AstraZeneca or any of its Sublicensees for a Principal Indication that is any of AD, MCI, AAMI or CDS;

(4) the IND-Ready Notice for such Option Compound specifies ADHD or a Primary Indication (other than AD, MCI, AAMI or CDS) and there is at that time an Option Compound for which (i) an IND-Ready Notice has been served previously, the Principal Indication which is ADHD or a Primary Indication (other than AD, MCI, AAMI or CDS) and in respect of which AstraZeneca has served the Option Maintenance Notice but it has not yet been determined whether such Option Compound shall be an Option Compound Candidate Drug, a Terminated Compound or an Unexercised Option Compound, or (ii) AstraZeneca has exercised an IND-Ready Option or POC Option and for which the resulting Option Compound Candidate Drug is being Developed or Option Compound Product is being (or has been) Commercialized, in each case, by AstraZeneca or any of its Sublicensees for a Principal Indication that is ADHD;

(5) the IND-Ready Notice for such Option Compound specifies Schizophrenia and there are at that time **[********]** Option Compounds for which (i) IND-Ready Notices have been served previously, the Principal Indication for each of which is Schizophrenia and in respect of which AstraZeneca has served the Option Maintenance Notice but it has not yet been determined whether such Option Compound shall be an Option Compound Candidate Drug, a Terminated Compound or an Unexercised Option Compound, or (ii) AstraZeneca has exercised an IND-Ready Option or POC Option and for which the resulting Option Compound Candidate Drug is being Developed or Option Compound Product is being (or has been) Commercialized, in each case, by AstraZeneca or any of its Sublicensees for a Principal Indication that is Schizophrenia; or

(6) it is an Excluded Zone Compound.

For purposes of clarity, (x) it is contemplated that each IND-Ready Notice will specify **[********]** Option Indication but, if an IND-Ready Notice specifies **[********]** Option Indication **[********]** shall be **[********]** for purposes of Sections 5.10.2(c)(2) through 5.10.2(c)(5). If AstraZeneca elects to Develop an IND-Ready Option Candidate Drug for an Option Indication other than the Option Indication specified in the applicable IND-Ready Notice, it shall notify Targacept in writing and Targacept shall have the right, on written notice to AstraZeneca within **[********]** of the delivery of such notice to Targacept, to designate the Option Indication specified in such IND-Ready Notice as the Principal Indication for such Option Compound Candidate Drug solely for purposes of this Section 5.10.2(c). Otherwise, the Principal Indication for such Option Compound Candidate Drug for purposes of this Section 5.10.2(c) shall be the Option Indication that is Developed by AstraZeneca.

(d) POC Option. Targacept shall provide AstraZeneca with written notice following completion of its execution of an Option Compound Development Plan, which notice shall (i) identify the Option Compound and describe Targacept's assessment of the Option Compound Profile at that time, (ii) include a summary of results of the Option Compound Development Plan, (iii) include a summary of the status existing Patent Rights with respect to

such Option Compound, whether Controlled by Targacept or controlled by a Third Party, Known to Targacept, (iv) include a description of all license agreements regarding, and other agreements relating to Targacept's Control of (including any financial or other obligations with respect thereto), such Option Compound and (v) specify whether Targacept has achieved Option Compound Proof of Concept (the "**POC Notice**"). If the POC Notice specifies that Targacept has achieved Option Compound Proof of Concept for the Option Indication specified in the Option Compound Development Plan, AstraZeneca shall thereafter have the option under this Section 5.10.2(d) to designate such Option Compound as a Candidate Drug (the "**POC Option**"). AstraZeneca shall notify Targacept if it desires to conduct due diligence at Targacept's offices with respect to such Option Compound and, if so, the Business Day(s) on which it will do so during normal business hours; provided that such date(s) shall be at least **[********]** following the date of Targacept's receipt of such notice from AstraZeneca. Each POC Option shall expire **[********]** following the date that the corresponding POC Notice is delivered to AstraZeneca or such later date as the Parties may agree in writing (such period, the "**POC Option Period**"), provided that, if AstraZeneca requests further information relating to such Option Compound as permitted by the next sentence and all such information is not provided **[********]** of any such request, then the POC Option Period with respect to such Option Compound shall be extended for any such delay in responding to such request (for example, if AstraZeneca requests certain information and and that information is not completely provided until **[********]** after the request, then the POC Option period would be extended by **[********]** to **[********]**). For a period of **[********]** after the POC Option Notice for an Option Compound, Targacept shall: (A) provide to AstraZeneca for review at Targacept's offices during normal business hours in a reasonable and prompt manner such data, documentation and other information in Targacept's possession or control regarding such Option Compound, including, including the activities conducted pursuant to the Option Development Plan and the results achieved as AstraZeneca reasonably requests for purposes of evaluating the POC Option for such Option Compound (including true, complete and correct copies of all license agreements (with financial terms redacted to the extent AstraZeneca has no responsibility therefor) regarding, and other agreements relating to Targacept's Control of (including any financial or other obligations with respect thereto), such Option Compound and applications for Patent Rights results of freedom to operate analyses and other information with respect to the

intellectual property status of such Option Compound; provided that Targacept shall not be required to provide privileged information with respect to such intellectual property status unless and until procedures reasonably acceptable to Targacept are in place to protect such privilege); and (B) respond in a prompt and reasonable manner to all reasonable queries raised by AstraZeneca in connection with its evaluation of such POC Option. For purposes of clarity, (x) except as permitted under Section 5.10.2(f), AstraZeneca shall not have a POC Option for any Compound other than an Option Compound for which AstraZeneca does not exercise the IND-Ready Option but pays the Option Maintenance Fee and (y) unless otherwise agreed in writing by the Parties, Targacept shall have no right to offer a POC Option for (i) any compound for any indication other than an Option Indication or (ii) any **[********]**. If AstraZeneca does not agree with Targacept's determination, as specified in the POC Notice, as to whether it has or has not achieved Option Compound Proof of Concept, it shall, prior to the end of the POC Option Period, refer such matter in writing to the ESC for resolution pursuant to Section 2.1.5 (and, if necessary, Section 14.3 (accelerated arbitration) and, in such event, all relevant time periods pursuant to this Section 5.10.2(d) shall be tolled pending such resolution and the POC Notice shall be deemed to be amended to reflect such resolution.

(1) Exercise of POC Option. AstraZeneca shall exercise the POC Option for an Option Compound, if at all, by giving written notice of exercise to Targacept and paying the Option Exercise Fee for a POC Option set forth in Section 6.2 at any time during the POC Option Period; provided that AstraZeneca agrees that, if it has determined not to exercise a POC Option prior to expiration of the POC Option Period, it shall in good faith provide written notice to Targacept promptly upon such determination and the date on which any such notice is given shall constitute the last day of the POC Option Period. Upon such exercise by AstraZeneca such Option Compound shall become a POC Option Candidate Drug and subject to AstraZeneca's obligations pursuant to Section 5.5.1(c).

(2) Failure to Exercise POC Option. If AstraZeneca does not exercise the POC Option for an Option Compound within the POC Option Period for an Option Compound for which Option Compound Proof of Concept was achieved, then, subject to Section 5.10.2(c), Targacept shall thereafter have the right in all respects, itself

or with, for the benefit of or sponsored by any Third Party, to research, develop, commercialize and otherwise Exploit, or to grant a license or other rights to any Third Party to develop, commercialize and otherwise Exploit, such Option Compound (A) if Option Compound Proof of Concept was achieved for such Option Compound for a Primary Indication, in or outside of the Field; or (B) if (x) Option Compound Proof of Concept was achieved for such Option Compound for Schizophrenia, solely outside the Field and (y) as of the last day of the POC Option Period for such Option Compound, (i) no Option Compound has or had become an Option Compound Candidate Drug for which the Principal Indication is Schizophrenia, (ii) there is no other Option Compound for which Targacept has delivered to AstraZeneca an IND-Ready Notice or a POC Notice or that otherwise is the subject of an Option Compound Development Plan or Targacept Option Compound Development Plan that specifies Schizophrenia as the Option Indication, and (iii) there is no other Option Compound Candidate Drug or Option Compound Product that AstraZeneca is otherwise Developing or Commercializing for Schizophrenia, the last day of the POC Option Period shall be the Schizophrenia Expiration Date. If (1) the last day of the POC Option Period is not the Schizophrenia Expiration Date because there is one or more Option Compounds for which Targacept has delivered to AstraZeneca an IND-Ready Notice or a POC Notice or that otherwise is the subject of an Option Compound Development Plan or Targacept Option Compound Development Plan that specifies Schizophrenia as the Option Indication or because AstraZeneca is Developing an Option Compound Candidate Drug for Schizophrenia (other than an Option Compound Candidate Drug for which the Principal Indication is Schizophrenia), (2) all such Option Compound(s) become Terminated Compound(s) or Unexercised Option Compound(s), (3) as of the date all such Option Compound(s) have become Terminated Compound(s) or Unexercised Option Compound(s), each of clauses (i), (ii) and (iii) above are true, (4) then, if not occurring earlier pursuant to Section 5.10.2(b)(2), the Schizophrenia Expiration Date shall be the date, if any, on which all such Option Compound(s) have become Terminated Compound(s) or Unexercised Option Compound(s). For purposes of clarity, if prior to the Schizophrenia Expiration Date, AstraZeneca has exercised an Option for an Option Compound Candidate Drug for which Schizophrenia is a Principal Indication or AstraZeneca otherwise Commercializes an Option Compound Product for Schizophrenia, there shall be no Schizophrenia Expiration Date. For purposes

of further clarity, a decision by AstraZeneca not to exercise a POC Option for an Option Compound (a) for which Option Compound Proof of Concept was not achieved or (b) with respect to which Targacept breached the applicable Option Compound Development Plan and AstraZeneca assumed and conducted such plan in accordance with Section 5.10.2(b)(5), in each case ((a) and (b)), shall not trigger the Schizophrenia Expiration Date.

(e) Option Compound ROFN Right. If the POC Notice for a particular Option Compound specifies that Option Compound Proof of Concept has not been achieved for the Option Indication specified in the Option Compound Development Plan (or Option Compound Proof of Concept is not obtained with respect to an Option Compound for which AstraZeneca assumes control of the Option Compound Development Plan pursuant to Section 5.10.2(b)(5)), AstraZeneca shall thereafter have the right to give Targacept written notice specifying whether it wishes to negotiate with Targacept **[********]** financial terms on which it would designate such Option Compound as an Option Compound Candidate Drug (the "**Option Compound ROFN Notice**"), it being acknowledged and agreed by both Parties that such financial terms relating to any such designation **[********]** the POC Option Candidate Drug terms set forth in Section 6.2, Section 6.5 and Section 6.6 **[********]** such Option Compound to achieve Option Compound Proof of Concept. AstraZeneca's right to give an Option Compound ROFN Notice shall expire **[********]** following the date that the corresponding POC Notice is delivered to AstraZeneca or amended by Targacept pursuant to Section 5.10.2(d) (or the date that AstraZeneca notifies Targacept that such Option Compound Proof of Concept is not obtained with respect to such Option Compound for which AstraZeneca assumed control of the Option Compound Development Plan pursuant to Section 5.10.2(b)(5)) (such period, the "**Option Compound ROFN Period**"); provided that, (i) if AstraZeneca determines not to give an Option Compound ROFN Notice prior to expiration of the Option Compound ROFN Period, it shall in good faith provide written notice to Targacept promptly upon such determination and the date on which any such notice is given shall constitute the last day of the Option Compound ROFN Period; and (ii) if such Option Compound was not subject to an Option Compound Development Plan assumed and conducted by AstraZeneca pursuant to Section 5.10.2(b)(5), AstraZeneca requests further information relating to such Option Compound as permitted by the next sentence, and all such information is not provided **[********]** of any such request, then the Option Compound ROFN Period with respect to such Option Compound shall be extended for

any such delay in responding to such request (for example, if AstraZeneca requests certain information and that information is not completely provided until **[********]** after the request, then the Option Compound ROFN period would be extended by **[********]** to **[********]**. For a period of **[********]** after the Option Compound ROFN Notice for an Option Compound, Targacept shall: (A) provide to AstraZeneca for review at Targacept's offices during normal business hours in a reasonable and prompt manner such data, documentation and other information in Targacept's possession or control regarding such Option Compound, including the activities conducted pursuant to the Option Development Plan and the results achieved as AstraZeneca reasonably requests for purposes of evaluating whether to give an Option Compound ROFN Notice to Targacept for such Option Compound (including true, complete and correct copies of all license agreements (with financial terms redacted to the extent AstraZeneca has no responsibility therefor) regarding, and other agreements relating to Targacept's Control of (including any financial or other obligations with respect thereto), such Option Compound and applications for Patent Rights, results of freedom to operate analyses and other information with respect to the intellectual property status of such Option Compound; provided that Targacept shall not be required to provide privileged information with respect to such intellectual property status unless and until procedures reasonably acceptable to Targacept are in place to protect such privilege); and (B) respond in a prompt and reasonable manner to all reasonable queries raised by AstraZeneca in connection with its evaluation thereof.

(1) If AstraZeneca gives Targacept an Option Compound ROFN Notice within the Option Compound ROFN Period, the Parties shall negotiate in good faith terms on which AstraZeneca would designate such Option Compound as an Option Compound Candidate Drug (including payment to Targacept) for a period of **[********]** from the date that the Option Compound ROFN Notice is given. If the Parties do not agree on such terms within the **[********]** negotiation period, AstraZeneca shall set forth in writing its final offer with respect to such Option Compound (the "**Final Option Compound Offer**") within **[********]** after expiration of such **[********]** negotiation period. If Targacept accepts such Final Option Compound Offer, such Option Compound shall, unless expressly specified otherwise in such Final Option Compound Offer, be deemed to be a POC Option Candidate Drug. If Targacept does not accept the Final Option Compound Offer submitted by AstraZeneca within

[********] after the Final Option Compound Offer is delivered to Targacept, either Party may at any time **[********]** after the expiration of such **[********]** negotiation period refer the matter to arbitration in accordance with Section 14.4 (expedited arbitration).

(2) If, in accordance with Section 14.4, the Expert determines that the proposal submitted by AstraZeneca pursuant to Section 14.4 (the "**AZ Proposal**") prevails, Targacept shall within **[********]** of such determination notify AstraZeneca that either (i) Targacept accepts the AZ Proposal in which event the Option Compound shall be deemed to be a POC Option Candidate Drug on the terms set forth in the AZ Proposal; or (ii) Targacept rejects the AZ Proposal in which event, unless the Parties agree in writing otherwise, such Option Compound shall cease to be an Option Compound and shall become a Terminated Compound (but not a Terminated AZ Compound) as set forth in Section 8.6.

(3) If, in accordance with Section 14.4, the Expert determines that the proposal submitted by Targacept pursuant to Section 14.4 (the "**Targacept Proposal**") prevails, AstraZeneca shall within **[********]** of such determination notify Targacept that either (i) AstraZeneca accepts the Targacept Proposal in which event the Option Compound shall be deemed to be a POC Option Candidate Drug on the terms of set forth in the Targacept Proposal; or (ii) AstraZeneca rejects the Targacept Proposal.

(4) If AstraZeneca (i) does not give Targacept an Option Compound ROFN Notice within the Option Compound ROFN Period, (ii) declines in writing during the Option Compound ROFN Period to enter into negotiations, or (iii), rejects the prevailing Targacept Proposal (if any) pursuant to Section 5.10.2(e)(3), unless the Parties agree in writing otherwise, Targacept shall thereafter have the right in all respects to research, develop, commercialize and otherwise Exploit, itself or with, for the benefit of or sponsored by any Third Party, or to grant a license or other rights to any Third Party to research, develop, commercialize and otherwise Exploit, such Option Compound, either (A) if the Option Indication specified in the Option Compound Development Plan is a Primary Indication, in or outside of the Field, or (B) if the Option Indication specified in the Option Compound Development Plan is Schizophrenia, solely

outside of the Field; provided that any decision by AstraZeneca not to exercise an Option under this Section 5.10.2(e) or Section 5.10.2(f) shall not trigger the Schizophrenia Expiration Date.

(f) Right of First Negotiation for Option Compound Following Targacept Option Compound Development Plan. If, with respect to any IND-Ready Option, (i) AstraZeneca gives Targacept an Option Maintenance Notice, (ii) the Parties do not agree to an Option Compound Development Plan within the Option Compound Development Plan Period for the IND-Ready Option Compound, and (iii) Targacept provides AstraZeneca a Targacept Option Compound Development Plan for the Option Indication specified in the applicable IND-Ready Option Notice, Targacept shall provide AstraZeneca, on at least a **[********]** basis, with written progress reports for each Targacept Option Compound Development Plan, which shall summarize the status of, and any results generated under, each Targacept Option Compound Development Plan, any updates or amendments to such Targacept Option Compound Development Plan (provided that, for clarity, no such update or amendment shall modify, substitute or otherwise change the Option Indication that was specified in the applicable IND-Ready Option Notice) and such additional information known to Targacept as may be reasonably requested from time to time by AstraZeneca. If and when Targacept completes such Targacept Option Compound Development Plan, Targacept shall promptly provide written notice to AstraZeneca. Any such written notice (the "**Targacept Plan POC Notice**") shall (A) identify the applicable Option Compound, (B) include a summary of results of the Targacept Option Compound Development Plan, (C) include a summary of the status of existing Patent Rights with respect to such Option Compound, whether Controlled by Targacept or controlled by a Third Party, that are Known to Targacept, (D) include a description of all license agreements regarding, and other agreements relating to Targacept's Control of (including any financial or other obligations with respect thereto), such Option Compound and (E) specify whether Targacept has obtained Option Compound Proof of Concept. AstraZeneca shall notify Targacept if it desires to conduct due diligence at Targacept's offices with respect to such Option Compound and, if so, the Business Day(s) on which it will do so during normal business hours; provided that such date(s) shall be at least **[********]** following the date of Targacept's receipt of such notice from AstraZeneca. For a period of **[********]** after the Targacept Plan POC Notice for an Option Compound, Targacept shall: (1) provide to AstraZeneca for review at

Targacept's offices during normal business hours in a reasonable and prompt manner such data, documentation and other information in Targacept's possession or control regarding such Option Compound, including the activities conducted pursuant to the Targacept Option Development Plan and the results achieved as AstraZeneca reasonably requests for purposes of evaluating such Option Compound (including true, complete and correct copies of all license agreements (with financial terms redacted to the extent AstraZeneca has no responsibility therefor) regarding, and other agreements relating to Targacept's Control of (including any financial or other obligations with respect thereto), such Option Compound, applications for Patent Rights, results of freedom to operate analyses and other information with respect to the intellectual property status of such Option Compound; provided that Targacept shall not be required to provide privileged information with respect to such intellectual property status unless and until procedures reasonably acceptable to Targacept are in place to protect such privilege); and (2) respond in a prompt and reasonable manner to all reasonable queries raised by AstraZeneca in connection with its evaluation of such Option Compound. Whether or not the Targacept Plan POC Notice specifies that Targacept believes it has achieved Option Compound Proof of Concept for the Option Indication specified in the Targacept Option Compound Development Plan (if any), AstraZeneca shall thereafter have the option to designate such Option Compound as an Option Compound Candidate Drug in accordance with the terms of Section 5.10.2(d)(1). Failing such designation by AstraZeneca, the Targacept Plan POC Notice shall be treated as a POC Notice that specifies that Targacept **[********]**, and the provisions of **[********]** shall apply. For purposes of clarity, Targacept shall have no obligation to complete all or any portion of any Targacept Option Compound Development Plan and, if it does not complete a Targacept Option Compound Development Plan or deliver to AstraZeneca the corresponding Targacept Plan POC Notice or such additional information as AstraZeneca may request pursuant to this Section 5.10.2(f), or if Targacept provides written notice to AstraZeneca that the Option Compound subject to such Targacept Option Compound Development Plan shall no longer be an Option Compound, the applicable Option Compound shall become a Terminated Compound (but not a Terminated AZ Compound) as set forth in Section 8.6.

(g) Cooperation with Notifications. In the event that either Party believes that, with respect to the exercise or potential exercise of any Option, notifications are required to be filed by each Party with the U.S. Federal Trade Commission and the U.S.

Department of Justice under the HSR Act or with relevant foreign governmental authorities under any similar foreign law, the Parties shall (i) reasonably cooperate with each other to coordinate and file such notifications in a timely manner, provided that all filing, registration or similar fees associated therewith shall be borne by AstraZeneca, and (ii) in the event of a filing, use reasonable efforts to respond promptly to any requests for additional information made by any such authority and to cause the waiting period under the HSR Act or any similar foreign law to terminate or expire at the earliest possible date after the date of filing. Targacept shall not take any action, directly or indirectly, that is intended to delay or interfere with the clearance of any filing under the HSR Act.

5.10.3 **Right of First Negotiation for ROFN Indications**. If at any time during the Term (subject to Section 15.2.2), Targacept determines to seek an ROFN Collaboration (the "**ROFN Indication Opportunity**"), Targacept shall give written notice to AstraZeneca specifying the particular ROFN Indication and the status of development of the particular compounds or products known to be involved, if any (the "**ROFN Indication Opportunity Notice**"). AstraZeneca shall have **[********]** following the date that the ROFN Indication Opportunity Notice is given by Targacept (the "**ROFN Notice Period**") to give written notice to Targacept that it wishes to enter into negotiations with Targacept with respect to such ROFN Indication Opportunity (an "**ROFN Notice**"); provided that, if AstraZeneca determines not to give an ROFN Notice prior to expiration of the ROFN Notice Period, it shall in good faith provide written notice to Targacept promptly upon such determination that it declines to enter into negotiations. If AstraZeneca gives notice within the ROFN Notice Period that it wishes to enter into negotiations with Targacept, the Parties shall negotiate in good faith **[********]** from the date such notice is given, and then, if the Parties are able to agree **[********]** within such period (or such longer period as the Parties may agree in writing), the Parties shall negotiate in good faith **[********]**. During such period, Targacept shall not discuss, or enter into any negotiations relating to, the ROFN Indication Opportunity, with any Third Party. If **[********]** with respect to the ROFN Indication Opportunity within the **[********]** negotiation period, or if **[********]** with respect to the ROFN Indication Opportunity within **[********]** negotiation period, AstraZeneca shall set forth in writing its final offer with respect to such ROFN Indication Opportunity within **[********]** after expiration of such **[********]** (the "**Final ROFN Offer**"). If Targacept does not accept such Final ROFN Offer within **[********]** (or, for purposes of

clarity, if AstraZeneca does not give Targacept notice that it wishes to enter into negotiations regarding the ROFN Indication Opportunity within the ROFN Notice Period or declines in writing during the ROFN Notice Period to enter into negotiations), Targacept shall thereafter have no obligation to AstraZeneca with respect to the ROFN Indication Opportunity and shall have the unencumbered right to negotiate and execute an agreement with any Third Party for the ROFN Indication Opportunity for a period of three (3) years after the expiration of AstraZeneca's **[********]** negotiation period, but only on terms more favorable to Targacept, when taken as a whole, than those set forth in the Final ROFN Offer. If Targacept does not enter into an agreement with a Third Party relating to such ROFN Indication Opportunity on such terms within such three (3)-year period and thereafter determines to seek an ROFN Collaboration for the same ROFN Indication, then **[********]**.

5.10.4 **Additional Obligations**. Promptly after the Effective Date, Targacept shall terminate its development agreement in effect as of the Execution Date with The Stanley Medical Research Institute (the "**SMRI Agreement**").

5.11 **Co-Promotion**.

5.11.1 **AstraZeneca Portfolio Products**. In the event that AstraZeneca determines in its sole discretion to seek, at any time after the date of Acceptance by the FDA of the first NDA for a Product Developed by AstraZeneca under this Agreement and prior to the **[********]**, a Third Party to promote (or to co-promote) in the United States to any group of specialist physicians or other specialist medical professionals (which, for purposes of clarity, shall not include primary care physicians or medical professionals, including family and general practitioners, internists (regardless of whether they have subspecialty in psychiatry or geriatrics) and pediatricians) that customarily prescribe or purchase, or that would reasonably be expected to prescribe or purchase, products to treat or prevent any nervous system disease or condition (the "**AZ Co-Promotion Opportunity**"), it shall give Targacept written notice of its determination together with a description of the product it is seeking to have a Third Party promote. Targacept shall have **[********]** from the date of such notice to provide a written response as to whether it wishes to participate in negotiations with AstraZeneca with respect to the AZ Co-Promotion Opportunity, provided that Targacept agrees that, if it determines not to

participate in such negotiations prior to the end of such period, it shall in good faith provide written notice to AstraZeneca promptly upon such determination. If Targacept's response indicating whether or not it wishes to participate in negotiations with respect to such AZ Co-Promotion Opportunity is not delivered to AstraZeneca within the **[********]** response period, Targacept shall no longer have any right to exercise such Co-Promotion Opportunity and shall have no right to receive any additional AZ Co-Promotion Opportunities with respect to other products under this Section 5.11.1. If Targacept indicates in its response delivered within such **[********]** period that it wishes to participate in negotiations with AstraZeneca with respect to such AZ Co-Promotion Opportunity, AstraZeneca shall grant Targacept the non-exclusive opportunity to negotiate an agreement with respect to such AZ Co-Promotion Opportunity and each Party shall participate in such negotiations in good faith; provided that AstraZeneca shall be under no obligation to enter into an agreement with Targacept with respect to such AZ Co-Promotion Opportunity. It is the understanding of the Parties that any selection by AstraZeneca of Targacept with respect to such AZ Co-Promotion Opportunity shall be subject, among other things, to Targacept's demonstration to AstraZeneca's reasonable satisfaction that Targacept has available an adequately-trained sales force for such AZ Co-Promotion Opportunity and negotiation of an agreement satisfactory to AstraZeneca.

5.11.2 **Products**.

(a) Exercise of Co-Promotion Option. Subject to Section 5.11.2(b)(3), Targacept shall have the option (the "**Co-Promotion Option**"), in its sole discretion, to Co-Promote any or all Products to the Co-Promotion Target Audience in the Co-Promotion Territory. Targacept may exercise its Co-Promotion Option for a Product by providing written notice (the "**Co-Promotion Option Notice**") to AstraZeneca at any time during the period commencing on the date of the Acceptance by the FDA of the first NDA for such Product and continuing for a period of **[********]** thereafter. If Targacept exercises its Co-Promotion Option with respect to any Product (each such Product, a "**Co-Promoted Product**"), the Parties shall (i) negotiate a Co-Promotion Agreement for such Co-Promotion in accordance with Section 5.11.2(b) and (ii) form, as soon as reasonably practicable thereafter but in any event within **[********]**, the Commercial Coordination Committee.

(b) Co-Promotion Agreement.

(1) Preparation, Negotiation, Execution and Delivery. Within **[********]** after Targacept gives a Co-Promotion Option Notice, the Parties shall commence the preparation of a Co-Promotion Agreement (the "**Co-Promotion Agreement**") that shall provide for the terms applicable to such Co-Promotion. The Co-Promotion Agreement shall conform in all material respects with the terms and conditions set forth in Schedule 5.11.2 and shall also include such additional provisions as are usual and customary in AstraZeneca's contract sales force agreements. For purposes of clarity, such additional terms shall supplement and not materially expand, limit or change the terms set forth on Schedule 5.11.2. The Parties shall negotiate the Co-Promotion Agreement in good faith and with sufficient diligence as is required to execute and deliver the Co-Promotion Agreement within **[********]** after Targacept gives the Co-Promotion Option Notice or such other period as the Parties may agree in writing.

(2) Co-Promotion Fees. The aggregate fees payable by AstraZeneca pursuant to any Co-Promotion Agreement(s) shall not exceed [********] Dollars (US $[********]) in any Calendar Year without AstraZeneca's consent, which AstraZeneca may withhold in its sole discretion.

(3) Targacept Sales Representatives. Targacept shall be required to field and maintain an adequately-trained sales force of at least **[********]** sales representatives to Detail the Co-Promoted Product(s). In no event shall Targacept be required, in any twelve (12)-month period, to field and maintain a sales force to Detail any Co-Promoted Product(s) that exceeds **[********]** sales representatives.

(4) Dispute Resolution. In the event the Parties fail to execute and deliver the Co-Promotion Agreement within the **[********]** or such longer period described in Section 5.11.2(b)(1), the Parties shall (A) use reasonable efforts to complete such negotiations and to execute and deliver the Co-Promotion Agreement as soon as possible after such period and (B) without limiting the generality of the foregoing, after the expiration of such period, each produce a list of issues on which they have failed to reach agreement and submit its list to the CCC to be resolved in accordance with Section 2.4.3(b).

(5) Breach of Co-Promotion Agreement. For purposes of clarity, following the effective date of any Co-Promotion Agreement, a determination that Targacept has breached such Co-Promotion Agreement shall not be deemed a breach of this Agreement and shall be governed solely by the terms of such Co-Promotion Agreement; provided, however, that, in the event that AstraZeneca terminates a Co-Promotion Agreement for Targacept's material breach or, to the extent permitted under such Co-Promotion Agreement, other failure to perform or Targacept's insolvency or bankruptcy in accordance with the terms of such Co-Promotion Agreement, Targacept shall have no further rights under this Section 5.11 with respect to any Co-Promotion Option or AZ Co-Promotion Opportunity, and AstraZeneca shall have the right to terminate any existing co-promotion agreement entered into pursuant to this Section 5.11, including any Co-Promotion Agreement.

(c) Executive Meetings. The Vice President, Business and Commercial Development of Targacept (or such other officer with comparable seniority and responsibility with respect to Targacept's promotional activities as Targacept may designate in writing to AstraZeneca from time to time) and the Vice President, Commercial Operations of AstraZeneca Pharmaceuticals, LP (or such other officer with comparable seniority and responsibility with respect to AstraZeneca's promotional activities as AstraZeneca may designate in writing to Targacept from time to time) shall meet at least semi-annually to review the Exploitation of any Co-Promoted Products.

5.12 **Product Recalls**. In the event that any Regulatory Authority issues or requests a recall or takes similar action in connection with a Product, or in the event a Party reasonably believes that an event, incident or circumstance has occurred that may result in the need for a recall, market withdrawal or other corrective action regarding a Product, such Party shall promptly advise the other Party thereof by telephone or facsimile. Following such notification, AstraZeneca shall decide and have control of whether to conduct a recall or market withdrawal (except in the event of a recall or market withdrawal mandated by a Regulatory Authority, in

which case it shall be required) or to take other corrective action in any country and the manner in which any such recall, market withdrawal or corrective action shall be conducted; provided that AstraZeneca shall keep Targacept regularly informed regarding any such recall, market withdrawal or corrective action. AstraZeneca shall bear all expenses of any such recall, market withdrawal or corrective action (including expenses for notification, destruction and return of the affected Product and any refund to customers of amounts paid for such Product); provided, however, that Targacept shall bear the expense of a recall to the extent that such recall resulted from any breach by Targacept of its obligations hereunder or under the applicable Co-Promotion Agreement or Targacept's or any of its Affiliates' negligence or willful misconduct, provided that Targacept shall not be deemed to be negligent or in breach solely for complying with the training provided by AstraZeneca under the applicable Co-Promotion Agreement, with AstraZeneca's standard operating procedures as may be provided under the applicable Co-Promotion Agreement or otherwise with direction from AstraZeneca if the activities required by such training, procedures or other direction would themselves constitute negligence or breach.

5.13 **Major Metabolite Cooperation**. Each Party shall, if reasonably requested by the other Party and at the cost of such other Party, reasonably cooperate with such other Party to assist such other Party to identify Major Metabolites for purposes of determining such other Party's rights and obligations under this Agreement, including **[********]**.

6. PAYMENTS

6.1 **Upfront Fee**. AstraZeneca shall pay Targacept an upfront fee in the amount of Ten Million Dollars (US $10,000,000) in immediately available funds within ten (10) Business Days of the Effective Date.

6.2 **Option Exercise Fees**. For each Option exercised by AstraZeneca pursuant to Section 5.10.2, AstraZeneca shall pay Targacept an option exercise fee (the "**Option Exercise Fee**"): (a) in the amount of **[********]** Dollars (US $**[********]**) (i) in the case of **[********]** or (ii) in the event **[********]** for an Option Compound **[********]** and such Option Compound **[********]**; (b) in the amount of **[********]** Dollars (US $**[********]**) (i) in the case of **[********]** or (ii) if **[********]** an Option Compound Candidate Drug **[********]**; or (c) in an amount to be negotiated by the Parties pursuant to Section 5.10.2(e) if **[********]** an Option

Compound that is (i) the subject of a POC Notice **[********]** the Option Compound Development Plan or (ii) the subject of a Targacept Option Compound Plan that AstraZeneca did not designate as an Option Compound Candidate Drug pursuant to Section 5.10.2(f).

6.3 **Option Maintenance Fees**. The Option Maintenance Fee contemplated by Section 5.10.2(b)(3) shall be **[********]** Dollars (US $**[********]**) (subject to **[********]** such Option Maintenance Fee **[********]** Option Compound Development Plan for an Option Compound **[********]**. If, with respect to any IND-Ready Option, AstraZeneca pays the Option Maintenance Fee, such Option Maintenance Fee (a) shall thereafter be fully creditable against the Option Exercise Fee payable by AstraZeneca for the Option for the same Option Compound, if such Option is exercised by AstraZeneca (including, for clarity, any Option Exercise Fee determined pursuant to Section 5.10.2(e)), and (b) otherwise, except as provided in Section 5.10.2(b)(4), shall be non-creditable and non-refundable.

6.4 **R&D Funding**.

6.4.1 **R&D Funding during the Pre-Phase IIb Period**. AstraZeneca shall pay Targacept fifty percent (50%) of (a) the aggregate FTE Cost for all FTEs, subject to this Section 6.4, based on the FTE Rate and (b) the amount of all External Targacept R&D Costs, if and to the extent such FTE Costs and External Targacept R&D Costs are incurred in accordance with the approved Targacept Research Budget (and, unless approved by the JRC, do not exceed the relevant amounts set forth in the Total Research Budget with respect thereto) and relate to activities conducted in, or were incurred during, the Pre-Phase IIb Period, provided that if AstraZeneca elects to proceed with the Development of Ispronicline by delivery of notice to Targacept in accordance with Section 3.3.1 or, subject to Section 3.3.2(b), neither Party terminates this Agreement in accordance with Section 11.2.1, AstraZeneca shall pay all of such costs that AstraZeneca has not already paid.

6.4.2 **R&D Funding after the Pre-Phase IIb Period**. If AstraZeneca elects to proceed with the Development of Ispronicline by delivery of notice to Targacept in accordance with Section 3.3, then from and after (i) the Commencement Date or (ii) if there is no Commencement Date, from and after the Sunset Date or if, subject to Section 3.3.2(b), neither Party terminates this Agreement in accordance with Section 11.2.1, from and after the first date

on which neither Party has the right to terminate this Agreement pursuant to Section 11.2.1, whichever is later, AstraZeneca shall pay Targacept (a) the aggregate FTE Cost for all FTEs, subject to this Section 6.4, based on the FTE Rate and (b) the amount of all External Targacept R&D Costs, if and to the extent such FTE Costs and External Targacept R&D Costs are incurred in accordance with an approved Targacept Research Budget (and, unless approved by the JRC, do not exceed the relevant amounts set forth in the Total Research Budget with respect thereto), ARP Budget or Targacept Development Budget.

6.4.3 **Reimbursement of Costs**. AstraZeneca shall pay the costs for which it is liable to Targacept pursuant to Section 6.4.1 and 6.4.2 **[********]**. Within **[********]** each Contract Quarter during the Research Program Term and any Additional Research Program Term and any Calendar Quarter during which Targacept undertakes any Targacept Development Activities, Targacept shall furnish to AstraZeneca a statement in a form reasonably acceptable to AstraZeneca showing (a) the number of FTEs engaged in activities allocated to Targacept in the then-current Annual Research Plan or Additional Research Plan and Targacept Development Activities under any Product Development Plan, in each case, if any, during the preceding quarter **[********]** consistent with the activities identified in the applicable Annual Research Plan, Additional Research Plan or Product Development Plan and (b) the External Targacept R&D Costs incurred by Targacept in the preceding quarter against the amount budgeted for such costs in the relevant Targacept Research Budget (and Total Research Budget), ARP Budget or Targacept Development Budget. At the end of the Contract Quarter following (i) the Commencement Date or (ii) if there is no Commencement Date, the Sunset Date, or if, subject to Section 3.3.2(b), neither Party terminates this Agreement in accordance with Section 11.2.1, the first date on which neither Party has the right to terminate this Agreement pursuant to Section 11.2.1, whichever is later, such statement shall include a reconciliation statement showing the amount previously paid by AstraZeneca in relation to activities conducted by Targacept in the performance of the Research Program during the Pre-Phase IIb Period and the additional amount payable by AstraZeneca pursuant to Section 3.3 and Section 6.4.1. Within thirty (30) days of receipt of such statement, together with such support for External Targacept R&D Costs as AstraZeneca may reasonably require, AstraZeneca shall make a payment equal to the FTE Costs and External Targacept R&D Costs for the relevant quarter, as set out in such statement; provided that in any Contract Year (or with respect to any Targacept Development Activities,

any Calendar Year), **[********]** with respect to that Contract Year (or, in the case of Targacept Development Activities, Calendar Year) **[********]** set forth in the applicable Targacept Research Budget (and Total Research Budget), ARP Budget or Targacept Development Budget (as the case may be) **[********]**. If, notwithstanding Targacept's exercise of Commercially Reasonable Efforts, in any year, the aggregate FTE Cost plus the External Targacept R&D Costs **[********]** FTE Costs and External Targacept R&D Costs in the applicable Targacept Research Budget (and the Total Research Budget), ARP Budget or Targacept Development Budget (as the case may be) **[********]** in accordance with the applicable Annual Research Plan, Additional Research Plan or Product Development Plan **[********]**. For purposes of clarity, Targacept shall have the right to conduct activities under the Research Program or an Additional Research Program in addition to those set forth in the Research Plan or the applicable Annual Research Plan or Additional Research Plan pursuant to Section 4.3.1 at its sole cost and expense, and AstraZeneca shall have no obligation to reimburse Targacept for the FTE Costs or External Targacept R&D Costs incurred with respect to such additional activities.

6.4.4 **R&D Funding Audit Rights**. Targacept shall keep accurate books and financial records pertaining to its costs and expenses of conducting the Research Program, the Additional Research Program, the Targacept Development Activities and any Targacept Manufacturing activities under Article 16 in sufficient detail to determine whether payments made by AstraZeneca were accurately calculated, which books and financial records shall be kept in accordance with GAAP and shall be retained by Targacept until **[********]** after the end of the Calendar Year to which they pertain (or such longer period as may be required by Applicable Laws). AstraZeneca shall have the right for a period of **[********]** after making any such payment to inspect or audit, or to appoint at its expense an independent certified public accounting firm reasonably acceptable to Targacept to inspect or audit, the books and financial records of Targacept relating to its costs and expenses of conducting the Research Program during any Contract Year, the Targacept Development Activities and any Targacept Manufacturing activities under Article 16 during any Calendar Year, in each case, to verify that the amount of such payment was correctly determined. Targacept shall make its records available for inspection or audit by AstraZeneca or such independent certified public accounting firm during regular business hours at such place or places where such records are customarily kept, upon reasonable notice from AstraZeneca; provided that AstraZeneca shall not have the

right to inspect or audit any Contract Year or any Calendar Year more than once or after the **[********]** of the end of such Contract Year or Calendar Year (unless a previous audit revealed an underpayment or overpayment with respect to such Contract Year or Calendar Year). All books and financial records made available for inspection or audit shall be deemed to be Confidential Information of Targacept and if any such inspection or audit is to be conducted by an independent certified public accounting firm, prior to such inspection such accounting firm shall enter into a non-disclosure agreement in a form reasonably acceptable to Targacept. The accounting firm shall disclose to the Parties whether or not the payment in question was accurately determined and the specific details concerning any discrepancies. No other information shall be provided to AstraZeneca. The results of each inspection or audit, if any, shall be binding on both Parties absent manifest error. In the event there was an underpayment by AstraZeneca hereunder, AstraZeneca shall promptly (but in any event no later than **[********]** after AstraZeneca's receipt of the report so concluding) make payment to Targacept of any shortfall. In the event that there was an overpayment by AstraZeneca hereunder, Targacept shall promptly (but in any event no later than **[********]** after Targacept's receipt of the AstraZeneca's or the independent accountant's report so concluding) refund to AstraZeneca the excess amount. AstraZeneca shall bear the full cost of such inspection or audit unless such inspection or audit discloses overcharging by Targacept of more than **[********]** of the amount that should have been paid by AstraZeneca in any Calendar Quarter or Contract Quarter, as applicable, in which case Targacept shall reimburse AstraZeneca for all costs incurred by AstraZeneca in connection with such inspection or audit.

6.5 **Milestone Payments**.

6.5.1 **Milestones**. Unless otherwise provided in Section 6.5.2, and subject to Sections 6.6.1(d)(2), 10.2.4 and 10.2.6, AstraZeneca shall make the following nonrefundable, non-creditable payments to Targacept:

(a) Full Milestone Stream. AstraZeneca shall, with respect to each Candidate Drug (other than a Licensed Derivative) or Product that contains such Candidate Drug, and each Licensed Derivative with respect to such Candidate Drug Derived during the Restricted Derivative Period for such Candidate Drug (each such Licensed Derivative, a

"**Milestone-Bearing Licensed Derivative**") or Product that contains such Licensed Derivative, make each of the following payments to Targacept within **[********]** after the first occurrence of the corresponding milestone event after (x) (i) the Commencement Date or (ii) if there is no Commencement Date, after the Sunset Date, or if, subject to Section 3.3.2(b), neither Party terminates this Agreement in accordance with Section 11.2.1, after the first date on which neither Party has the right to terminate this Agreement pursuant to Section 11.2.1, whichever is later, or (y) solely with respect to Option Compound Candidate Drugs (other than Licensed Derivatives) or Option Compound Products that contain any such Option Compound Candidate Drug, and any Milestone-Bearing Licensed Derivatives (or Products that contain any such Milestone-Bearing Licensed Derivative) with respect thereto, the Effective Date; provided that if a milestone event with respect to a Candidate Drug (other than a Licensed Derivative) or a Product that contains such Candidate Drug, or a Milestone-Bearing Licensed Derivative with respect thereto or Product that contains such Milestone-Bearing Licensed Derivative, in each case, other than an Option Compound Candidate Drug or Option Compound Product, occurs prior to (A) the Commencement Date, AstraZeneca shall pay such milestone payment within **[********]** after the Commencement Date or (B) if there is no Commencement Date, the Sunset Date, or if, subject to Section 3.3.2(b), neither Party terminates this Agreement in accordance with Section 11.2.1, the first date on which neither Party has the right to terminate this Agreement pursuant to Section 11.2.1, whichever is later, AstraZeneca shall pay such milestone payment within **[********]** after the Sunset Date or such later date (as applicable):

	Candidate Drugs/Products			
Milestone Event	**A Ispronicline/ Ispronicline Products**	**B IND-Ready Option Candidate Drugs/IND-Ready Option Products**	**C POC Option Candidate Drugs/POC Option Products**	**D All Other Candidate Drugs/ Products**
1. Commencement of **[********]**	**[********]**	**[********]**	**[********]**	**[********]**
2. **[********]**	**[********]**	**[********]**	**[********]**	**[********]**

Milestone Event	Candidate Drugs/Products A Ispronicline/ Ispronicline Products	B IND-Ready Option Candidate Drugs/IND-Ready Option Products	C POC Option Candidate Drugs/POC Option Products	D All Other Candidate Drugs/ Products
3. Election to Commence Development of Ispronicline pursuant to Section 3.3.1	$ 20 million	[********]	[********]	[********]
4. [********] of [********]	[********]	[********]	[********]	[********]
5. Initiation of [********]	[********]	[********]	[********]	[********]
6. [********] of [********]	[********]	[********]	[********]	[********]
7. First Commercial Sale [********]	[********]	[********]	[********]	[********]
8. First Commercial Sale [********]	[********]	[********]	[********]	[********]
9. First Commercial Sale [********]	[********]	[********]	[********]	[********]

With respect to each of (A) Ispronicline and any Ispronicline Product, collectively, (B) each Candidate Drug (other than Ispronicline or an Option Compound Candidate Drug, which are addressed in clauses (A) and (C), respectively, and other than a Milestone-Bearing Licensed Derivative, which is addressed in the next sentence) and any Product that contains such Candidate Drug, collectively, and (C) each Option Compound Candidate Drug (other than a Licensed Derivative) and any Option Compound Product that contains such Option Compound Candidate Drug, collectively, AstraZeneca shall make a payment corresponding to each of the foregoing milestone events only once under this Section 6.5.1(a), regardless of (1) the number of times such milestone event occurs for such Candidate Drug(s) and Product(s), (2) the number of Primary Indications for which any such Candidate Drug or Product is Developed or Commercialized, (3) whether or not any such Candidate Drug or Product is Developed or

Commercialized for Schizophrenia and (4) the number of Candidate Drugs contained in a Product. Each Milestone-Bearing Licensed Derivative with respect to any Candidate Drug(s) or Product(s) set forth in clause (A), (B) or (C) above, shall be individually eligible for each milestone payment under this Section 6.5.1(a) **[********]**, subject to the same conditions set forth in clauses (1), (2) and (3) above, subject, in the event such Milestone-Bearing Licensed Derivative is selected to replace a terminated or discontinued Candidate Drug or Product, to Section 6.5.2.

Milestones with respect to: (w) Ispronicline or any Ispronicline Product shall be owed only under column A of the above chart; (x) each IND-Ready Option Candidate Drug or IND-Ready Option Product shall be owed only under column B of the above chart; (y) each POC Option Candidate Drug or POC Option Product (except with respect to POC Option Candidate Drugs resulting from the application of Section 5.10.2(e) and any POC Option Products that contain such POC Option Candidate Drugs, which shall be subject to the financial terms determined in accordance with Section 5.10.2(e)) shall be owed only under column C of the above chart; provided, however, that solely with respect to such POC Option Candidate Drugs or POC Option Products where the Development or Commercialization for the indication for which it had achieved Option Compound Proof of Concept, or for which Targacept conducted a Targacept Option Compound Development Plan (AstraZeneca having elected to designate it as an Option Compound Candidate Drug under Section 5.10.2(d)(1)), **[********]**, subject to Section 5.5.1(c), and AstraZeneca Develops or Commercializes such POC Option Compound Candidate Drug or POC Option Product for a **[********]**, payments by AstraZeneca not previously made under this Section 6.5.1(a), if any, and subject to Section 6.5.2, shall be owed as though such POC Option Candidate Drug or POC Option Product were an IND-Ready Option Candidate Drug or IND-Ready Option Product as set forth under column B of the above chart; and (z) each other Candidate Drug (other than a Licensed Derivative) or any Product that contains such Candidate Drug and each Milestone-Bearing Licensed Derivative (or Product that contains such Milestone-Bearing Licensed Derivative) shall be owed only under column D of the above chart. AstraZeneca shall, however, make additional payments if and as provided in Section 6.5.1(b) and Section 6.5.1(c), subject to Section 6.5.2.

(b) Additional Primary Milestone Stream. In addition to the milestone payments required by Section 6.5.1(a) and Section 6.5.1(c), AstraZeneca shall, with respect to each Candidate Drug (other than a Licensed Derivative) or Product that contains such Candidate Drug, and each Milestone-Bearing Licensed Derivative with respect to such Candidate Drug (or Product that contains such Milestone-Bearing Licensed Derivative), make each of the following payments **[********]** after each occurrence of the corresponding milestone event after (x) (i) the Commencement Date or (ii) if there is no Commencement Date, the day after the Sunset Date, or if, subject to Section 3.3.2(b), neither Party terminates this Agreement in accordance with Section 11.2.1, after the first date on which neither Party has the right to terminate this Agreement pursuant to Section 11.2.1, whichever is later, or (y) solely with respect to Option Compound Candidate Drugs (other than Licensed Derivatives) or Option Compound Products that contain any such Option Compound Candidate Drug, and any Milestone-Bearing Licensed Derivatives (or Products that contain such Milestone-Bearing Licensed Derivatives) with respect thereto, the Effective Date; provided that if a milestone event with respect to a Candidate Drug (other than a Licensed Derivative) or a Product that contains such Candidate Drug, or a Milestone-Bearing Licensed Derivative with respect thereto or Product that contains such Milestone-Bearing Licensed Derivative, in each case, other than an Option Compound Candidate Drug or Option Compound Product, occurs prior to (A) the Commencement Date, AstraZeneca shall pay such milestone payment within **[********]** after the Commencement Date or (B) if there is no Commencement Date, the Sunset Date, or if, subject to Section 3.3.2(b), neither Party terminates this Agreement in accordance with Section 11.2.1, the first date on which neither Party has the right to terminate this Agreement pursuant to Section 11.2.1, whichever is later, AstraZeneca shall pay such milestone payment within **[********]** after the Sunset Date or such later date (as applicable).

	Candidate Drugs/Products	
Milestone Event	**A Ispronicline/Ispronicline Products/POC Optoin Candidate Drugs/POC Option Products**	**B All Other Candidat Drugs/Products**
1. Initiation of **[********]**	**[********]**	**[********]**
2. Receipt of **[********]** Regulatory Approval **[********]**	**[********]**	**[********]**
3. **[********]**	**[********]**	**[********]**

With respect to each of (i) Ispronicline and any Ispronicline Product, collectively, (ii) each Candidate Drug (other than Ispronicline or an Option Compound Candidate Drug, which are addressed in clauses (i) and (iii), respectively, and other than a Milestone-Bearing Licensed Derivative (or Product that contains such Milestone-Bearing Licensed Derivative), which is addressed in the next sentence) and any Product that contains such Candidate Drug, collectively, and (iii) each Option Compound Candidate Drug (other than a Licensed Derivative), and any Option Compound Product that contains such Option Compound Candidate Drug, collectively, AstraZeneca shall make a payment corresponding to each of the foregoing milestone events only once for each compensable indication under this Section 6.5.1(b), regardless of the number of Candidate Drugs contained in a Product. Each Milestone-Bearing Licensed Derivative with respect to any Candidate Drug(s) or Product(s) set forth in clause (i), (ii) or (iii) above, shall be individually eligible for each milestone under this Section 6.5.1(b) **[********]**, subject to the same conditions set forth above, subject, in the event such Milestone-Bearing Licensed Derivative is selected to replace a terminated or discontinued Candidate Drug or Product, to Section 6.5.2.

Milestones with respect to (x) (1) Ispronicline or any Ispronicline Product and (2) each POC Option Candidate Drug or POC Option Product (except with respect to POC Option Candidate Drugs resulting from the application of Section 5.10.2(e) and any POC Option Products that contain such POC Option Candidate Drugs, which shall be subject to the financial terms determined in accordance with Section 5.10.2(e)), in each case ((1) and (2)), shall be owed only under column A of the above chart; provided, however, that solely with respect to such POC Option Candidate Drugs or POC Option Products where the Development or Commercialization for an indication for which it had achieved Option Compound Proof of Concept, or for which Targacept conducted a Targacept Option Compound Development Plan (AstraZeneca having elected to designate it as an Option Compound Candidate Drug under Section 5.10.2(d)(1)), **[********]**, subject to Section 5.5.1(c), and AstraZeneca Develops or Commercializes such POC Option Candidate Drug or POC Option Product for, payments by AstraZeneca not previously made under this Section 6.5.1(b), if any, and subject to Section 6.5.2, shall be owed as

though such POC Option Candidate Drug or POC Option Product were an IND-Ready Option Candidate Drug or IND-Ready Option Product as set forth under column B of the above chart and (y) each other Candidate Drug (other than a Licensed Derivative) or any Product that contains such Candidate Drug and each Milestone-Bearing Licensed Derivative (or Product that contains such Milestone-Bearing Licensed Derivative) shall be owed only under column B of the above chart.

For purposes of this Section 6.5.1(b) (and Section 6.5.1(a)), AD and MCI shall be considered the same indication.

(c) Small Market Indication Milestone. In addition to the milestone payments required by Section 6.5.1(a) and Section 6.5.1(b), AstraZeneca shall, with respect to each (i) Candidate Drug (other than a Licensed Derivative) or Product that contains such Candidate Drug and each Milestone-Bearing Licensed Derivative (or Product that contains such Milestone-Bearing Licensed Derivative), in each case for which **[********]** Regulatory Approval has been received for **[********]**, make the following payment within **[********]** after each occurrence of the corresponding milestone event:

	Candidate Drugs/Products	
	A	
Milestone Event	**Ispronicline/Ispronicline Products/POC Option Candidate Drugs/POC Option Products**	**B All Other Candidate Drugs/Products**
1. Receipt of **[********]** Regulatory Approval **[********]**	**[********]**	**[********]**

With respect to each of (i) Ispronicline and any Ispronicline Product, collectively, (ii) each Candidate Drug (other than Ispronicline or an Option Compound Candidate Drug, which are addressed in clauses (i) and (iii), respectively, and other than a Milestone-Bearing Licensed Derivative (or Product that contains such Milestone-Bearing Licensed Derivative), which is addressed in the next sentence) and any Product that contains such Candidate Drug, collectively, and (iii) each Option Compound Candidate Drug (other than a Licensed Derivative) and any Option Compound Product that contains such Option Compound Candidate Drug, collectively,

AstraZeneca shall make a payment corresponding to each of the foregoing milestone events only once for each Small Market Indication under this Section 6.5.1(c), regardless of the number of Candidate Drugs contained in a Product. Each Milestone-Bearing Licensed Derivative with respect to any Candidate Drug(s) or Product(s) set forth in clause (i), (ii) or (iii) above, shall be individually eligible for each milestone under this Section 6.5.1(c) **[********]**, subject to the same conditions set forth above, subject, in the event such Milestone-Bearing Licensed Derivative is selected to replace a terminated or discontinued Candidate Drug or Product, to Section 6.5.2.

Milestones with respect to (x) (1) Ispronicline or any Ispronicline Product and (2) each POC Option Candidate Drug or POC Option Product (except with respect to POC Option Candidate Drugs resulting from the application of Section 5.10.2(e) and any POC Option Products that contain such POC Option Candidate Drugs, which shall be subject to the financial terms determined in accordance with Section 5.10.2(e)), in each case ((1) and (2)), shall be owed only under **[********]** of the above chart; provided, however, that solely with respect to such POC Option Candidate Drugs or POC Option Products where the Development or Commercialization for an indication for which it had achieved Option Compound Proof of Concept, or for which Targacept conducted a Targacept Option Compound Development Plan (AstraZeneca having elected to designate it as an Option Compound Candidate Drug under Section 5.10.2(d)(1)), **[********]**, subject to Section 5.5.1(c), and AstraZeneca Develops or Commercializes such POC Option Candidate Drug or POC Option Product for, payments by AstraZeneca not previously made under Section 6.5.1(c), if any, and subject to Section 6.5.2, shall be owed as though such POC Option Candidate Drug or POC Option Product were an IND-Ready Option Candidate Drug or IND-Ready Option Product as set forth under **[********]** of the above chart and (y) each other Candidate Drug (other than a Licensed Derivative) or any Product that contains such Candidate Drug and each Milestone-Bearing Licensed Derivative (or Product that contains such Milestone-Bearing Licensed Derivative) shall be owed only under column B of the above chart.

(d) Notwithstanding anything herein to the contrary, AstraZeneca shall have no obligation to make any milestone payments under this Section 6.5.1 with respect to any Licensed Derivative that is not a Milestone-Bearing Licensed Derivative.

6.5.2 **Effect of Discontinued Development of Candidate Drugs and Indications on Obligation to Pay Milestones; No Payment for Label Expansions**.

(a) Notwithstanding Sections 6.5.1(a) and 6.5.1(b), and subject to Sections 6.6.1(d)(2), 10.2.4 and 10.2.6, if (i) AstraZeneca makes payments for any of milestone events 1, 2, 4, 5 and 6 under Section 6.5.1(a) or for milestone event 1 under Section 6.5.1(b) for a Candidate Drug in Development for a particular Primary Indication or for Schizophrenia, (ii) AstraZeneca subsequently terminates Development of such Candidate Drug for any reason, and (iii) AstraZeneca subsequently Develops, or is Developing, another Candidate Drug (including a Licensed Derivative with respect to the Candidate Drug for which Development was terminated), for which milestones would be due under Sections 6.5.1(a) and 6.5.1(b) but for this Section 6.5.2, for the same Primary Indication for which it was Developing the Candidate Drug for which Development was terminated, or if the Candidate Drug for which Development was terminated was being Developed for Schizophrenia, Schizophrenia, then: (x) AstraZeneca shall only be obligated to make payments corresponding to those milestone events that occur for the non-terminated Candidate Drug for which it had not previously made payments under Section 6.5.1(a) or Section 6.5.1(b), as applicable, with respect to the terminated Candidate Drug; and (y) AstraZeneca may **[********]** any milestone payments that were made under Section 6.5.1(a) or 6.5.1(b) for the non-terminated Candidate Drug, but which are no longer owed by operation of this Section 6.5.2(a) **[********]** to Targacept for **[********]**. For purposes of clarity and by way of example, if (A) AstraZeneca is Developing Candidate Drug n for AD, (B) AstraZeneca pays the applicable amounts upon the occurrence of milestone events 1, 2, 4 and 5 under Section 6.5.1(a) for Candidate Drug n, (C) AstraZeneca terminates the Development of Candidate Drug n in a Phase III Clinical Trial, and (D) AstraZeneca subsequently Develops Candidate Drug n+1 for AD, and such Candidate Drug n+1 achieves any of milestone events 1, 2, 4 or 5 under Section 6.5.1(a), AstraZeneca shall not have any obligation to pay any milestone upon the occurrence of milestone events 1, 2, 4 or 5 under Section 6.5.1(a) for Candidate Drug n+1; provided that, if Candidate Drug n+1 (or a Product that contains Candidate Drug n+1) receives **[********]** Regulatory Approval for AD in any Major Market Country, AstraZeneca shall have an obligation to pay the applicable milestone upon the occurrence of each of milestone events 1, 2, 4 and 5 pursuant to Section 6.5.1(a) (as well as upon the occurrence of each of milestone

events 6, 7, 8 and 9) for Candidate Drug n+2 and each subsequent Candidate Drug Developed for AD, except as otherwise provided in this Section 6.5.2.

(b) Notwithstanding Sections 6.5.1(a) and 6.5.1(b), and subject to Sections 6.6.1(d)(2), 10.2.4 and 10.2.6, if (i) AstraZeneca is Developing a Candidate Drug for two (2) indications (whether for two (2) Primary Indications or for one (1) Primary Indication and Schizophrenia) and makes a payment for milestone event 5 under Section 6.5.1(a) for one such indication and a payment for milestone event 1 under Section 6.5.1(b) for the other such indication, and (ii) AstraZeneca subsequently terminates Development of either such indication for any reason, then AstraZeneca may **[********]** the payment made for milestone event 1 under Section 6.5.1(b) **[********]** to Targacept **[********]**. For purposes of clarity and by way of example, if (A) AstraZeneca is Developing Candidate Drug n for AD and CDS, (B) AstraZeneca pays the applicable amount upon the occurrence of milestone event 5 under Section 6.5.1(a) for Candidate Drug n for AD and milestone 1 under Section 6.5.1(b) for Candidate Drug n for CDS, and (C) AstraZeneca terminates the Development of Candidate Drug n for either AD or CDS in a Phase III Clinical Trial, AstraZeneca may **[********]** the payment for milestone event 1 under Section 6.5.1(b) **[********]** to Targacept **[********]**. For purposes of further clarity, if, in the scenario described in the immediately preceding sentence, AD was terminated, the continued Development of Candidate Drug n (or the Commercialization of a Product that contains Candidate Drug n) for CDS would be subject to the payment of milestones under Section 6.5.1(a) upon the occurrence of each milestone event for which a milestone payment has not been made for Candidate Drug n at the time its Development for AD was terminated, as well as milestones under Sections 6.5.1(b) and 6.5.1(c) upon the occurrence of the milestone events set forth therein with respect to additional indications, if any, for Candidate Drug n (or a Product that contains Candidate Drug n).

(c) AstraZeneca shall not be obligated to make milestone payments as a result of any Label Expansion.

6.5.3 **Sublicensees**. AstraZeneca shall retain, and Targacept shall have no right in or to, any payments made to AstraZeneca or its Affiliates, including any license fees and milestone payments (other than royalties and Sales-Based Milestones, which shall be governed

by Section 6.6.1(c)), however characterized, by any Sublicensee in consideration of rights sublicensed under Section 8.1 (in accordance with Section 8.3.1). AstraZeneca shall not structure any agreement with a Sublicensee with an intent to avoid sharing amounts received thereunder with Targacept.

6.5.4 **Determination that Milestone Events have Occurred**. AstraZeneca shall provide Targacept with prompt written notice upon each occurrence of a milestone event set forth in Section 6.5.1. In the event that, notwithstanding the fact that AstraZeneca has not given such a notice, Targacept believes any such milestone event has occurred, it shall so notify AstraZeneca in writing and shall provide to AstraZeneca data, documentation or other information that supports its belief. Any dispute under this Section 6.5.4 that relates to whether or not a milestone event has occurred shall be referred to the ESC to be resolved in accordance with Section 2.1.5.

6.6 **Payment of Royalties; Royalty Rates; Accounting and Records**.

6.6.1 **Payment of Royalties by AstraZeneca**.

(a) Royalty Rates. Subject to the treatment of Combination Products as provided in the definition of Net Sales in Section 1.186, for each Product or Other Licensed Product, AstraZeneca shall pay Targacept a royalty based on AZ Net Sales of such Product or Other Licensed Product in each Calendar Year (or partial Calendar Year) at the following rates:

(1) Ispronicline Products, IND-Ready Option Products and POC Option Products:

	Royalty Rate (%)		
AZ Net Sales of such Product in the Territory	**A Ispronicline Products**	**B IND-Ready Option Products**	**C POC Option Products**
For that portion of AZ Net Sales of such Product that are less than or equal to [********]	[********]	[********]	[********]
For that portion of AZ Net Sales of such Product that exceed [********] and are less than or equal to [********]	[********]	[********]	[********]
For that portion of AZ Net Sales of such Product that exceed [********] and are less than or equal to [********]	[********]	[********]	[********]
For that portion of AZ Net Sales of such Product that exceed [********] and are less than or equal to [********]	[********]	[********]	[********]
For that portion of AZ Net Sales of such Product that exceed [********]	[********]	[********]	[********]

(2) All other Products (other than Products that only contain Other Licensed Compounds), including, for clarity, Products containing any Licensed Derivatives with respect to Ispronicline, IND-Ready Option Candidate Drugs and POC Option Candidate Drugs:

AZ Net Sales in the Territory	Royalty Rate (%)
For that portion of AZ Net Sales of such Product that are less than or equal to [********]	[********]
For that portion of AZ Net Sales of such Product that exceed [********] and are less than or equal to [********]	[********]
For that portion of AZ Net Sales of such Product that exceed [********]	[********]

(3) For each product that contains one or more Other Licensed Compounds, the Exploitation of which would infringe one or more Other Licensed Product Royalty-Bearing Claims in the absence of the license grants under the Targacept Patent Rights set forth in Section 8.1 (each, an "**Other Licensed Product**"), the Parties shall negotiate in good faith an appropriate royalty rate for the licenses granted under Section 8.1 with respect to such Targacept Patent Right(s) based on such rates as are then customary for unblocking patent licenses for comparable Patent Rights and, if and to the extent that such Targacept Patent Rights provide exclusivity with respect to such Other Licensed Product, the value of such exclusivity; provided that in the event the Parties are

unable to agree, such matter shall be referred to an Expert for resolution in accordance with Section 14.4 (expedited arbitration). For purposes of clarity, no royalties shall be owed to Targacept with respect to any Other Licensed Compounds other than an Other Licensed Product; provided that nothing in this Section 6.6.1(a)(3) shall be deemed to permit the Exploitation of any Other Licensed Product where such Exploitation would constitute a breach of Section 8.6.3 or any other provision of this Agreement.

(4) Notwithstanding anything in the contrary in this Section 6.6.1(a), with respect to each Product that is (i) labeled for one or more diagnostic uses, veterinary uses and any other uses other than as a prophylactic or therapeutic pharmaceutical product in humans and (ii) not labeled for use as a prophylactic or therapeutic pharmaceutical product in humans, the Parties shall negotiate in good faith an appropriate royalty rate for sales thereof based on such rates as are then customary for products for such use(s) and, if and to the extent that Targacept Patent Rights provide exclusivity with respect to such use(s), the value of such exclusivity; provided that in the event the Parties are unable to agree, such matter shall be referred to an Expert for resolution in accordance with Section 14.4 (expedited arbitration).

(b) Royalty Term.

(1) Products other than Other Licensed Products. AstraZeneca's obligation to pay royalties under Sections 6.6.1(a)(1), (a)(2), (a)(4) and (c) (with respect to Products other than Other Licensed Products) shall commence, on a country-by-country basis, with respect to each separate Product, on the date of the First Commercial Sale of such Product by AstraZeneca, its Affiliates or Sublicensees in such country. The obligation shall expire, on a country-by-country basis, with respect to each separate Product, when that Product becomes a Terminated Compound with respect to such country or, if earlier, on the last to occur of (A) the twelfth (12th) anniversary of the First Commercial Sale of the first Product that is in the same Compound Family as such Product by AstraZeneca, its Affiliates or Sublicensees in such country; (B) the expiration date in such country of the last to expire of (i) any Targacept Patent Right, Joint Patent Right, AstraZeneca Research Program Patent Right or AstraZeneca Pre-Phase IIb

Program Patent Right, in each case that includes at least one Valid Claim covering the composition of matter of such Product, a pharmaceutical preparation comprising such Product or a method of use of such Product for the indication for which Commercialization Regulatory Approval is obtained with respect to such Product in such country or (ii) any AstraZeneca Derivative Patent Right that includes at least one Valid Claim covering the composition of matter of the Candidate Drug contained in such Product (each of (i) and (ii), a "**Royalty-Bearing Claim**") and (C) solely with respect to Products that are not Licensed Derivatives the expiration or earlier termination of the applicable Data Exclusivity Period. Upon termination of the royalty obligations of AstraZeneca under this Section 6.6.1(b)(1) in a country with respect to a Product, the license grants to AstraZeneca in Section 8.1 shall become fully paid-up and AZ Net Sales of such Product in such country shall be excluded from the royalty calculations set forth in Section 6.6.1(a) (including the thresholds and ceilings). For purposes of clarity, if on the date of the First Commercial Sale of a Product (other than an Other Licensed Product), (i) there is no Royalty-Bearing Claim with respect to such Product, (ii) such First Commercial Sale is after the twelfth (12th) anniversary of the First Commercial Sale of the first Product that is in the same Compound Family as such Product by AstraZeneca, its Affiliates or Sublicensees in such country and (iii) either (x) the Candidate Drug contained in such Product is not a Licensed Derivative, but there is no Data Exclusivity Period with respect to such Product or (y) the Candidate Drug contained in such Product is a Licensed Derivative, then no royalties shall be owed under this Section 6.6.1 until such time, if any, as there is a Royalty-Bearing Claim with respect to such Product.

(2) Other Licensed Products. AstraZeneca's obligation, if any, to pay royalties under Section 6.6.1(a)(3) with respect to each Other Licensed Product shall commence, on a country-by-country basis, with respect to each separate Other Licensed Product, on the date of the First Commercial Sale of such Other Licensed Product by AstraZeneca, its Affiliates or Sublicensees in such country. The obligation shall expire, on a country-by-country basis, with respect to each separate Other Licensed Product, when such Other Licensed Product becomes a Terminated Compound with respect to such country or, if earlier, on the expiration date in such country of the last to

expire of any Targacept Patent Right that includes at least one Valid Claim covering the composition of matter of the applicable Other Licensed Compound(s) contained in such Other Licensed Product, a pharmaceutical preparation comprising such Other Licensed Compound(s) or a method of use of such Other Licensed Compound(s) for the indication for which Commercialization Regulatory Approval is obtained with respect to such Other Licensed Product in such country (each, an "**Other Licensed Product Royalty-Bearing Claim**"). Upon termination of the royalty obligations of AstraZeneca under this Section 6.6.1(b)(2) in a country with respect to an Other Licensed Product, the license grants to AstraZeneca in Section 8.1 shall become fully paid-up and AZ Net Sales of such Other Licensed Product in such country shall be excluded from the royalty calculations set forth in Section 6.6.1(a)(2).

(c) Net Sales by Sublicensees. Any and all AZ Net Sales by Sublicensees shall shall be excluded from the royalty calculations in Sections 6.6.1(a)(1) and 6.6.1(a)(2) (including, for purposes of clarity, the royalty threshold and ceiling calculations). With respect to AZ Net Sales of Product (other than Other Licensed Product) by Sublicensees to Third Parties on which royalties or milestone payments that are based solely on achieving certain sales thresholds for a Product (such milestone payments, "**Sales-Based Milestones**"), are paid to AstraZeneca, royalties to Targacept hereunder with respect to such AZ Net Sales, for any Calendar Year, shall, subject to Sections 6.6.1(d), 10.2.4 and 10.2.6, be equal to **[********]** royalties and Sales-Based Milestones paid to AstraZeneca or its Affiliates by such Sublicensees with respect to such AZ Net Sales during such Calendar Year; provided, however, that no such royalties shall be due under this Section 6.6.1(c) with respect to any AZ Net Sales on which royalties would not be owed by AstraZeneca under Section 6.6.1(a)(1) or 6.6.1(a)(2) were such sales made by AstraZeneca (*e.g.*, after the end of the royalty term set forth in Section 6.6.1(b)). For the avoidance of doubt, no royalty payments shall be due under this Section 6.6.1 with respect to (a) any upfront license fees or milestone payments (other than Sales-Based Milestones) made to AstraZeneca or its Affiliates (which are addressed in Section 6.5.3), or (b) any payments made to AstraZeneca or its Affiliates: (i) under a credit facility; (ii) in consideration of (A) any issuance of equity or debt securities by AstraZeneca or its Affiliates, (B) any supply of Product (including Other Licensed Product) by or on behalf of AstraZeneca or its Affiliates, or (C) any research, development or other activities relating to such Product

(including Other Licensed Product) that AstraZeneca or its Affiliates may perform on behalf of a Sublicensee, provided that such payments do not exceed the fair market value of such securities, supply or activities, as applicable; (iii) in consideration of any grant of rights or licenses (including royalties) other than a sublicense under the licenses granted under Section 8.1 (such consideration to be allocated based on the fair market value only of the rights sublicensed under Section 8.1 (in accordance with Section 8.3.1) to such Sublicensee and the fair market value only of the other rights of AstraZeneca licensed to such Sublicensee); (iv) as reimbursement of actual patent prosecution and maintenance costs and expenses; or (v) in connection with awards or judgments in patent or other intellectual property right enforcement, which shall be allocated between the Parties in accordance with Section 10.2.1(e).

(d) **Reduction of Royalty**.

(1) No Royalty-Bearing Claim. From and after (A) the date on which a Product (or an Other Licensed Product) is either (1) not covered by a Royalty-Bearing Claim or (2) covered only by a Royalty-Bearing Claim based on a method of use of such Product for an indication for which Commercialization Regulatory Approval is obtained with respect to such Product in a given country, which Royalty-Bearing Claim is not capable of providing market exclusivity with respect to such Product in such country (*e.g.,* such Product is approved or is reasonably likely to be approved in the future, by the Regulatory Authorities in such country for another indication and neither such indication nor the composition of matter of the Candidate Drug included in such Product is covered by a Royalty Bearing Claim) and (B) solely with respect to Products that are not Licensed Derivatives (and are not Other Licensed Products) if later, the last day of the Data Exclusivity Period, if any, for such Product in such country, (i) the royalty rate(s) payable to Targacept by AstraZeneca under Section 6.6.1(a) with respect to such AZ Net Sales of such Product in such country shall be reduced by [********] and (ii) the royalties and other payments paid to Targacept under Section 6.6.1(c) with respect to AZ Net Sales of such Product (other than an Other Licensed Product) by Sublicensees to Third Parties on which royalties or Sales-Based Milestones, if any, are paid to AstraZeneca, for any Calendar Year shall be reduced by [********] (*i.e.*, [********] of any amounts paid to AstraZeneca or its Affiliates by such Sublicensees with respect to such AZ Net Sales

during such Calendar Year). For purposes of this Section 6.6.1(d)(1), the royalty rate(s) payable to Targacept with respect to Net Sales of a Product in a given country shall be deemed to be the rate(s) which would apply if Net Sales of such Product in such country subject to each of the royalty rates under Section 6.6.1(a) were proportional to Net Sales of such Product in all countries subject to each of the royalty rates under Section 6.6.1(a).

(2) Royalty Stacking. AstraZeneca shall have the right to reduce the amount of (A) royalties owing to Targacept under Section 6.6.1(a) (as such royalties may be adjusted pursuant to the other provisions of this Section 6.6.1(d) and Section 10.2.4 and 10.2.6) and (B) royalties or other payments owing to Targacept under Section 6.6.1(c) (as such payments may be adjusted pursuant to the other provisions of this Section 6.6.1(d) and Section 10.2.4 and 10.2.6), in each case, for any Product by [********] of the amount of royalties (if any), or other amounts (including license fees and milestones) paid by AstraZeneca or any of its Affiliates (including on behalf of any Sublicensee) or, solely with respect to Other Licensed Products, Sublicensees, to any Third Party in consideration for the license of Patent Rights in any country if, at the time such license was granted such Patent Rights would, or might reasonably be expected to, be infringed by the Exploitation of the Product in the Territory in the Field or, if the Product is being Developed for Schizophrenia, Schizophrenia in the absence of such a license (for clarity, payments by AstraZeneca to such Third Party with respect to AZ Net Sales by AstraZeneca and its Affiliates shall only be applied to reduce the amounts owing to Targacept under Section 6.6.1(a) and payments by AstraZeneca or its Affiliates to such Third Party with respect to AZ Net Sales by AstraZeneca's or its Affiliates' Sublicensees shall only be applied to reduce the amounts owed to Targacept under Section 6.6.1(c)); provided, however, that, except as otherwise provided in the next proviso, in no event shall the royalties owed under Section 6.6.1(a) (and not Section 6.6.1(c), which shall not be subject to this [********] limitation) with respect to a Product in a country be reduced solely by operation of this Section 6.6.1(d)(2), together with Section 10.2.4 and 10.2.6, by more than [********] of what would otherwise be owed under 6.6.1(a) (as such royalties may be adjusted pursuant to the other provisions of this Section 6.6.1(d)) with respect to such Product; and provided further that to the extent that the need for any such license arises from or relates to a breach by Targacept of its representations and

warranties under this Agreement with respect to a Collaboration Compound, Candidate Drug or Product, and notwithstanding Sections 10.2.4 and 10.2.6 and the preceding proviso, [********] of any such royalties, license fees or milestones with respect to such Collaboration Compound, Candidate Drug or Product may be credited against such royalties under clause (A) or royalties or other payments under clause (B), above, as well as against any milestones under Section 6.5 with respect to such Collaboration Compound, Candidate Drug or Product. For purposes of this Section 6.6.1(d)(2), the amount of royalties owing to Targacept under Section 6.6.1(a) (as such royalties may be adjusted pursuant to the other provisions of this Section 6.6.1(d) and Sections 10.2.4 and 10.2.6) for Net Sales of any Product in a given country shall be deemed to be that amount which would be owed if Net Sales of such Product in such country subject to each of the royalty rates under Section 6.6.1(a) (as such royalty rates may be adjusted pursuant to the other provisions of this Section 6.6.1(d)) were proportional to Net Sales of such Products in all countries subject to each of the royalty rates under Section 6.6.1(a).

(3) Compulsory Licenses. In the event that a court or a governmental agency of competent jurisdiction requires AstraZeneca or an AstraZeneca Affiliate or Sublicensee to grant a compulsory license to a Third Party permitting such Third Party to make and sell a Product in a country in the Territory, then (x) all Net Sales of such Product in such country, or if such country is in Europe, Europe, shall be excluded from the thresholds and ceilings and the royalty calculations set forth in Sections 6.6.1(a) and 6.6.1(c) and (y) the royalties and other payments to be paid by AstraZeneca on such AZ Net Sales and, if applicable, Sales-Based Milestones of such Product in such country under Section 6.6.1(a) or 6.6.1(c), as applicable, or, if such country is in Europe, Europe, shall automatically be the lesser of (A) the positive difference of the royalties and other payments that would have been payable under Sections 6.6.1(a) and 6.6.1(c), as applicable, but for the exclusion of such AZ Net Sales under clause (x) of this Section 6.6.1(d)(3) (as such payments may be adjusted pursuant to the other provisions of this Section 6.6.1(d) and Sections 10.2.4 and 10.2.6) over the royalties and other payments that would be payable under Sections 6.6.1(a) and 6.6.1(c), as applicable, after giving effect to the exclusion of such AZ Net Sales under clause (x) of this Section 6.6.1(d)(3) (as such payments may be adjusted pursuant to the other

provisions of this Section 6.6.1(d) and Sections 10.2.4 and 10.2.6) and (B) the product of the royalty rate under such compulsory license times such AZ Net Sales without regard to Section 6.6.1(c), in each case ((x) and (y)) during the time period when such compulsory license is in effect and being exercised.

(4) Non-AZ Sales by Targacept or Licensee. Except as provided in this Section 6.6.1(d)(4), in the event that, at any time during the royalty term for a particular Product or Other Licensed Product is commercially sold in any country in the Territory by (A) Targacept or its Affiliates (other than in the case of a Co-Promoted Product) or (B) a Third Party that has licensed the right to sell such Product or Other Licensed Product from Targacept, including any Sublicensee, (x) the royalty rate(s) payable to Targacept by AstraZeneca under Section 6.6.1(a) (as such royalties may be adjusted pursuant to the other provisions of Section 6.6.1(d) and Sections 10.2.4 and 10.2.6) with respect to all AZ Net Sales of such Product in the Territory shall be reduced by [********] and (y) the royalties and other payments paid to Targacept under Section 6.6.1(c) with respect to AZ Net Sales of such Product (other than Other Licensed Product) by Sublicensees to Third Parties on which royalties or Sales-Based Milestones, if any, are paid to AstraZeneca, for any Calendar Year shall be reduced by [********] (*i.e.*, [********] of any amounts paid to AstraZeneca or its Affiliates by such Sublicensees with respect to such AZ Net Sales during such Calendar Year) (as such royalties and other payments may be adjusted pursuant to the other provisions of Section 6.6.1(d) and Sections 10.2.4 and 10.2.6). For purposes of clarity, this Section 6.6.1(d)(4) shall not apply in the event of sale of Terminated Compounds (including Terminated AZ Compounds), Unexercised Option Compounds or any product to the extent that it contains a Terminated Compound (including a Terminated AZ Compound) or Unexercised Option Compound.

(5) Application of Reductions. Any reductions set forth in this Section 6.6.1(d) (or in Section 10.2.4 or 10.2.6 or any other provision of this Agreement permitting the reduction of royalties) shall be applied to royalties payable to Targacept under Section 6.6.1(a) in the order in which the event triggering such reduction occurs. For purposes of clarity, the reductions set forth in this Section 6.6.1(d) and Sections

10.2.4 and 10.2.6 (except as otherwise expressly provided in Sections 6.6.1(d)(2), 10.2.4 and 10.2.6) are are intended to be **[********]** reduction may be **[********]** reduction). Credits not exhausted in any Calendar Quarter may be carried into future Calendar Quarters, subject to the foregoing sentence.

(e) Payment Dates and Reports. Royalty payments shall be made by AstraZeneca within **[********]** after the end of each Calendar Quarter commencing with the Calendar Quarter in which the First Commercial Sale of a Product by AstraZeneca, its Affiliates or Sublicensees occurs. All payments shall be made by wire transfer in accordance with instructions given in writing from time to time by Targacept. AstraZeneca shall also provide, at the same time each such payment is made, a report showing: (i) the AZ Net Sales of each Product by country in the Territory; (ii) the basis for any deductions from gross amounts billed or invoiced to determine AZ Net Sales; (iii) the applicable royalty rates for such Product; (iv) the exchange rates used in calculating any of the foregoing; (v) a calculation of the amount of royalty due to Targacept; and (vi) payments from Sublicensees on which payments are owed to Targacept under Section 6.6.1(c).

(f) Acknowledgement. The Parties recognize and acknowledge that each of the following, separately and together, has substantial economic benefit to AstraZeneca: (i) Targacept's expertise concerning the discovery and optimization of compounds that become Collaboration Compounds and Candidate Drugs; (ii) the performance by Targacept of the Research Program and any Additional Research Program; (iii) the disclosure to AstraZeneca of results obtained in the Research Program and any Additional Research Program by Targacept; (iv) the licenses granted to AstraZeneca hereunder with respect to Targacept Technology and Joint Technology that are not within the claims of any Patent Rights Controlled by Targacept; (v) the licenses granted to AstraZeneca under Patent Rights Controlled by Targacept; (vi) the restrictions on Targacept pursuant to Section 8.6.1; and (vii) the exclusivity afforded to AstraZeneca by each of the foregoing. The Parties agree that the royalty rates set forth in Section 6.6.1 reflect an efficient and reasonable blended allocation of the values provided by Targacept to AstraZeneca.

6.6.2 **Records; Audit Rights**. AstraZeneca shall (and shall use reasonable efforts to ensure that its Affiliates and Sublicensees shall) keep and maintain for **[********]** from the date of each payment of royalties hereunder (or such longer period as may be required by Applicable Law) records of AZ Net Sales by AstraZeneca, its Affiliates and Sublicensees (as the case may be) of each Product in sufficient detail to allow royalties to be determined accurately. Targacept shall have the right for a period of **[********]** after receiving any such payment to inspect or audit, or to appoint at its expense an independent certified public accountant reasonably acceptable to AstraZeneca to inspect or audit, the relevant records of AstraZeneca and its Affiliates to verify that the amount of such payment was correctly determined. AstraZeneca and its Affiliates shall each make its records available for inspection or audit by such independent certified public accountant during regular business hours at such place or places where such records are customarily kept, upon reasonable notice from Targacept, solely to verify that royalty payments hereunder were correctly determined. Such inspection or audit right shall not be exercised by Targacept more than **[********]** in any Calendar Year more than **[********]** with respect to sales of a particular Product in a particular period or more than **[********]** years after the end of such period. All records made available for inspection or audit shall be deemed to be Confidential Information of AstraZeneca and prior to any such inspection or audit the accountant shall enter into a non-disclosure agreement in a form reasonably acceptable to AstraZeneca. The accounting firm shall disclose to the Parties whether the royalty reports are correct or incorrect and the specific details concerning any discrepancies. No other information shall be provided to Targacept. The results of each inspection or audit, if any, shall be binding on both Parties absent manifest error. In the event there was an underpayment by AstraZeneca hereunder, AstraZeneca shall promptly (but in any event no later than **[********]** after AstraZeneca's receipt of the report so concluding) make payment to Targacept of any shortfall. In the event that there was an overpayment by AstraZeneca hereunder, Targacept shall promptly (but in any event no later than **[********]** after Targacept's receipt of the independent accountant's report so concluding) refund to AstraZeneca the excess amount. Targacept shall bear the full cost of such audit unless such audit discloses an underreporting by AstraZeneca of more than **[********]** of the aggregate amount of royalties payable in any Calendar Year, in which case AstraZeneca shall reimburse Targacept for all costs incurred by Targacept in connection with such inspection or audit.

6.6.3 **Overdue Royalties and Milestones**. All royalty payments not made within the time period set forth in Section 6.6.1(e), and all milestone payments not made within the time period specified in Section 6.5.1, shall bear interest at a rate equal to the lesser of the prime rate as published in *The Wall Street Journal*, Eastern United States Edition, on the first day of each Calendar Quarter in which such payments are overdue, plus **[********]**, calculated on the number of days such payment is delinquent, compounded annually or, if less, the maximum interest rate permitted by Applicable Laws. Any such overdue royalty or milestone payment shall, when made, be accompanied by, and credited first to, all interest so accrued.

6.6.4 **Withholding Taxes**. The royalties, milestones and other amounts payable by AstraZeneca to Targacept pursuant to this Agreement ("**Payments**") shall not be reduced on account of any taxes unless required to be so reduced by Applicable Laws. Targacept alone shall be responsible for paying any and all taxes (other than withholding taxes required by Applicable Laws to be paid by AstraZeneca) levied on account of, or measured in whole or in part by reference to, any Payments it receives. AstraZeneca shall deduct or withhold from the Payments any taxes that it is required by Applicable Laws to deduct or withhold. Notwithstanding the foregoing, if Targacept is entitled under any applicable tax treaty to a reduction of rate of, or the elimination of, applicable withholding tax, it may deliver to AstraZeneca or the appropriate governmental authority (with the assistance of AstraZeneca to the extent reasonably required and expressly requested in writing) the prescribed forms necessary to reduce the applicable rate of withholding or to relieve AstraZeneca of its obligation to withhold tax, and AstraZeneca shall apply the reduced rate of withholding, or dispense with withholding, as the case may be; provided that AstraZeneca has received evidence, in a form satisfactory to AstraZeneca, of Targacept's delivery of all applicable forms (and, if necessary, its receipt of appropriate governmental authorization) at least fifteen (15) days prior to the date that the applicable Payment is due. If, in accordance with the foregoing, AstraZeneca withholds any amount, it shall pay to Targacept the balance when due, make timely payment to the proper taxing authority of the withheld amount, and send to Targacept proof of such payment within sixty (60) days following that payment. For purposes of this Agreement, the stated amount of the Payments payable by AstraZeneca shall include any sales tax that Targacept may be required to collect.

6.6.5 **Indirect Taxes**. Notwithstanding anything contained in Section 6.6.4, this Section 6.6.5 shall apply with respect to Indirect Taxes. All Payments are exclusive of Indirect Taxes. If any Indirect Taxes are chargeable in respect of any Payments, AstraZeneca shall pay such Indirect Taxes at the applicable rate in respect of any such Payments following the receipt, where applicable, of an Indirect Taxes invoice in the appropriate form issued by Targacept in respect of those Payments, such Indirect Taxes to be payable on the due date of the payment of the Payments to which such Indirect Taxes relate.

6.6.6 **Foreign Currency Exchange**. All royalties shall be payable in full in United States Dollars, regardless of the countries in which sales are made. If, in any Calendar Quarter, AZ Net Sales are made in any currency other than United States Dollars, such AZ Net Sales (including amounts payable to Targacept under Section 6.6.1(c)) shall be converted into United States Dollars in accordance with AstraZeneca's standard accounting policies approved by its independent auditors for use in its financial statements. All milestone payments shall similarly be payable in United States Dollars, regardless of the country in which the milestone event is achieved.

6.6.7 **Financial Obligations Under In-License Agreements**. Notwithstanding anything in this Agreement to the contrary, Targacept shall be solely responsible for all payments owed to Third Parties under the In-License Agreements.

7. TREATMENT OF CONFIDENTIAL INFORMATION; PUBLICITY; NON-SOLICITATION

7.1 **Confidentiality**

7.1.1 **Confidentiality Obligations**. Targacept and AstraZeneca each recognizes that the other Party's Confidential Information and Proprietary Materials constitute highly valuable assets of such other Party. Targacept and AstraZeneca each agrees that, subject to Section 7.1.2, it will not disclose, and will cause its Affiliates and Sublicensees not to disclose, any Confidential Information or Proprietary Materials of the other Party and it will not use, and will cause its Affiliates and Sublicensees not to use, any Confidential Information or Proprietary Materials of the other Party except as expressly permitted hereunder; provided that such obligations shall apply (a) during the Term and for an additional [********] thereafter, in the

case of Confidential Information, and (b) during and after the Term, in the case of Proprietary Materials. Without limiting the generality of the foregoing, each Party shall take such action, and shall cause its Affiliates and Sublicensees to take such action, to preserve the confidentiality of the other Party's Confidential Information and Proprietary Materials as such Party would customarily take to preserve the confidentiality of its own Confidential Information and Proprietary Materials and shall, in any event, use at least reasonable care to preserve the confidentiality the other Party's Confidential Information and Proprietary Materials.

7.1.2 **Limited Disclosure**. Targacept and AstraZeneca each agrees that disclosure of its Confidential Information or any transfer of its Proprietary Materials may be made by the other Party to any employee, consultant or Affiliate of such other Party to enable such other Party to exercise its rights or to carry out its responsibilities under this Agreement; provided that any such disclosure or transfer shall only be made to Persons who are bound by written obligations as described in Section 7.1.3. In addition, except as otherwise provided in Section 7.5, Targacept and AstraZeneca each agrees that the other Party may disclose its Confidential Information (a) on a need-to-know basis to such other Party's legal and financial advisors, (b) as reasonably necessary in connection with an actual or potential (i) permitted sublicense of such other Party's rights hereunder, (ii) debt or equity financing of such other Party or (iii) Change of Control involving such other Party and (c) to any Third Party to enable a Party to exercise its rights and perform its obligations under this Agreement; if, in each case, the Person receiving such Confidential Information or Proprietary Materials of the other Party agrees in writing to maintain the confidentiality of such Confidential Information or Proprietary Materials of the other Party with terms at least as restrictive as those contained in Section 7.1.1. In addition, each Party agrees that the other Party may disclose such Party's Confidential Information or Proprietary Materials (A) as reasonably necessary to file, prosecute or maintain Patent Rights, or to file, prosecute or defend litigation related to Patent Rights, in accordance with this Agreement; or (B) as required by Applicable Laws; provided that, in the case of any disclosure under this clause (B), the disclosing Party shall (1) provide the other Party with reasonable advance notice of and an opportunity to comment on any such required disclosure, and the disclosing Party shall take into consideration in good faith any such comments (or any reasonably requested redactions) in connection with such disclosure and (2) if requested by the other Party, cooperate in all reasonable respects with the other Party's efforts to obtain

confidential treatment or a protective order with respect to any such disclosure, at the other Party's expense. Notwithstanding anything to the contrary in this Section 7.1.2, if a Party is required to disclose the terms of this Agreement, it shall provide the other Party with reasonable advance notice and shall make such redactions from the disclosed copy of this Agreement, or any summary thereof, as such other Party reasonably requests in a timely manner.

7.1.3 **Employees and Consultants**. Targacept and AstraZeneca each hereby represents that all of its employees and consultants, and all of the employees and consultants of its Affiliates, who participate in the activities of the Collaboration or have access to Confidential Information or Proprietary Materials of the other Party are or will, prior to their participation or access, be bound by written obligations to maintain such Confidential Information or Proprietary Materials in confidence and not to use such information except as expressly permitted hereunder. Each Party agrees to use, and to cause its Affiliates to use, reasonable efforts to enforce such obligations.

7.2 **Publicity**. The Parties acknowledge that the terms of this Agreement constitute Confidential Information of each Party and may not be disclosed except as permitted by Section 7.1.2. However, notwithstanding anything to the contrary in Section 7.1, the Parties, upon the execution of this Agreement, shall agree to a press release with respect to this Agreement and either Party may make subsequent public disclosure of the contents of such press release without further approval of the other Party. After issuance of such press release, except as required by Applicable Laws, neither Party shall issue a press or news release or make any similar public announcement (it being understood that publication in scientific journals, presentation at scientific conferences and meetings and the like are intended to be covered by Section 7.3 and not subject to this Section 7.2) related to **[********]** without the prior written consent of the other Party; provided that, notwithstanding the foregoing, (a) **[********]**, Targacept shall be expressly permitted to **[********]** and (b) **[********]**, AstraZeneca shall be expressly permitted to **[********]**.

7.3 **Publications and Presentations**. The Parties acknowledge that scientific publications and presentations must be strictly monitored to prevent any adverse effect from premature publication or dissemination of results of the activities hereunder. Each Party agrees that, except as required by Applicable Laws, it shall **[********]**. Each Party shall provide to the

other Party the opportunity to review each of the submitting Party's proposed abstracts, manuscripts or presentations (including information to be presented verbally) that relate to the Research Program **[********]** at least **[********]** prior to its intended presentation or submission for publication, and such submitting Party agrees, upon written request from the other Party given within such **[********]** period, not to submit such abstract or manuscript for publication or to make such presentation until the other Party is given up to **[********]** from the date of such written request to seek appropriate patent protection for any material in such publication or presentation that it reasonably believes may be patentable. Further, AstraZeneca shall **[********]**. Once an abstract, manuscript or presentation has been reviewed and, in the case of any abstract, manuscript or presentation that relates to the Research Program, approved by a Party **[********]**, the same abstract, manuscript or presentation does not have to be provided again to the other Party for review for a later submission for publication. Each Party also shall have the right to require that any of its Confidential Information that is disclosed in any such proposed publication or presentation be deleted prior to such publication or presentation. In any permitted publication or presentation by a Party, the other Party's contribution shall be duly recognized, and co-authorship shall be determined in accordance with customary standards. All such abstracts, manuscripts and presentations by or on behalf of Targacept shall **[********]**. Notwithstanding anything in this Section 7.3 to the contrary, Targacept shall **[********]** publication in connection with the Ongoing Ispronicline Trial; provided that Targacept shall (a) coordinate its activities in connection therewith with AstraZeneca in good faith and (b) permit AstraZeneca to review and comment on any such publication.

7.4 **Prohibition on Solicitation**. Without the written consent of the other Party, neither Party nor its Affiliates shall, commencing on the Effective Date and ending **[********]**, solicit any employee of the other Party or its Affiliates who participated in the Research Program at any time during the Research Program Term. This provision shall not restrict either Party or its Affiliates from advertising employment opportunities, engaging head-hunters or engaging in any other activity directed towards recruitment, in each case if and to the extent that such advertising or activities do not directly target the other Party or its Affiliates.

7.5 **Excluded Data**. To the extent any Targacept Technology or AstraZeneca Technology comprises Excluded Data with respect to a compound (regardless of the Party that

generated such Excluded Data), such Technology shall **[********]** unless and until such compound becomes a Terminated AZ Compound or an Unexercised Option Compound or Targacept is otherwise permitted to develop and commercialize such compound or product in the Field or Schizophrenia, as applicable, pursuant to Section 8.6 and, notwithstanding Section 7.1.2 or any other provision of this Agreement, Targacept shall **[********]**.

8. LICENSE GRANTS; EXCLUSIVITY

8.1 **Targacept License Grants**.

8.1.1 **Research Program and Tail Period**. Subject to the other terms of this Agreement, Targacept shall, and hereby does, grant to AstraZeneca, with effect on the Effective Date, a co-exclusive (with Targacept and its Affiliates), royalty-free, worldwide license, without the right to grant sublicenses (except to its Affiliates and as reasonably necessary in connection with any engagement by AstraZeneca of a Third Party to conduct work in the Research Program or any Additional Research Program as permitted in Section 4.1), during the Research Program Term and the Tail Period, under Targacept Technology and Targacept Patent Rights and Targacept's interest in Joint Technology and Joint Patent Rights, solely to conduct the AstraZeneca Research Activities. For purposes of clarity, the co-exclusivity granted by Targacept under this Section 8.1.1 is limited to the sole purpose referenced in the preceding sentence and shall have no effect on Targacept's ability to Exploit Targacept Technology, Targacept Patent Rights and Targacept's interest in Joint Technology and Joint Patent Rights for any other purpose, to the extent permitted by Section 8.6 and consistent with the exclusive and co-exclusive grants set forth in this Agreement.

8.1.2 **Option Compounds**. Subject to the other terms of this Agreement, Targacept shall, and hereby does, grant to AstraZeneca, with effect on the Effective Date, a co-exclusive (with Targacept and its Affiliates), royalty-free, worldwide license, without the right to grant sublicenses, during the Option Term, under Targacept Technology and Targacept Patent Rights and Targacept's interest in Joint Technology and Joint Patent Rights, solely (a) **[********]** and (b) to develop, or have developed, any Option Compound in respect of which AstraZeneca has elected to complete the Option Compound Development Plan pursuant to, and

to the extent permitted by, Section 5.10.2(b)(5). For purposes of clarity, the co-exclusivity granted by Targacept under this Section 8.1.2 is limited to the sole purpose referenced in the preceding sentence and shall have no effect on Targacept's ability to Exploit Targacept Technology, Targacept Patent Rights and Targacept's interest in Joint Technology and Joint Patent Rights for any other purpose, to the extent permitted by Section 8.6 and consistent with the exclusive and co-exclusive grants set forth in this Agreement.

8.1.3 **Development and Exploitation**. Subject to the other terms of this Agreement, Targacept shall, and hereby does, grant to AstraZeneca, with effect on the Effective Date, an exclusive (even as to Targacept and its Affiliates), royalty-bearing, worldwide license, with the right to grant sublicenses, under Targacept Technology and Targacept Patent Rights and Targacept's interest in Joint Technology and Joint Patent Rights:

(a) to Exploit (i) Ispronicline and Ispronicline Products (including conducting the Pre-Phase IIb Program), (ii) any Licensed Derivatives with respect to Ispronicline, and (iii) any Additional Compounds with respect to the foregoing;

(b) to Exploit (i) Collaboration Candidates and Active+ Compounds until such time, with respect to each such Collaboration Candidate and Active+ Compound, as it becomes a Terminated Compound, (ii) Collaboration Compounds, Candidate Drugs, and Products (other than Ispronicline or Ispronicline Products (or any Licensed Derivatives with respect thereto), Option Compound Candidate Drugs or Option Compound Products), and (iii) any Additional Compounds with respect to the foregoing; and

(c) to Exploit (i) Option Compound Candidate Drugs and Option Compound Products and (ii) any Additional Compounds with respect to the foregoing;

provided that: (i) AstraZeneca and its Sublicensees shall not have the right under this Section 8.1.3 to Develop, file Drug Approval Applications or obtain or maintain Regulatory Approvals for, promote (which, for clarity, shall not include responses by AstraZeneca's Medical Resources Department or any equivalent department outside the United States to unsolicited inquiries with respect to any Candidate Drug or Product) or market any Candidate Drugs or Products outside the Field and outside Schizophrenia; (ii) such licenses granted under this Section 8.1.3 shall

terminate, with respect to any compound or product, at such time as such compound or product becomes a Terminated Compound; and (iii) such licenses granted under this Section 8.1.3 shall not preclude Targacept from such actions as may be necessary: (A) to conduct the Research Program or any Additional Research Program; (B) to conduct the Ongoing Ispronicline Trial; (C) to conduct Targacept Development Activities under any Product Development Plan; (D) subject to Section 5.10.2(c)(1), to identify, research and develop potential Back-Up Option Compounds (which, for purposes of clarity, are Additional Compounds with respect to the applicable Option Compound Candidate Drugs) with respect to Option Compound Candidate Drugs, in each case ((A) through (D)) in accordance with this Agreement; and (E) otherwise for purposes of performing Targacept's obligations with respect to AstraZeneca under this Agreement.

8.1.4 **Derivatives**. Subject to the other terms of this Agreement (including Section 8.6.3), Targacept shall, and hereby does, grant to AstraZeneca, with effect on the Effective Date, a non-exclusive, royalty-free, worldwide license, with the right to grant sublicenses, under Targacept Technology and Targacept Patent Rights and Targacept's interest in Joint Technology and Joint Patent Rights: (a) to Derive compounds from Collaboration Compounds, Candidate Drugs and Products (other than Terminated Compounds and products to the extent that they contain Terminated Compounds), which shall become effective (i) as of the Effective Date with respect to Ispronicline, Ispronicline Products, Option Compound Candidate Drugs and Option Compound Products and (ii) after the end of the Tail Period or, if there is no Tail Period, the Research Program Term, with respect to all other Candidate Drugs and Products and all Collaboration Compounds; and (b) to Exploit any such Derived compound; provided, however, that in each case ((a) and (b)) AstraZeneca and its Sublicensees shall not have the right, under this Section 8.1.4, to Develop, file Drug Approval Applications or obtain or maintain Regulatory Approvals for, sell, offer for sale or have sold (other than to an Affiliate in an intra-company transfer), promote or market (i) any such Derived compound or any product that contains such Derived compound (for purposes of clarity, any such Derived compound that is a Collaboration Compound, Candidate Drug, Product or any Additional Compound or Additional Product with respect to any of the foregoing shall be covered by Section 8.1.3) or (ii) any Excluded Derivative, in each case ((i) or (ii)) in or outside the Field.

8.1.5 **Post-Restricted Derivative Period Technology License**. Subject to Section 8.6.3, Targacept shall, and hereby does, grant to AstraZeneca a non-exclusive, royalty-free, worldwide license, with the right to grant sublicenses, under Targacept Technology (but not Targacept Patent Rights) and Targacept's interest in Joint Technology (but not Joint Patent Rights), to Exploit compounds Derived from (a) Ispronicline, (b) Collaboration Compounds or Candidate Drugs, (c) IND-Ready Option Candidate Drugs and (d) POC Option Candidate Drugs, in each case ((a) through (d)) after the expiration of the applicable Restricted Derivative Period, **[********]**. Nothing in this Section 8.1.5 shall require Targacept to provide or disclose any Targacept Technology or Joint Technology to AstraZeneca. For purposes of clarity, AstraZeneca shall not have any rights under this Section 8.1.5 to Exploit (i) Ispronicline, (ii) Lead Collaboration Compounds or Related Collaboration Compounds, (iii) IND-Ready Option Candidate Drugs, (iv) POC Option Candidate Drugs, or (v) any Licensed Derivatives with respect to any of the foregoing Derived prior to the end of the applicable Restricted Derivative Period.

8.1.6 **Regulatory Filings**. Subject to the other terms of this Agreement, each of Targacept and its Affiliates shall, and hereby does, grant to AstraZeneca and its Affiliates:

(a) an exclusive (even as to Targacept and its Affiliates) license and right of reference in the Territory, with the right to grant sublicenses or further rights of reference, under Targacept's and its Affiliates' rights, titles and interests in and to the Regulatory Filings for or relating to any Candidate Drug (including Ispronicline) or Product (including any Ispronicline Product), to the extent not otherwise assigned pursuant to Section 8.4, so as to enable AstraZeneca to exercise its rights under the grants set forth in Sections 8.1.1, 8.1.2, 8.1.3 8.1.4 and 8.1.5; provided, however, Targacept expressly reserves for itself such rights as may be necessary to conduct the Ongoing Ispronicline Trial; and

(b) a co-exclusive (with Targacept and its Affiliates) license and right of reference in the Territory, without the right to grant sublicenses or further rights of reference (except to its Affiliates and as reasonably necessary in connection with any engagement by AstraZeneca of a Third Party to conduct work in the Research Program or any Additional Research Program as permitted in Section 4.1), under Targacept's and its Affiliates' rights, titles

and interests in and to the Regulatory Filings, if any, for or relating to any Option Compounds, so as to enable AstraZeneca (i) **[********]** and (ii) to develop, or have developed, any Option Compound in respect of which AstraZeneca has elected to complete the Option Compound Development Plan pursuant to, and to the extent permitted by, Section 5.10.2(b)(5).

In each case ((a) and (b)), Targacept shall, as soon as reasonably practicable following AstraZeneca's written request, provide AstraZeneca with full access to all such Regulatory Filings, all data and other information contained therein, and correspondence relating thereto.

8.1.7 **Additional Assurance**. Targacept shall not enter into any agreement, whether written or oral, with respect to, or otherwise assign, transfer, license, convey or otherwise encumber its right, title or interest in or to, the Targacept Patent Rights, Targacept Technology, Targacept's interest in Joint Patent Rights and Joint Technology, Regulatory Filings, Compounds, Candidate Drugs or Products (including by granting any covenant not to sue with respect thereto) to any Person that is inconsistent with the rights and licenses granted to AstraZeneca under this Agreement. Notwithstanding the foregoing, in no event shall this Section 8.1.7 be deemed to prevent or restrict, or be deemed breached solely as the result of, a Change of Control of Targacept; provided that the terms of this Agreement (including Section 8.6) shall continue to apply to Targacept and Targacept's acquiror or successor in the Change of Control.

8.2 **AstraZeneca Grants**.

8.2.1 **Research Program**. Subject to the other terms of this Agreement, AstraZeneca shall, and hereby does, grant to Targacept a co-exclusive (with AstraZeneca and its Affiliates), royalty-free, worldwide license during the Research Program Term and the Tail Period, without the right to grant sublicenses (except as reasonably necessary in connection with any engagement by Targacept of an Affiliate or Third Party to conduct work in the Research Program or any Additional Research Program as permitted in Section 4.1.1), under AstraZeneca Technology and AstraZeneca Patent Rights and AstraZeneca's interest in Joint Technology and Joint Patent Rights, solely to conduct the Research Program and any Additional Research Program. For purposes of clarity, the co-exclusivity granted by AstraZeneca under this Section 8.2.1 is limited to the sole purpose referenced in the preceding sentence and shall have no effect

on AstraZeneca's ability to Exploit AstraZeneca Technology, AstraZeneca Patent Rights and AstraZeneca's interest in Joint Technology and Joint Patent Rights for any other purpose to the extent permitted by Section 8.6.3 and consistent with the co-exclusive grants set forth in this Agreement.

8.2.2 **Development Program**. Subject to the other terms of this Agreement, AstraZeneca shall, and hereby does, grant to Targacept and its Affiliates a non-exclusive, royalty-free, worldwide license during the Term, without the right to grant sublicenses (except as reasonably necessary in connection with any engagement by Targacept of a Third Party to conduct any Targacept Development Activity as permitted in Section 5.3, under AstraZeneca Technology and AstraZeneca Patent Rights and AstraZeneca's interest in Joint Technology and Joint Patent Rights solely to conduct Targacept Development Activities under any Product Development Plan.

8.2.3 **Terminated Compounds**.

(a) License Grant. Subject to the other terms of this Agreement and in particular Sections 8.6.1, 8.6.2 and 11.4.4(a), AstraZeneca shall, and hereby does, grant to Targacept a co-exclusive (with AstraZeneca and its Affiliates), worldwide license, with the right to grant sublicenses (i) under AstraZeneca Patent Rights (excluding the AstraZeneca Other Patent Rights) and AstraZeneca's interest in Joint Patent Rights in each country (but, with respect to each Terminated Compound (but not a Terminated AZ Compound) or product to the extent that it contains such Terminated Compound **[********]** (x) **[********]** such Terminated Compound, in each case as of the date **[********]**, or (y) **[********]** such Terminated Compound, to the extent such Technology relates to such Terminated Compound and **[********]** on or prior to the date **[********]**) **[********]** (other than a Terminated AZ Compound, which shall be governed by Article 11) **[********]**, and (ii) under AstraZeneca Technology (excluding the AstraZeneca Other Technology) and AstraZeneca's interest in Joint Technology (but, with respect to each Terminated Compound (but not a Terminated AZ Compound) or product to the extent that it contains such Terminated Compound **[********]** (x) **[********]** such Terminated Compound, in each case as of the date **[********]**, or (y) **[********]** of such Terminated Compound, to the extent such Technology solely relates to such

Terminated Compound and **[********]** on or prior to the date **[********]** such Terminated Compound became a Terminated Compound), in each case ((i) and (ii)) to Exploit Terminated Compounds (other than Terminated AZ Compounds, which shall be governed by Article 11) and products that contain such Terminated Compounds, in each case (A) during the Term, **[********]** and (1) with respect to Option Compounds that become Terminated Compounds pursuant to Section 5.10.2 **[********]** and (2) with respect to all other Terminated Compounds, **[********]** (whether or not **[********]**), and (B) after expiration of the Term pursuant to Section 11.1 or termination of this Agreement in its entirety by AstraZeneca pursuant to Section 11.2.1 or Section 11.2.3, or by Targacept pursuant to Section 11.2.4 or Section 11.2.5(a), **[********]**; provided, however, that Targacept's rights under this Section 8.2.3(a) with respect to any Excluded Data Controlled by AstraZeneca or any of its Affiliates or Sublicensees shall be subject to Section 7.5. For purposes of clarity, the co-exclusivity granted by AstraZeneca under this Section 8.2.3(a) is limited to the sole purpose referenced in the preceding sentence and shall have no effect on AstraZeneca's ability to Exploit AstraZeneca Technology, AstraZeneca Patent Rights and AstraZeneca's interest in Joint Technology and Joint Patent Rights for any other purpose, to the extent consistent with Section 8.6.3 and the co-exclusivity grants set forth in this Agreement.

(b) Regulatory Filings. Subject to the other terms of this Agreement and in particular Sections 8.6.1, 8.6.2 and 11.4.4(a), AstraZeneca shall, as soon as reasonably practicable following Targacept's written request, provide Targacept with full access to all Regulatory Filings (including all data and other information contained therein, and correspondence relating thereto) for or relating to each Terminated Compound (other than a Terminated AZ Compound, which filings shall be governed by Article 11) and all information contained therein (but, with respect to each Terminated Compound (but not a Terminated AZ Compound) or product to the extent that it contains such Terminated Compound, **[********]** as (i) **[********]** such Terminated Compound, in each case **[********]** such Terminated Compound became a Terminated Compound, or (ii) **[********]** such Terminated Compound, to the extent such Technology relates to such Terminated Compound and **[********]** such Terminated Compound became a Terminated Compound), and AstraZeneca shall, and hereby does, grant to Targacept a co-exclusive (with AstraZeneca and its Affiliates) license and right of reference in the Territory, with the right to grant sublicenses or further rights of reference, under

AstraZeneca's and its Affiliates' rights, titles and interests in and to such requested Regulatory Filings, so as to enable Targacept to exercise its rights under the grants set forth in Section 8.2.3(a); provided that Targacept's rights with respect to Excluded Data included or referenced in such Regulatory Filings shall be subject to Section 7.5.

8.2.4 **AstraZeneca Assigned Technology**. AstraZeneca shall, and hereby does, assign to Targacept all of AstraZeneca's and its Affiliates' rights, titles and interests in and to all AstraZeneca Assigned Technology and all AstraZeneca Assigned Patent Rights that solely cover such AstraZeneca Assigned Technology: (a) with respect to any compounds that (i) are Derived by or on behalf of AstraZeneca from a Collaboration Candidate, Active+ Compound, Collaboration Compound or Candidate Drug (other than Ispronicline or a Licensed Derivative with respect thereto, or an Option Compound Candidate Drug) and (ii) then become Terminated Compounds during the Research Program or Tail Period or as of the end of the Tail Period, when and as such compounds become Terminated Compounds; (b) with respect to any Excluded Derivatives that are Derived by or on behalf of AstraZeneca during the applicable Restricted Derivative Period, on the date each such Excluded Derivative is determined to be an Excluded Derivative; and (c) with respect to any Technology made, developed or conceived by or on behalf of AstraZeneca in **[********]**. AstraZeneca shall duly execute and deliver, or cause to be duly executed and delivered, such instruments and shall do and cause to be done such acts and things, including the filing of such assignments, agreements, documents and instruments, as may be necessary for, or as Targacept may reasonably request, to carry out more effectively the purpose of this Section 8.2.4.

8.3 **Additional Rights**.

8.3.1 **Right to Sublicense**. To the extent either Party is permitted to grant sublicenses under the licenses granted to it under Section 8.1 or 8.2, as applicable, such Party shall have the right to grant such sublicenses through multiple tiers of sublicensees; provided that: (a) any such sublicense is consistent with the terms of this Agreement (including this Article 8); (b) such Party shall provide written notice to the other Party of any such sublicense and provide copies to the other Party of each such sublicense (with confidential and financial information redacted) promptly after the execution thereof; and (c) except as provided in

Sections 6.5.3 and 6.6.1(c) with respect to AstraZeneca, neither Party shall be relieved of its obligations pursuant to this Agreement as a result of such sublicense.

8.3.2 **Distributorships**. AstraZeneca shall have the right, in its sole discretion, to appoint its Affiliates, and AstraZeneca and its Affiliates shall have the right, in their sole discretion, to appoint any other Persons, in any country in the Territory, to distribute, market and sell the Products (with or without packaging rights), in circumstances where the Person purchases its requirements of Products from AstraZeneca or its Affiliates but does not otherwise make any royalty or other payment to AstraZeneca with respect to its intellectual property rights. Where AstraZeneca or its Affiliates appoints such a Person that is not an Affiliate of AstraZeneca, that Person shall be a "**Distributor**" for purposes of this Agreement. The term "packaging rights" in this Section 8.3.2 shall mean the right for the Distributor to package Products supplied in unpackaged bulk form into individual ready-for-sale packs. To the extent Targacept has the right under this Agreement to distribute, market and sell a Product (including a Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product) that contains a Terminated Compound or a Partially-Terminated Product in a country, Targacept shall have the right, in its sole discretion, to appoint its Affiliates, and Targacept and its Affiliates shall have the right, in their sole discretion, to appoint Third Parties to distribute, market and sell such products in such country(ies).

8.4 **Assignment of Regulatory Documentation**. If and to the extent requested by AstraZeneca, and except as otherwise provided on Schedule 8.4, Targacept shall, and hereby does, assign to AstraZeneca all of Targacept's and its Affiliates' rights, titles and interests in and to all Regulatory Filings Controlled by Targacept or its Affiliates as of the Effective Date and at any time thereafter during the Term for or relating to any Candidate Drug. Targacept shall duly execute and deliver, or cause to be duly executed and delivered, such instruments and shall do and cause to be done such acts and things, including the filing of such assignments, agreements, documents and instruments, as may be necessary, or as AstraZeneca may reasonably request, to carry out more effectively the purpose of this Section 8.4. If, at any time, AstraZeneca believes that its Development of Ispronicline under the applicable Product Development Plan, including any of the Pre-Phase IIb Program, would be delayed or otherwise impaired as a result of the fact that Targacept has not yet assigned **[********]** to AstraZeneca, the Parties shall work together in

good faith, and in the best interests of the Ispronicline, to permit AstraZeneca to conduct such activities in a timely manner as contemplated by the Product Development Plan.

8.5 **No Other Rights**. AstraZeneca shall have no rights to use or otherwise Exploit Targacept Technology, Targacept Patent Rights, or Targacept Proprietary Materials, and Targacept shall have no rights to use or otherwise exploit AstraZeneca Technology, AstraZeneca Patent Rights or AstraZeneca Proprietary Materials, in each case, except as expressly set forth in this Agreement.

8.6 **Exclusivity**.

8.6.1 **Targacept Restrictions**. Except as permitted pursuant to Section 8.6.2, with effect on the Execution Date, Targacept shall not, and shall cause each of its Affiliates not to, conduct any activity, either on its own, or with, for the benefit of, or sponsored by, any Third Party, that is designed to research, develop or commercialize, or grant any license or other rights (including any covenant not to sue) to any Third Party to utilize any Technology or Patent Rights Controlled by Targacept or any of its Affiliates for the purpose of researching, developing, commercializing or otherwise Exploiting, in each case in the Territory:

(a) any Alpha4Beta2 Agonist or any compound or product **[********]** an Alpha4Beta2 Agonist (including any Terminated Compound other than a Terminated AZ Compound), in the Field or in Schizophrenia, until the date, if any, on which AstraZeneca Initiates a Clinical Trial for any Alpha4Beta2 Agonist that is not a Collaboration Compound, Candidate Drug or Product;

(b) during the Option Term, any Secondary Pharmacology Compound or any Other NNR Compound (including any Terminated Compound other than a Terminated AZ Compound) in the Field or **[********]** in Schizophrenia;

(c) during the Research Program Term, **[********]**;

(d) during the Research Program Term and the Tail Period, any Collaboration Candidate until, subject to the penultimate paragraph of Section 1.309, the date, if any, on which such Collaboration Candidate becomes a Terminated Compound;

(e) during the Research Program Term and the Tail Period, any Active+ Compound until, subject to the penultimate paragraph of Section 1.309, the date, if any, on which such Active+ Compound becomes a Terminated Compound;

(f) any Collaboration Compound, Candidate Drug or Product or Additional Compound with respect to any of the foregoing (including TC-1827), in the Field or in Schizophrenia;

(g) any Terminated Compound beyond **[********]**;

(h) any compound or product for which a Major Metabolite (i) is a Collaboration Compound or Candidate Drug, (ii) is an Additional Compound with respect to a Collaboration Compound or Candidate Drug or (iii) is **[********]** (A) a Collaboration Compound, (B) a Candidate Drug or (C) an Additional Compound with respect to a Collaboration Compound or a Candidate Drug, in each case ((A), (B) and (C)) that satisfies Section 1.9(a)(iii), 1.9(b)(iii), 1.9(c)(iii) or 1.9(d)(iii), whichever is applicable to such compound or product, in each case ((i), (ii) and (iii)) if such Collaboration Compound, Candidate Drug, Additional Compound **[********]** for such compound or product in the Field or in Schizophrenia; and

(i) any Excluded Zone Compound in the Field or Schizophrenia.

8.6.2 **Targacept Permitted Activities**. Section 8.6.1 shall not apply:

(a) if and to the extent that Targacept or any of its Affiliates is undertaking research activities, the Targacept Development Activities or the Co-Promotion of Products, in each case if and only to the extent permitted by this Agreement and in accordance with this Agreement and, if applicable, any Co-Promotion Agreement;

(b) to the Exploitation of Unexercised Option Compounds (i) if the Option Indication designated in the applicable Option Notice is a Primary Indication, in or outside of the Field, or (ii) if the Option Indication designated in the applicable Option Notice is Schizophrenia, solely outside the Field from and after the date that they become Unexercised Option Compounds;

(c) to the Exploitation of the Compounds known to Targacept as of the Execution Date as **[********]**, **[********]** (**[********]**) and **[********]** (unless and until, in each case, the Parties agree in writing to designate such Compound as a Collaboration Compound or Candidate Drug), including in each case any salt form, polymorph, crystalline form, Prodrug, metabolite (other than any such metabolite that is an Excluded Zone Compound), hydrate, solvate or formulation thereof, outside the Field and outside Schizophrenia;

(d) to any Secondary Pharmacology Compound or Other NNR Compound in connection with non-clinical research and non-clinical development activities undertaken to enable Targacept to assess whether to designate such Secondary Pharmacology Compound or Other NNR Compound as a Potential Option Compound or an Option Compound, but excluding, for purposes of clarity, any Option Compound Candidate Drug or any Additional Compound with respect thereto (other than Back-Up Option Compounds to the extent permitted under Section 5.10.2(c)(1));

(e) to any Option Compound in connection with the performance of the Option Compound Development Plan (if any) or Targacept Option Compound Development Plan (if any) relating to such Option Compound, but excluding, for purposes of clarity, any Option Compound Candidate Drug or any Additional Compound with respect thereto (other than Back-Up Option Compounds to the extent permitted under Section 5.10.2(c)(1));

(f) subject to Sections 11.3 and 11.5, to the Exploitation of any Partially-Terminated Product, including any salt form, polymorph, crystalline form, hydrate, Prodrug, metabolite (other than any such metabolite that is an Excluded Zone Compound), solvate or formulation thereof, outside of the applicable Partially-Terminated Product Territory;

(g) subject to Section 11.3 and 11.5, to the Exploitation of any Terminated AZ Compound in the Territory;

(h) after the first anniversary of the end of the Research Program Tail Period, **[********]** any Alpha4Beta2 Agonist or any compound or product for which a Major Metabolite is an Alpha4Beta2 Agonist (other than (x) (i) Collaboration Compounds, (ii) Candidate Drugs, (iii) Products or (iv) Additional Compounds with respect to any of the

foregoing (including TC-1827), (y) any Excluded Zone Compound or (z) any compound or product that is subject to Section 8.6.1(h)) in the Field or in Schizophrenia; provided that, **[********]**; or

(i) after the Term.

8.6.3 **AstraZeneca**. With effect on the date first above written, AstraZeneca shall not, and shall cause each of its Affiliates not to, from the Effective Date until the first anniversary of the end of the Research Program Tail Period, conduct any activity, either on their own, or with, for the benefit of, or sponsored by any Third Party, that is designed to research, develop or commercialize, or grant any license or other rights to any Third Party to utilize any Technology or Patent Rights Controlled by AstraZeneca or any of its Affiliates for the purpose of developing or commercializing any compound or product that is optimized to be, or that AstraZeneca Knows to be, an Alpha4Beta2 Agonist in the Field or in Schizophrenia or conducting any research or other Exploitation in support of such activities, except to the extent AstraZeneca or any of its Affiliates is undertaking any activities (a) pursuant to the Research Plan, any Annual Research Plan, any Additional Research Plan or the Pre-Phase IIb Plan, or (b) in connection with the Exploitation of any Option Compound, Collaboration Candidate, Active+ Compound, Collaboration Compound, Candidate Drug or Product or any compounds or products Derived from any of the foregoing (including the making and Exploiting of Derivatives with respect to any of the foregoing to determine whether they are Collaboration Candidates during the Research Program Term and Tail Period, and thereafter, to determine whether they are Licensed Derivatives), in each case to the extent permitted by, and in accordance with, this Agreement.

8.7 **Notice of Release of Targacept Exclusivity Obligations**. If AstraZeneca Initiates a Clinical Trial for (a) any Alpha4Beta2 Agonist other than a Collaboration Compound, Candidate Drug or Product or (b) any Other NNR Compound that is not an Option Compound Candidate Drug or Option Compound Product (other than with respect to an Option Compound that is the subject of an Option Compound Development Plan that AstraZeneca has elected to complete pursuant to Section 5.10.2(b)(5)), in each case in the Field or in Schizophrenia, AstraZeneca shall promptly (but in no event later than thirty (30) days following such Initiation)

provide written notice to Targacept thereof; provided that AstraZeneca shall have such obligation (x) with respect to Alpha4Beta2 Agonist, only for the first such Alpha4Beta2 Agonist and (y) with respect to Other NNR Compounds, only if it has not previously provided a notice under this Section 8.7 for an Alpha4Beta2 Agonist, and then only for the first such Other NNR Compound for which it Initiates a Clinical Trial.

8.8 **[********] Program**. Targacept agrees that it shall not consent to the use of Ispronicline in any Clinical Trial or other study conducted under the **[********]** Program without the prior written consent of AstraZeneca.

8.9 **[********]**.

8.9.1 **[********]**.

(a) If at any time Targacept or any of its Affiliates wishes to conduct any activity, either on its own, or with, for the benefit of, or sponsored by, any Third Party, that is designed to research, develop or commercialize, or to grant any license or other rights (including any covenant not to sue) to any Third Party to utilize any Technology or Patent Rights Controlled by Targacept or any of its Affiliates for the purpose of researching, developing, commercializing or otherwise Exploiting any (x) Collaboration Compound, Candidate Drug or Product or Additional Compound with respect to any of the foregoing (including TC-1827), (y) compound or product **[********]** (i) is a Collaboration Compound or Candidate Drug, (ii) is an Additional Compound with respect to a Collaboration Compound or Candidate Drug or (iii) is **[********]** (A) a Collaboration Compound, (B) a Candidate Drug or (C) an Additional Compound with respect to a Collaboration Compound or a Candidate Drug, in each case ((A), (B) and (C)) that satisfies Section 1.9(a)(iii), 1.9(b)(iii), 1.9(c)(iii) or 1.9(d)(iii), whichever is applicable to such compound or product, in each case ((i), (ii) and (iii)) if such Collaboration Compound, Candidate Drug, Additional Compound **[********]** for such compound or product or (z) any Excluded Zone Compound (collectively ((x), (y) and (z)), the "**AZ Compounds**") **[********]**, Targacept shall provide AstraZeneca with **[********]** advance written notice, which notice shall identify the affected AZ Compounds **[********]**, describe the reasons for Targacept's interest in conducting such activity or granting such license or other rights and

include **[********]**. Thereafter, Targacept shall provide AstraZeneca with such other information as AstraZeneca may reasonably request.

(b) AstraZeneca shall have the right, on written notice to Targacept within **[********]** after receipt of a notice from Targacept with respect to an AZ Compound(s) for an indication(s) pursuant to Section 8.9.1(a), to **[********]**. For purposes of clarity and notwithstanding anything herein to the contrary, (i) Targacept shall have no rights under this Section 8.9.1 with respect to **[********]**, (ii) **[********]**, and (iii) unless AstraZeneca expressly agrees otherwise in writing, (A) AstraZeneca shall **[********]** and (B) Targacept shall **[********]**.

(c) If, with respect to **[********]** AstraZeneca **[********]**, then Targacept shall have the right to independently develop and commercialize such AZ Compound **[********]**, but, unless the Parties otherwise agree in writing and notwithstanding anything in this Agreement to the contrary, not under any Regulatory Approval that is in the name of AstraZeneca or any of its Affiliates, Sublicensees or Distributors.

(d) In consideration for AstraZeneca's obligation to fund the Research Program and any Additional Research Programs and to Develop and Commercialize Candidate Drugs and Products, including AZ Compounds, under this Agreement, which activities will expand the understanding of the role that NNRs and the Exclusivity Mechanism generally, and the AZ Compounds specifically, play in human health both in and outside the Field, and in consideration for Targacept's rights under this Agreement, including with respect to the Targacept Technology and the Targacept Patent Rights, Targacept shall pay to AstraZeneca a royalty on Targacept Net Sales of any such AZ Compound or any product that contains such AZ Compound at the same rate and on the same terms as AstraZeneca would pay Targacept royalties on such Net Sales under Section 6.6.1(a) were they AZ Net Sales without regard to Section 6.6.1(d)(4), and the other provisions of Sections 6.6 and the other relevant provisions of this Agreement shall apply to such royalty obligations *mutatis mutandis,* except that all AstraZeneca Patent Rights shall be royalty bearing and the First Commercial Sale of such AZ Compound or Product shall be the First Commercial Sale by Targacept or its Affiliates or Sublicensees, for purposes of Section 6.6.1(b), Section 6.6.1(d) and the other relevant provisions of this Agreement.

(e) Targacept shall not, and shall cause each of its Affiliates not to, conduct any activity, either on its own, or with, for the benefit of, or sponsored by, any Third Party, that is designed to research, develop or commercialize, or grant any license or other rights (including any covenant not to sue) to any Third Party to utilize any Technology or Patent Rights Controlled by Targacept or any of its Affiliates for the purpose of researching, developing, commercializing or otherwise Exploiting, an AZ Compound **[********]** with respect to such AZ Compound as provided herein.

Notwithstanding anything in this Section 8.9.1 to the contrary, Exploitation permitted pursuant to Section 8.6.2(c) or 8.6.2(g) shall not trigger application of this Section 8.9.1.

8.9.2 **Potential Expansion**. In the event that: (a) (i) **[********]** of any Collaboration Compound, Candidate Drug or Product, or any Licensed Derivative with respect thereto, **[********]**, or (ii) **[********]** any Collaboration Compound, Candidate Drug or Product, or any Licensed Derivative with respect thereto, **[********]**; and (b) **[********]**, AstraZeneca gives notice to Targacept that **[********]**, Targacept shall engage in good faith discussions with AstraZeneca with respect to **[********]**; provided that, for purposes of clarity, (A) Targacept's obligation under this Section 8.9.2 shall be to engage in good faith discussions with AstraZeneca, and Targacept shall have no duty or obligation, fiduciary or otherwise, to **[********]**, (B) Section 8.9.1 shall not apply to **[********]** pursuant to this Section 8.9.2, (C) neither Party shall be deemed in breach hereunder of any activity in respect of **[********]**, to the extent such activities were permitted under this Agreement **[********]**, and (D) unless the Parties otherwise agree in writing, no right granted or assigned under this Agreement **[********]** shall be revoked, reduced or limited as the result of **[********]**.

9. INTELLECTUAL PROPERTY RIGHTS

9.1 **Ownership of Intellectual Property Rights**

9.1.1 **Targacept Intellectual Property Rights**. Subject to Section 9.1.3 and Section 9.1.4 and the license grants and assignment to AstraZeneca under Article 8, as between the Parties, Targacept shall own and retain all right, title and interest in and to any and all: (a) Technology conceived, discovered, developed or otherwise made, as necessary to establish

authorship, inventorship or ownership under Applicable Laws in the United States, by or on behalf of Targacept or its Affiliates or, to the extent permitted by their agreements therewith, their respective licensees and Sublicensees (other than AstraZeneca or its Affiliates or Sublicensees); and (b) Patent Rights and other intellectual property rights that are Controlled by Targacept and its Affiliates or, to the extent permitted by their agreements therewith, their respective licensees and Sublicensees (other than AstraZeneca or its Affiliates or Sublicensees).

9.1.2 **AstraZeneca Intellectual Property Rights**. Subject to Section 9.1.3 and the license grants and assignments to Targacept under Article 8, as between the Parties, AstraZeneca shall own and retain all right, title and interest in and to any and all: (a) Technology conceived, discovered, developed or otherwise made, as necessary to establish authorship, inventorship or ownership under Applicable Laws in the United States, by or on behalf of AstraZeneca or its Affiliates or, to the extent permitted by their agreements therewith, their respective licensees and Sublicensees (other than Targacept or its Affiliates or Sublicensees); (b) Patent Rights and other intellectual property rights that are Controlled by AstraZeneca, its Affiliates or, to the extent permitted by their agreements therewith, their respective licensees and Sublicensees (other than Targacept or its Affiliates or Sublicensees); and (c) unless otherwise agreed by the Parties, Regulatory Filings made on or after the Effective Date and such Regulatory Filings made prior to the Effective Date as may be assigned to AstraZeneca pursuant to Section 8.4.

9.1.3 **Joint Technology Rights**. Subject to the license grants and assignments under Article 8 and except as provided in Section 9.1.4, the Parties shall each own an equal, undivided interest in (a) any and all Technology conceived, discovered, developed or otherwise made, as necessary to establish authorship, inventorship or ownership under Applicable Laws in the United States, by or on behalf of a Party (or its Affiliates), jointly by or on behalf of Targacept (or its Affiliates or, to the extent permitted by their agreements therewith, their respective licensees and Sublicensees), on the one hand, and AstraZeneca (or its Affiliates or, to the extent permitted by their agreements therewith, their respective licensees and Sublicensees) on the other hand, in connection with the work conducted under or in connection with this Agreement, whether or not patented or patentable (the "**Joint Technology**"), and (b) Patent Rights that contain one or more claims that cover Joint Technology (the "**Joint Patent Rights**").

Each Party shall have the right to Exploit, subject to limitations as to Targacept's use of any Excluded Data, and to grant licenses to Third Parties to Exploit, Joint Patent Rights and Joint Technology not exclusively licensed to a Party hereunder outside the scope of this Agreement without the consent of, or accounting to, the other Party, to the extent, with respect to either Party, such Exploitation would not be prohibited hereunder if such Joint Technology were solely such Party's own Technology. Each Party shall promptly disclose to the other Party in writing, and cause its Affiliates to so disclose, the development, making, conception or reduction to practice of any Joint Patent Rights or Joint Technology, and shall, and outside the United States does hereby, assign, and cause its Affiliates to so assign (or, if such assignment is not possible, grant, and cause its Affiliates to so grant, a fully-paid exclusive license in) to the other Party, without additional compensation, such right, title and interest in and to any Joint Patent Rights and Joint Technology as is necessary to fully effect the joint ownership provided for in the first sentence of this Section; provided, however, that AstraZeneca shall have no obligation to assign any right, title or interest in or to any Excluded Data under this Section 9.1.3.

9.1.4 **Product Trademarks**. AstraZeneca shall have the sole right to select the Product Trademarks for the marketing and sale of Products in the Territory. AstraZeneca shall own such Product Trademarks and all rights and goodwill with respect thereto. Targacept shall not, and shall not permit its Affiliates to, use any Trademark that is the same as or confusingly similar to, misleading or deceptive with respect to or that dilutes the Product Trademarks.

9.2 **Patent Coordinators**. Targacept and AstraZeneca shall each appoint a patent coordinator reasonably acceptable to the other Party (each, a "**Patent Coordinator**") to serve as such Party's primary liaison with the other Party on matters relating to patent filing, prosecution, maintenance and enforcement. Each Party may replace its Patent Coordinator at any time by notice in writing to the other Party. The initial Patent Coordinators shall be:

For Targacept: **[********]**

For AstraZeneca: **[********]**

9.3 **Inventorship**. In case of a dispute between Targacept and AstraZeneca over inventorship and, as a result, whether any particular Technology is Targacept Technology, AstraZeneca Technology or Joint Technology, such dispute shall be resolved by patent counsel

reasonably acceptable to the Parties who (and whose firm) is not at the time of the dispute, and was not at any time during the five (5) years prior to such dispute, performing services for either of the Parties. Expenses of such patent counsel shall be shared equally by the Parties.

9.4 **Employees and Agents**.

9.4.1 Each Party shall obtain from each of its Affiliates, sublicensees, employees and agents, and from the employees and agents of its Affiliates, who are engaged in research or Development activities conducted pursuant to this Agreement or who otherwise have access to the other Party's Confidential Information or Technology, such undertakings and agreements as are necessary to ensure that each Party shall, by virtue of this Agreement, receive from the other, without payments beyond those required by Article 6 and Section 11.4, the licenses and other rights granted to the other Party hereunder.

9.4.2 Neither Party will use in any capacity, in connection with the performance of the activities contemplated by this Agreement, any Person who has been debarred pursuant to Section 306 of the United States Federal Food, Drug, and Cosmetic Act, or who is the subject of a conviction described in such section. Each Party agrees to inform the other in writing immediately if it or any Person who is performing services hereunder on its behalf is debarred or is the subject of a conviction described in Section 306, or if any action, suit, claim, investigation or legal or administrative proceeding is pending or, to such Party's Knowledge, is threatened, relating to the debarment or conviction of such Party or any Person performing services hereunder.

9.5 **In-Licenses**. During the Term, Targacept shall not encumber or diminish the rights granted to AstraZeneca hereunder with respect to the Targacept Patent Rights or the Targacept Technology, including by not (a) knowingly committing any acts or knowingly permitting the occurrence of any omissions that would cause the material breach or termination of any In-License Agreement, or (b) amending or otherwise modifying or permitting to be amended or modified, any In-License Agreement. Targacept shall promptly provide AstraZeneca with notice of any alleged, threatened or actual breach of any In-License Agreement.

10. FILING, PROSECUTION AND MAINTENANCE OF PATENT RIGHTS

10.1 **Patent Filing, Prosecution and Maintenance**.

10.1.1 **Targacept Patent Rights**. Subject to Section 10.1.5, Targacept, acting through patent counsel or agents reasonably acceptable to AstraZeneca, shall, at its sole expense (except as otherwise provided in this Section 10.1.1), diligently prepare, file, prosecute (including any interferences, reissue proceedings and re-examinations) and maintain, in the best interests of the Collaboration, all Targacept Patent Rights (other than Targacept Excluded Patent Rights) in each case in the United States and all other countries set forth on Schedule 10.1.1; provided that:

(a) with respect to Ispronicline from and after the Commencement Date (or, if there is no Commencement Date, but neither Party terminates this Agreement in accordance with Section 11.2.1 and Targacept makes the election pursuant to Section 3.3.2(b)(A), from and after the first date on which neither Party has the right to terminate this Agreement pursuant to Section 11.2.1), (i) AstraZeneca shall have the right, in its sole discretion to assume control of, and responsibility for, the diligent preparation, filing and prosecution (including interferences, re-examinations, reissues, revocations, observations or oppositions) and maintenance, in the best interest of the Collaboration, of all Targacept Product Patent Rights covering Ispronicline (or any Ispronicline Product), any Licensed Derivative with respect thereto or any Additional Compound (or Additional Product) with respect to any of the foregoing; (ii) AstraZeneca shall be responsible for, (A) if AstraZeneca controls the filing and prosecution of such a Targacept Patent Right (or if AstraZeneca does not control the filing and prosecution of such a Targacept Patent Right, but such Targacept Patent Right covers only one or more Other Licensed Compounds), one hundred percent (100%) and (B) if AstraZeneca does not control the filing and prosecution of a Targacept Patent Right, **[********]**, in each case ((A) and (B)), of the reasonable and verifiable out-of-pocket costs incurred by Targacept in the preparation, filing, prosecution and maintenance of such Targacept Patent Rights (or by AstraZeneca with respect to any such activities conducted on behalf of, or otherwise at the request of, Targacept); provided that, solely in the case of clause (B), such Targacept Patent Rights contain one or more Valid Claims that cover Ispronicline (or any Ispronicline Product), any Licensed Derivative (or any

Product that contains such a Licensed Derivative) with respect thereto or any Additional Compound (or Additional Product) with respect to any of the foregoing, in each case (1) as a composition of matter, (2) a method of its use in the Field or in Schizophrenia or (3) if such Targacept Patent Right would, or is reasonably expected to, provide future exclusivity, as a pharmaceutical preparation or a method of its manufacture; and (iii) AstraZeneca shall have no obligation to reimburse Targacept for any costs incurred by Targacept in the preparation, filing, prosecution and maintenance of any such Targacept Patent Rights prior to the Commencement Date (or such later date, as applicable);

(b) with respect to each Option Compound Candidate Drug from and after the date of AstraZeneca's exercise of an IND-Ready Option or a POC Option, as applicable, with respect thereto, (i) AstraZeneca shall have the right, in its sole discretion to assume control of, and responsibility for, the diligent preparation, filing and prosecution (including interferences, re-examinations, reissues, revocations, observations or oppositions) and maintenance, in the best interest of the Collaboration, of all Targacept Product Patent Rights covering such Option Compound Candidate Drug (or Option Compound Product that contains such Option Compound Candidate Drug) or any Additional Compound (or Additional Product) with respect thereto; (ii) from and after the date of AstraZeneca's exercise of an IND-Ready Option or a POC Option, as applicable, AstraZeneca shall be responsible for (A) if AstraZeneca controls the filing and prosecution of such a Targacept Patent Right (or if AstraZeneca does not control the filing and prosecution of such a Targacept Patent Right, but such Targacept Patent Right covers only one or more Other Licensed Compounds), one-hundred percent (100%) and (B) if AstraZeneca does not control the filing and prosecution of a Targacept Patent Right, **[********]**, in each case ((A) and (B)), of the reasonable and verifiable out-of-pocket costs incurred by Targacept in the preparation, filing, prosecution and maintenance of such Targacept Patent Right (or by AstraZeneca with respect to any such activities conducted on behalf of, or otherwise at the request of, Targacept); provided that, solely in the case of clause (B), such Targacept Patent Rights contain one or more Valid Claims that cover such Option Compound Candidate Drug (or any Option Compound Product that contains such Option Compound Candidate Drug), any Licensed Derivative of such Option Compound Candidate Drug (or any Product that contains such a Licensed Derivative as an active ingredient) or any Additional Compound (or Additional Product) with respect to any of the foregoing, in each case (1) as a

composition of matter, (2) a method of its use in the Field or in Schizophrenia or (3) if such Targacept Patent Right would, or is reasonably expected to, provide future exclusivity, as a pharmaceutical preparation or a method of its manufacture; and (iii) AstraZeneca shall have no obligation to reimburse Targacept for any costs incurred by Targacept in the preparation, filing, prosecution and maintenance of any such Targacept Patent Rights prior to the date of AstraZeneca's exercise of an IND-Ready Option or a POC Option, as applicable;

(c) with respect to each Active+ Compound and Collaboration Compound, (i) from and after the designation of a Compound as an Active+ Compound (unless and until such Compound becomes a Terminated Compound), AstraZeneca shall be responsible for **[********]** of the reasonable and verifiable out-of-pocket costs incurred by Targacept in the preparation, filing, prosecution and maintenance, in the best interest of the Collaboration, of Targacept Patent Rights that contain one or more Valid Claims that cover such Active+ Compound as a composition of matter, a pharmaceutical preparation, a method of its manufacture or a method of its use in the Field or in Schizophrenia; and (ii) from and after the designation of an Active+ Compound as a Collaboration Compound (unless and until such Compound becomes a Terminated Compound), (A) AstraZeneca shall have the right, in its sole discretion to assume control of, and responsibility for, the diligent preparation, filing and prosecution (including interferences, re-examinations, reissues, revocations, observations or oppositions) and maintenance, in the best interest of the Collaboration, of all Targacept Product Patent Rights covering such Collaboration Compound or any Additional Compound (or Additional Product) with respect thereto; (B) AstraZeneca shall be responsible for, (1) if AstraZeneca controls the filing and prosecution of such a Targacept Patent Right (or if such a Targacept Patent Right relates to only one or more Other Licensed Compounds), one-hundred percent (100%) and (2) if AstraZeneca does not control the filing and prosecution of a Targacept Patent Right, **[********]**, in each case ((1) and (2)), of the reasonable and verifiable out-of-pocket costs incurred by the Parties in the preparation, filing, prosecution and maintenance of such Targacept Patent Right; provided that, solely in the case of clause (2), such Targacept Patent Rights contain one or more Valid Claims that cover such Collaboration Compound (or any Product that contains such Collaboration Compound), any Licensed Derivative (or any Product that contains such a Licensed Derivative) with respect thereto or any Additional Compound (or Additional Product) with respect to any of the foregoing, in each case (1) as a

composition of matter, (2) a method of its use in the Field or in Schizophrenia or (3) if such Targacept Patent Right would, or is reasonably expected to, provide future exclusivity, as a pharmaceutical preparation or a method of its manufacture; and (C) AstraZeneca shall reimburse Targacept for all reasonable and verifiable out-of-pocket costs incurred by Targacept in the preparation, filing, prosecution and maintenance of such Targacept Patent Rights prior to the date such Collaboration Compound was designated as an Active+ Compound;

(d) with respect to pending applications for Targacept Patent Rights (other than Targacept Product Patent Rights) that have not yet issued and that contain claims that cover compounds or products other than Collaboration Compounds, Candidate Drugs or Products (including Option Compound Candidate Drugs and Option Compound Products) or Additional Compounds (or Additional Products) with respect to any of the foregoing, whenever reasonably possible without materially weakening or reducing the scope or coverage of the Targacept Patent Rights, Targacept shall take such actions as are necessary to generate Targacept Product Patent Rights from such Targacept Patent Rights, including by filing divisionals, continuations and continuations-in-part, so as to separate the claims that cover such other compounds or products into separate patent applications; provided that, with respect to any Targacept Patent Rights that have issued and contain claims that cover compounds or products other than Collaboration Compounds, Candidate Drugs or Products (including Option Compound Candidate Drugs and Option Compound Products), or Additional Compounds (or Additional Products) with respect to any of the foregoing, (i) Targacept shall (A) give priority to such Collaboration Compounds, Candidate Drugs, Products, Additional Compounds or Additional Products over such other compounds or products with respect to any patent term extensions, restorations or the like that may be available now or in the future and (B) not give priority to such other compounds or products over such Collaboration Compounds, Candidate Drugs, Products, Additional Compounds or Additional Products where Targacept knows or reasonably believes that such priority has or would have a material adverse effect on the Exploitation hereunder of such Collaboration Compounds, Candidate Drugs, Products, Additional Compounds or Additional Products, and (ii) Targacept shall not enter into any agreement that is inconsistent with this Section 10.1.1(d); and

(e) in no event shall AstraZeneca have the right to control the preparation, filing, prosecution (including interferences, re-examinations, reissues, revocations, observations or oppositions) or maintenance of any Targacept Patent Rights that claim only, or be responsible for any costs incurred by the Parties in the preparation, filing, prosecution or maintenance of any Targacept Patent Rights with respect to, a Terminated Compound from and after the date that it becomes a Terminated Compound, and AstraZeneca shall, and shall cause its Affiliates to, reasonably cooperate with Targacept to transfer responsibility with respect to such Targacept Patent Rights to Targacept, including by promptly (and in any event so as to provide Targacept a reasonable amount of time to meet any deadline by which an action must be taken to establish or preserve any such rights in such Targacept Patent Rights) delivering to Targacept copies of all necessary files with respect to which responsibility has been transferred and taking all actions and executing all documents reasonably necessary for Targacept to assume such responsibility, including any powers of attorney required by applicable patent offices.

Notwithstanding the foregoing, AstraZeneca may decline to pay such costs incurred by Targacept in the preparation, filing, prosecution and maintenance of Targacept Patent Rights in any country in the Territory, in which case Targacept may elect to exclude such Targacept Patent Rights from the licenses granted to AstraZeneca under Sections 8.1.1 through 8.1.5 in such country. At a Party's request, the other Party shall cooperate with the requesting Party in all reasonable respects in connection with such preparation, filing, prosecution and maintenance of Targacept Patent Rights.

Notwithstanding anything in this Article 10 to the contrary, (i) Targacept shall not have any obligation to synthesize any compound or otherwise take any action to determine whether a compound is an Additional Compound or Licensed Derivative for purposes of determining its obligations under this Article 10, or (ii) all obligations under this Article 10 with respect to Targacept Patent Rights that relate to Additional Compounds or Licensed Derivatives shall be operative only with respect to those Additional Compounds or Licensed Derivatives that Targacept Knows are Additional Compounds or Licensed Derivatives and only, in each such case, from and after the date on which Targacept Knows.

10.1.2 **AstraZeneca Patent Rights**. Subject to Section 10.1.5, AstraZeneca, at its sole expense and acting through patent counsel or agents of its choice, shall be responsible for the preparation, filing, prosecution (including interferences, re-examinations, reissues, revocations, observations or oppositions) and maintenance of all AstraZeneca Patent Rights in its sole discretion. At AstraZeneca's request, Targacept shall cooperate with and assist AstraZeneca in all reasonable respects, at AstraZeneca's expense, in connection with such preparation, filing, prosecution and maintenance of AstraZeneca Patent Rights.

10.1.3 **Joint Patent Rights**.

(a) Unless the Parties otherwise agree, and subject to Section 10.1.3(b) and 10.1.5, AstraZeneca shall have the first right, but not the obligation, acting through patent counsel or agents of its choice, to prepare, file, prosecute (including interferences, re-examinations, reissues, revocations, observations or oppositions) and maintain all Joint Patent Rights (other than Joint Terminated Compound Patent Rights) in its sole discretion. AstraZeneca and Targacept shall, and shall cause their respective Affiliates, as applicable, to assist and cooperate with one another in, and share equally the expense of, filing, prosecuting and maintaining such Joint Patent Rights; provided that either Party may decline to pay its share of costs for filing, prosecuting and maintaining any Joint Patent Rights in a particular country or particular countries, in which case the declining Party shall, and shall cause its Affiliates to, assign (or, if such assignment is not possible, grant a fully-paid exclusive license in) to the other Party all or their rights, titles and interests in and to any such Joint Patent Rights in the applicable country or countries, whereupon such Joint Patent Rights shall become AstraZeneca Patent Rights or Targacept Patent Rights in such country or countries, as the case may be.

(b) Where AstraZeneca exercises its first right pursuant to Section 10.1.3(a), AstraZeneca shall, whenever reasonably possible without materially weakening or reducing the scope or coverage of the Joint Patent Rights (other than Joint Terminated Compound Patent Rights), take such actions as are necessary to generate Joint Terminated Compound Patent Rights from such Joint Patent Rights, including by filing divisionals, continuations and continuations-in-part, so as to separate the claims that cover (i) one or more Terminated Compounds or the Exploitation thereof from (ii) one or more other compounds or products or the Exploitation thereof; provided that whenever it is not reasonably possible to

generate Joint Terminated Compound Patent Rights without materially weakening or reducing the scope or coverage of the Joint Patent Rights, (A) AstraZeneca shall, in preparing, filing, prosecuting and maintaining such Joint Patent Rights, give good faith consideration to the effect of any particular action or inaction on the scope or coverage of such Joint Patent Rights as applied to compounds or products other than Collaboration Compounds, Candidate Drugs or Products (including Option Compound Candidate Drugs and Option Compound Products) or Additional Compounds (or Additional Products) with respect to any of the foregoing, or the Exploitation thereof, and, in consultation with Targacept, use reasonable efforts to minimize any weakening effect on or reduction to the scope or coverage thereof; provided, however, that AstraZeneca shall have the right to **[********]** Collaboration Compounds, Candidate Drugs, Products, Additional Compounds or Additional Products **[********]**; and (B) AstraZeneca shall not enter into any agreement that is inconsistent with this Section 10.1.3(b).

(c) Subject to Section 10.1.5, Targacept shall have the first right, but not the obligation, acting through patent counsel or agents of its choice, at its sole expense, to prepare, file, prosecute (including any interferences, reissue proceedings and re-examinations) and maintain, in the best interests of the Collaboration, all Joint Terminated Compound Patent Rights in its sole discretion. AstraZeneca shall, and shall cause its Affiliates to, reasonably cooperate with Targacept, at Targacept's expense, to file, prosecute and maintain such Joint Terminated Compound Patent Rights; provided that Targacept may decline to file, prosecute or maintain any Joint Terminated Compound Patent Rights in a particular country or particular countries, in which case Targacept shall, and shall cause its Affiliates to, assign (or, if such assignment is not possible, grant a fully-paid exclusive license in) to AstraZeneca all or their rights, titles and interests in and to any such Joint Terminated Compound Patent Rights in the applicable country or countries, whereupon such Joint Terminated Compound Patent Rights shall become AstraZeneca Patent Rights in such country or countries, as the case may be.

10.1.4 **Information and Cooperation**. Except with respect to Targacept Excluded Patent Rights, AstraZeneca Excluded Patent Rights and AstraZeneca Other Patent Rights (other than those specific AstraZeneca Other Patent Rights that cover a Terminated AZ Compound and for which Targacept provides AstraZeneca with written notice that Targacept expressly wishes to include within the scope of this Section 10.1.4, from and after the later of the

date that such Terminated AZ Compound became a Terminated AZ Compound and the date that AstraZeneca receives such written notice), in connection with the activities set forth in Sections 10.1.1, 10.1.2, 10.1.3 and 10.1.5: (a) each Party shall consult with the other as to the strategy and prosecution of applications for Patent Rights and the maintenance or extension of the Targacept Patent Rights, the AstraZeneca Patent Rights and the Joint Patent Rights (provided that, if, in such consultation, AstraZeneca reasonably believes that an action Targacept proposes to take in connection with the prosecution of a Targacept Patent Right that is not a Targacept Product Patent Right would materially weaken or reduce the scope or coverage of such Targacept Patent Right as applied to Collaboration Compounds, Candidate Drugs or Products (including Option Compound Candidate Drugs and Option Compound Products), or Additional Compounds (or Additional Products) with respect to any of the foregoing, or the Exploitation thereof, **[********]**); (b) each filing Party shall regularly provide the other Party with copies of all patent applications filed hereunder and other material submissions and correspondence with the patent offices in sufficient time to allow for review and comment by the other Party, and in any event at least **[********]** in advance of the due date of any payment or other administrative action that is required to obtain or maintain a Patent Right; (c) such filing Party shall provide the other Party and its patent counsel with an opportunity to consult with the filing Party and its patent counsel regarding the filing and contents of any such application, amendment, submission or response; and (d) such filing Party shall notify the other Party as early as reasonably practicable, and in any event at least **[********]** in advance of all meetings and material communications with any patent authorities concerning the Targacept Patent Rights, the AstraZeneca Patent Rights or Joint Patent Rights and shall permit the other Party to participate in such meetings, and the advice and suggestions of the other Party and its patent counsel shall be taken into consideration in good faith by such Party and its patent counsel in connection with such filing. Each Party shall also provide the other Party, upon its request, with copies of any patentability search reports generated by its patent counsel with respect to the Research Program Technology or Development Program Technology, including relevant Third Party patents and patent applications located; provided that neither Party shall be required to provide privileged information with respect to such intellectual property status unless and until procedures reasonably acceptable to such Party are in place to protect such privilege. The Parties shall consult in good faith and cooperate in gaining patent term extension(s), restoration(s) or the like

that may be available now or in the future to the Targacept Patent Rights (other than the Targacept Excluded Patent Rights), AstraZeneca Patent Rights (other than the AstraZeneca Excluded Patent Rights and, except as provided above, the AstraZeneca Other Patent Rights) or Joint Patent Rights in any part of the Territory (including under a supplementary protection certificate in European countries) so as to provide the longest period of patent protection in each country in the Territory.

10.1.5 **Abandonment; Failure to Pursue**.

(a) If the responsible Party under Section 10.1.1 decides not to (i) file a Patent Right with respect to any Targacept Technology (or Joint Technology that is Known by the Parties to relate solely to Terminated Compounds) or pursue the filing, prosecution (including interferences, re-examinations, reissues, revocations, observations or oppositions) or maintenance of any of the Targacept Patent Rights (other than Targacept Excluded Patent Rights) in any country listed on Schedule 10.1.1, or (ii) take any other action with respect to any of the Targacept Patent Rights (other than Targacept Excluded Patent Rights) or the Joint Terminated Compound Patent Rights in any country in the Territory that is necessary or useful to establish or preserve rights thereto (including by seeking any patent term extension, restoration or the like that may be available now or in the future), then in each such case such Party shall inform the other Party of such decision in writing promptly and, in any event, so as to provide such other Party a reasonable amount of time to meet any deadline by which an action must be taken to establish or preserve any such rights in such Targacept Patent Rights or Joint Terminated Compound Patent Rights in such country. Such other Party shall have the right but not the obligation to pursue the filing or registration, or to support the continued prosecution or maintenance of such Targacept Patent Rights or, subject to Section 10.1.3, such Joint Terminated Compound Patent Rights, as applicable, in such country and to pay any required fees to maintain such Targacept Patent Rights or, subject to Section 10.1.3, such Joint Terminated Compound Patent Rights, as applicable, in such country or defending such Targacept Patent Rights, in each case with costs to be allocated as set forth in Section 10.1.1(a)(ii)(B), 10.1.1(b)(ii)(B), 10.1.1(c)(ii)(B) or 10.1.3(c), as applicable, and through patent counsel or agents of its choice. If such other Party elects to pursue such filing or registration, as the case may be, or continue such support, then such other Party shall notify such first Party of such election and such first Party

shall, and shall cause its Affiliates to, reasonably cooperate with such other Party in this regard (including by promptly delivering to such other Party copies of all necessary files related to the Targacept Patent Rights or the Joint Terminated Compound Patent Rights, as applicable, with respect to which responsibility has been transferred and taking all actions and executing all documents reasonably necessary for such other Party to assume such responsibility, including any powers of attorney required by applicable patent offices.

(b) If AstraZeneca decides not to (i) file a Patent Right with respect to any AstraZeneca Technology or Joint Technology (other than Joint Technology that is Known by the Parties to relate solely to Terminated Compounds) or pursue the filing, prosecution (including interferences, re-examinations, reissues, revocations, observations or oppositions) or maintenance of any of the AstraZeneca Patent Rights (other than AstraZeneca Excluded Patent Rights) or Joint Patent Rights in any country in the Territory, or (ii) take any other action with respect to any of the AstraZeneca Patent Rights (other than AstraZeneca Excluded Patent Rights) or Joint Patent Rights (other than Joint Terminated Compound Patent Rights) in any country in the Territory that is necessary or useful to establish or preserve rights thereto (including by seeking any patent term extension, restoration or the like that may be available now or in the future), in each case ((i) and (ii)) other than any AstraZeneca Other Patent Rights unless, with respect to any such AstraZeneca Other Patent Right that covers a Terminated AZ Compound, Targacept provides AstraZeneca with written notice that Targacept expressly wishes to include such AstraZeneca Other Patent Right within the scope of this Section 10.1.5, from and after the later of the date that such Terminated AZ Compound became a Terminated AZ Compound and the date that AstraZeneca receives such written notice, then in each such case AstraZeneca shall inform Targacept of such decision in writing promptly, and in any event, so as to provide Targacept a reasonable amount of time to meet any deadline by which an action must be taken to establish or preserve any such rights in such AstraZeneca Patent Rights or, subject to Section 10.1.3, Joint Patent Rights in such country. Targacept shall have the right but not the obligation to pursue the filing or registration, or support the continued prosecution or maintenance of such AstraZeneca Patent Rights or, subject to Section 10.1.3, Joint Patent Rights in such country and to pay any required fees to maintain such AstraZeneca Patent Rights or Joint Patent Rights in such country or defending such AstraZeneca Patent Rights or Joint Patent Rights, in each case at Targacept's sole expense and through patent counsel or agents of its choice. If Targacept elects

to pursue such filing or registration, as the case may be, or to continue such support, then Targacept shall notify AstraZeneca of such election and AstraZeneca shall, and shall cause its Affiliates to, reasonably cooperate with Targacept in this regard (including by promptly delivering to Targacept copies of all necessary files related to the AstraZeneca Patent Rights or Joint Patent Rights with respect to which responsibility has been transferred and taking all actions and executing all documents reasonably necessary for Targacept to assume such responsibility, including any powers of attorney required by applicable patent offices.

10.1.6 **CREATE Act**. Notwithstanding anything to the contrary in this Section 10.1, neither Party shall have the right to make an election under the Cooperative Research and Technology Enhancement Act of 2004, 35 U.S.C. 103(c)(2)-(c)(3) (the "**CREATE Act**") when exercising its rights under this Section 10.1 without the prior written consent of the other Party. With respect to any such permitted election, the Parties shall use reasonable efforts to cooperate and coordinate their activities with respect to any submissions, filings or other activities in support thereof. The Parties acknowledge and agree that this Agreement is a "joint research agreement" as defined in the CREATE Act.

10.2 **Legal Actions**.

10.2.1 **Third Party Infringement**.

(a) In the event either Party becomes aware of any possible infringement of, or the submission by any Third Party of an abbreviated new drug application under the Hatch-Waxman Act that is covered by, any Targacept Patent Rights (an "**Infringement**"), that Party shall promptly (and if with respect to the filing of an abbreviated new drug application under the Hatch-Waxman Act or any certification thereunder, no later than five (5) Business Days of its first becoming aware thereof) notify the General Counsel of the other Party (or such person as the General Counsel may designate in writing from time to time) and provide it with all details of such Infringement of which it is aware (each, an "**Infringement Notice**"). AstraZeneca shall have the first right and option, but not the obligation, to eliminate such Infringement by reasonable steps, which may include the institution of legal proceedings, the granting of a sublicense or other action; provided that, notwithstanding the foregoing, and without limiting AstraZeneca's rights under Section 10.2.2, AstraZeneca agrees to cooperate in

good faith with Targacept or any Third Party to which Targacept has licensed Targacept Patent Rights outside of the Field, as permitted in this Agreement, in all reasonable respects to determine and pursue the most reasonable method of eliminating the Infringement (and in responding to an invalidity or unenforceablity defense or counterclaim in connection therewith) in view of the parties' respective interests. All costs, including attorneys' fees, relating to such legal proceedings or other action controlled by AstraZeneca shall be borne by AstraZeneca, subject to its rights under Section 10.2.4. If AstraZeneca notifies Targacept that it does not intend to exercise its rights pursuant to the preceding sentence or otherwise does not take commercially reasonable steps to eliminate the Infringement within one hundred twenty (120) days from any Infringement Notice (or to commence preparation of a suit within twenty-five (25) days in the case of an Infringement under the Hatch-Waxman Act), then Targacept shall have the right and option, but not the obligation, to do so at its sole expense, upon written notice to AstraZeneca; provided that if AstraZeneca has commenced good faith negotiations with an alleged infringer for elimination of such Infringement within such one hundred twenty (120)-day (or, if applicable twenty-five (25)-day) period, AstraZeneca shall have an additional ninety (90) days to conclude its negotiations before Targacept may take steps to eliminate such Infringement. Neither Party shall settle or otherwise compromise any Infringement claim or proceeding under this Section 10.2.1(a) without the prior written consent of the other Party, which consent shall not be unreasonably withheld, conditioned or delayed.

(b) Each Party shall have the right, at its sole expense, to be represented by counsel that it selects in any legal proceedings or other action instituted under this Section 10.2.1 by the other Party. If a Party with the right to initiate legal proceedings under Section 10.2.1 to eliminate an Infringement lacks standing to do so and the other Party has standing to initiate such legal proceedings, then the Party with standing shall initiate such legal proceedings at the request and sole expense, and under the control, of the other Party.

(c) In the event of an Infringement of a Joint Patent Right, the Parties shall enter into discussions as to whether and how to eliminate the Infringement. If the Parties cannot agree, AstraZeneca shall have the first right, but not the obligation, to seek to eliminate any Infringement that adversely affects its Exploitation of a Collaboration Compound, Candidate Drug or Product, or otherwise adversely affects its rights under this Agreement. If AstraZeneca

notifies Targacept that it does not intend to exercise its rights pursuant to the preceding sentence or otherwise does not take commercially reasonable steps to eliminate the Infringement within one hundred twenty (120) days from the date on which it is determined that the Parties cannot agree, then Targacept shall have the right and option, but not the obligation, to do so, upon written notice to AstraZeneca; provided that if AstraZeneca has commenced good faith negotiations with an alleged infringer for elimination of such Infringement within such one hundred twenty (120)-day, AstraZeneca shall have an additional ninety (90) days to conclude its negotiations before Targacept may take steps to eliminate such Infringement. The Party that pursues an action, suit or proceeding under this Section 10.2.1(c) to eliminate such infringement shall bear **[********]** the costs thereof and shall be entitled to **[********]** amounts recovered, except if, and to the extent, that any amount is recovered specifically on account of lost profits with respect to (i) Product(s) or Other Licensed Product(s), in which case **[********]** AstraZeneca's historic profits on AZ Net Sales of the Product(s) or Other Licensed Product(s) affected by the Infringement (inclusive of royalties paid to Targacept under this Agreement on such AZ Net Sales) bears to such royalties, in each case as determined by **[********]** in good faith or (ii) Royalty-Bearing Terminated AZ Product(s) or Royalty-Bearing Terminated Compound(s), in which case **[********]** Targacept's historic profits on Targacept Net Sales of the Royalty-Bearing Terminated AZ Product(s) or Royalty-Bearing Terminated Compound(s) affected by the Infringement (inclusive of royalties paid to AstraZeneca under this Agreement on such Targacept Net Sales) bears to such royalties, in each case as determined by **[********]** in good faith. Each Party shall have the right, at its sole expense, to be represented by counsel of its own selection in any action, suit or proceeding instituted under this Section 10.2.1(c) by the other Party. If a Party lacks standing and the other Party has standing to bring any such action, suit or proceeding, then the Party with standing shall bring such suit at the request and sole expense, and under the control, of the other Party.

(d) In any action, suit or proceeding instituted under this Section 10.2.1, the Parties shall cooperate with and assist each other in all reasonable respects. Upon the reasonable request of the Party instituting such action, suit or proceeding, the other Party shall join such action, suit or proceeding and shall be represented using counsel of its own choice, at the requesting Party's sole expense.

(e) Except as otherwise provided in Section 10.2.1(c), any amounts recovered by either Party pursuant to this Section 10.2.1, whether by settlement or judgment, shall be allocated in the following order: (i) first, to reimburse AstraZeneca and Targacept (including, for clarification, to reimburse Targacept for any AstraZeneca expenses with respect thereto that were offset against payments to Targacept pursuant to Section 10.2.4) for their reasonable out-of-pocket expenses in making such recovery (which amounts shall be allocated pro rata if insufficient to cover the totality of such expenses); (ii) then, if and to the extent that any amount recovered is on account of lost profits with respect to (A) Product(s) or Other Licensed Product(s), to AstraZeneca and Targacept in the same proportion as AstraZeneca's historic profits on AZ Net Sales of the Product(s) affected by the Infringement (inclusive of royalties paid to Targacept under this Agreement on such AZ Net Sales) bears to such royalties, in each case as determined by AstraZeneca in good faith consistent with its then-current practices or (B) Royalty-Bearing Terminated AZ Product(s) or Royalty-Bearing Terminated Compound(s), to AstraZeneca and Targacept in the same proportion as Targacept's historic profits on Targacept Net Sales of the Royalty-Bearing Terminated AZ Product(s) or Royalty-Bearing Terminated Compound(s) affected by the Infringement (inclusive of royalties paid to AstraZeneca under this Agreement on such Targacept Net Sales) bears to such royalties, in each case as determined by Targacept in good faith consistent with its then-current practices; and (iii) any remainder, **[********]** to each Party. Any license fees, royalties, milestones or other payments received by Targacept under a license granted to remove an Infringement shall be **[********]**.

10.2.2 **Invalidity or Unenforceability Defenses or Actions**. In the event that a Third Party or Sublicensee asserts, as a defense or as a counterclaim in any infringement action under Section 10.2.1 or otherwise, that any Targacept Patent Rights (other than Targacept Excluded Patent Rights) or Joint Patent Rights are invalid or unenforceable, then the Party pursuing such infringement action shall promptly give written notice to the other Party. AstraZeneca shall have the first right, but not the obligation, through counsel of its choice and at its sole expense (subject to Section 10.2.4), to respond to and control such defense or defend against such counterclaim (as applicable), including the right to settle or otherwise compromise such claim at its sole expense (subject to Section 10.2.4). If AstraZeneca notifies Targacept in writing that it does not wish to respond to such defense or defend against, or settle or otherwise

compromise, such counterclaim (as applicable), Targacept shall have the right, but not the obligation, through counsel of its choice and at its sole expense, upon written notice to AstraZeneca, to respond to such defense or defend against such counterclaim (as applicable); provided, however, that Targacept shall provide written notice to AstraZeneca reasonably in advance of ceasing to defend or prosecute such defense or counterclaim so as to enable AstraZeneca to assume control of such defense or counterclaim if it so elects, and shall obtain the written consent of AstraZeneca, not to be unreasonably withheld, conditioned or delayed, prior to settling or otherwise compromising, such defense or counterclaim. Further, if a Third Party or Sublicensee asserts, in a declaratory judgment action or similar action or claim filed by such Third Party or Sublicensee, that any Targacept Patent Rights (other than Targacept Excluded Patent Rights) or Joint Patent Rights are invalid or unenforceable, then the Party first becoming aware of such action or claim shall promptly give written notice to the other Party. AstraZeneca shall have the first right, but not the obligation, through counsel of its choice, and at its sole expense (subject to Section 10.2.4), to defend against such action or claim, including the right to settle or otherwise compromise such claim. If AstraZeneca notifies Targacept in writing that it does not wish to respond to or defend against or settle or otherwise compromise such action or claim, Targacept shall have the right, but not the obligation, through counsel of its choice and at its sole expense, upon written notice to AstraZeneca, to defend against and control such action or claim; provided, however, that Targacept shall provide written notice to AstraZeneca reasonably in advance of ceasing to defend such action or claim so as to enable AstraZeneca to assume control of such defense if it so elects, and shall obtain the written consent of AstraZeneca, not to be unreasonably withheld, conditioned or delayed, prior to settling or otherwise compromising, such action or claim. Any amounts recovered in connection with any action, claim or suit under Section 10.2.2 shall be allocated between the Parties as provided in Section 10.2.1(e). Any license fees, royalties, milestones or other payments received by Targacept under a license granted to remove an Infringement shall be **[********]**.

10.2.3 **Defense of Claims**. In the event that either Party becomes aware of any action, suit or proceeding brought or threatened against either Party or any Affiliate or Sublicensee of either Party, or any Distributor or customer of AstraZeneca, alleging the infringement of, or otherwise has reason to believe that either Party may be infringing, the Technology or Patent Rights of a Third Party by reason of the conduct of the Pre-Phase IIb

Program, the Research Program, any Additional Research Program, or the Development, Commercialization or other Exploitation of any Candidate Drug or Product, that Party shall promptly notify the General Counsel of the other Party (or such person as the General Counsel may designate in writing from time to time) and provide him or her with all details of such action, suit or proceeding of which it is aware. AstraZeneca shall have the first right, but not obligation, through counsel of its choice, to assume direction and control of the defense of any such action, suit or proceeding at its sole expense. Targacept or any of its Affiliates or Sublicensees shall have the right to separate counsel at its own expense in any such action, suit or proceeding and, if such action, suit or proceeding has been brought against Targacept or any of its Affiliates or Sublicensees, such party may elect to defend itself at its sole expense. In any event, the Parties shall cooperate with each other in all reasonable respects in any such action, suit or proceeding. Each Party shall provide the other Party with prompt written notice of the commencement of any such suit, action or proceeding, or of any allegation of infringement of which such Party becomes aware, and shall promptly furnish the other Party with a copy of each communication relating to the alleged infringement that is received by such Party. In no event shall either Party settle or otherwise compromise or resolve any such action, suit or proceeding brought against the other Party or any of its Affiliates or Sublicensees (or, with respect to AstraZeneca, its Distributors or customers) without that other Party's prior written consent. Any amounts recovered in connection with any action, claim or suit under Section 10.2.3 shall be allocated between the Parties as provided in Section 10.2.1(e). Any license fees, royalties, milestones or other payments received by Targacept under a license granted to remove an Infringement shall be **[********]**.

10.2.4 **Set-Off**. AstraZeneca shall have the right to credit against the royalty payments to be paid by AstraZeneca to Targacept with respect to the sale of Products under Article 6 as follows:

(a) without limiting AstraZeneca's rights under Section 10.2.4(c), with respect to the prosecution of a suit against a Third Party for Infringement of a Targacept Patent Right (other than a Targacept Excluded Patent Right) under Section 10.2.1, AstraZeneca shall have the right to credit, (i) if such suit relates to (A) Ispronicline (or an Ispronicline Product) or an Option Compound Candidate Drug (or an Option Compound Product), **[********]** and (B) any other Candidate Drug or Product or any Collaboration Compound, **[********]** in each case

((A) and (B)) of all reasonable costs, including Indirect Taxes if applicable, and expenses incurred by AstraZeneca in connection with prosecuting such suit and (ii) all damages awarded against AstraZeneca or its Affiliates resulting from actions or omissions of Targacept or its licensors;

(b) without limiting AstraZeneca's rights under Section 10.2.4(c), with respect to the defense of a Third Party suit or claim that a Targacept Patent Right (other than a Targacept Excluded Patent Right) is invalid or unenforceable, including any interference or opposition, AstraZeneca shall have the right to credit, (i) if such suit or claim relates to a Targacept Patent Right (A) that covers Ispronicline (or an Ispronicline Product) or an Option Compound Candidate Drug (or an Option Compound Product), **[********]** and (B) that covers any other Candidate Drug or Product or any Collaboration Compound, **[********]** in each case ((A) and (B)) of all reasonable costs, including Indirect Taxes if applicable, and expenses incurred by AstraZeneca in connection with defending against such suit or claim and (ii) all damages awarded against AstraZeneca or its Affiliates resulting from actions or omissions of Targacept or its licensors; and

(c) with respect to the defense of a suit or claim under Section 10.2.3, AstraZeneca shall have the right to credit **[********]** of: (i) all reasonable costs, including Indirect Taxes if applicable, and expenses incurred by or on behalf of AstraZeneca or its Affiliates in connection with defending against such suit or claim; (ii) all damages or costs awarded against, or otherwise borne by, AstraZeneca or its Affiliates; and (iii) all payments or royalties that AstraZeneca is ordered to or agrees to pay to a Third Party that are necessary to secure the right to continue the conduct of the Pre-Phase IIb Program, the Research Program or any Additional Research Program, or the Development, Commercialization or other Exploitation of any Candidate Drug or Product, as the case may be (which royalties shall be subject to Section 6.6.1(d)(2));

provided, however, without limiting Sections 6.6.1(d)(2)(B) or 6.6.1(d)(5), and except as provided in the next proviso, that in no event shall the aggregate reductions under this Section 10.2.4, when combined with any reductions in Sections 6.6.1(d)(2)(A) and 10.2.6, reduce the royalty payments due to Targacept under Section 6.6.1(a) (but not Section 6.6.1(c), which shall

not be subject to **[********]**) with respect to a product (as such royalty payments may be reduced pursuant to the other provisions of Section 6.6.1(d)), regardless of the amount or number of credits available to AstraZeneca in accordance with Section 6.6.1(d)(2)(A), this Section 10.2.4 or Section 10.2.6, by more than **[********]**; and provided further that, for clarity, to the extent that any prosecution or defense under this Section 10.2 arises from or relates to a breach by Targacept of its representations and warranties under this Agreement with respect to a Collaboration Compound, Candidate Drug or Product, notwithstanding Section 6.6.1(d)(2) or 10.2.6, (x) any costs, expenses and damages incurred by AstraZeneca under this Section 10.2 with respect to such Collaboration Compound, Candidate Drug or Product may be credited against **[********]** to be paid by AstraZeneca pursuant to Article 6 with respect to such Collaboration Compound, Candidate Drug or Product and (z) the percentages set forth in Sections 10.2.4(a), (b) and (c) and the preceding proviso shall each be increased to **[********]** with respect thereto. Credits not exhausted in any Calendar Quarter may be carried into future Calendar Quarters, subject to the foregoing sentence. For the avoidance of doubt, where Indirect Taxes apply to milestones, royalties or costs, the Parties shall invoice these sums according to Applicable Laws.

Notwithstanding anything in this Agreement to the contrary, (A) AstraZeneca shall not have the right under this Section 10.2.4 to credit against the royalty payments to be paid by AstraZeneca to Targacept with respect to the sale of Products under Article 6, any expenses incurred by or on behalf of, or damages or costs awarded against, AstraZeneca (or its Affiliates) as a result of (x) invalidity or enforceability proceedings under Section 10.2.2 with respect to Licensed Derivatives Derived, or any Additional Compounds made, developed or conceived, by AstraZeneca or its Affiliates or Sublicensees (other than Targacept or its Affiliates or Sublicensees), (y) any action, claim or suit under Section 10.2.3 to the extent that such action, claim or suit alleges that a Licensed Derivative Derived, or Additional Compound made, developed or conceived, by AstraZeneca or its Affiliates or Sublicensees (other than Targacept or its Affiliates or Sublicensees), or any Technology or Patent Rights (other than Targacept Technology, Targacept Patent Rights or a Candidate Drug) that AstraZeneca or its Affiliates or Sublicensees incorporates into a Product, infringes the Technology or Patent Rights of a Third Party and (z) any enhanced damages (*e.g.*, treble damages) awarded as a result of a determination that AstraZeneca or its Affiliates or Sublicensees willfully infringed a Third Party's Patent

Rights, and (B) a payment of a royalty or other payments to a Third Party shall be credited only once, regardless of the number of provisions of this Agreement (including Sections 6.6.1(d)(2), 10.2.4 and 10.2.6) that may apply to such payment.

10.2.5 **Cooperation**. Targacept shall provide to AstraZeneca all assistance reasonably requested by AstraZeneca in connection with any action, claim or suit under Section 10.2.1, 10.2.2 or Section 10.2.3, including allowing AstraZeneca reasonable access during normal business hours to Targacept's files and documents and to Targacept's personnel who may have possession of relevant information. In particular Targacept shall promptly make available to AstraZeneca, free of charge, all information in its possession or control that it is aware shall assist AstraZeneca in responding to any such action, claim or suit under Section 10.2.1, 10.2.2 or 10.2.3. Targacept shall cause any Third Parties owning Targacept Patent Rights licensed to Targacept, and any Third Parties that are licensees of any Targacept Patent Rights, to use reasonable efforts to assist and cooperate with AstraZeneca in connection with the response to such action, claim or suit under Section 10.2.1, 10.2.2 or 10.2.3.

10.2.6 **Third Party Licenses**. If, in the reasonable opinion of AstraZeneca, the Exploitation of Candidate Drugs or Products by AstraZeneca, its Affiliates or any of their Sublicensees infringes or misappropriates any Patent Rights, trade secret or other intellectual property right of a Third Party in any country in the Territory, such that AstraZeneca or any of its Affiliates, Distributors or Sublicensees cannot Exploit the Candidate Drugs or the Products in such country without infringing the Patent Rights, trade secret or other intellectual property right of such Third Party, then, AstraZeneca shall have the first right, but not the obligation, through counsel of its choice at its sole expense subject to the last sentence of this Section, and in its sole discretion, to negotiate and obtain a license from such Third Party as necessary for AstraZeneca and its Affiliates and Sublicensees to Exploit the Collaboration Compounds, Candidate Drugs and Products in such country. In the event that AstraZeneca obtains such a license, AstraZeneca shall be entitled to offset any royalties, license fees, milestones or other payments made to a Third Party under any such license against royalties payable by AstraZeneca hereunder as provided in Sections 6.6.1(d)(2) and 6.6.1(d)(5); provided, however, without limiting Sections 6.6.1(d)(2)(B) or 6.6.1(d)(5), and except as provided in the next proviso, that in no event shall the aggregate reductions under this Section 10.2.6, when combined with any reductions in

Sections 6.6.1(d)(2)(A) and 10.2.4, reduce the royalty payments due to Targacept under Section 6.6.1(a) (but not Section 6.6.1(c), which shall not be subject to **[********]**) with respect to a product (as such royalty payments may be reduced pursuant to the other provisions of Section 6.6.1(d)), regardless of the amount or number of credits available to AstraZeneca in accordance with Section 6.6.1(d)(2)(A), Section 10.2.4 or this Section 10.2.6, by more than **[********]**, provided that, for clarity, to the extent that the need for any such license arises from or relates to a breach by Targacept of its representations and warranties under this Agreement with respect to a Collaboration Compound, Candidate Drug or Product, and notwithstanding Sections 6.5.1, 6.6.1(d)(2) and 10.2.4, **[********]** of any such royalties, license fees or milestones with respect to such Collaboration Compound, Candidate Drug or Product may be credited against milestones as well as royalties to be paid by AstraZeneca hereunder with respect to such Collaboration Compound, Candidate Drug or Product.

10.3 **Trademark Prosecution**. AstraZeneca shall have the sole right to file, prosecute, defend and maintain the Product Trademarks, at AstraZeneca's expense, except with respect to Partially-Terminated Products, where the Parties shall reasonably cooperate with one another and Targacept shall bear such expense outside the applicable Partially-Terminated Product Territory.

11. TERM, TERMINATION AND REMEDIES FOR BREACH

11.1 **Term**. This Agreement shall commence on the Effective Date and shall continue in full force and effect until the later of (a) the expiration of the last royalty obligation pursuant to Section 6.6.1 with respect to the first Product (other than an Option Compound Product that contains an Option Compound Candidate Drug, unless pursuant to Section 5.5.1(c) such Option Compound Candidate Drug is sufficient to satisfy AstraZeneca's diligence obligation set forth in Section 5.5.1(b)) for which the First Commercial Sale occurs (or, if earlier, another Product for which the First Commercial Sale occurs) and (b) the Obligation Expiration Date, unless earlier terminated (i) in accordance with this Article 11 or (ii) by the mutual agreement of the Parties (the "**Term**").

11.2 **Termination**.

11.2.1 **Termination in connection with the Pre-Phase IIb Program**.

(a) **Termination by AstraZeneca**. Subject to Section 3.3.2, AstraZeneca may terminate this Agreement with immediate effect upon written notice to Targacept stating its intention to terminate this Agreement under this Section 11.2.1(a) (i) at any time on or prior to the Sunset Date if AstraZeneca determines, in its sole discretion, to not proceed with the Development of Ispronicline, in accordance with Section 3.3.2(a), or (ii) thereafter, if neither Party terminates this Agreement as set forth in Section 3.3.2(a), within ten (10) Business Days of delivery of notice of Targacept's election in accordance with Section 3.3.2(b).

(b) **Termination by Targacept**. Targacept may terminate this Agreement, for any reason or no reason, with immediate effect upon written notice to AstraZeneca stating its intention to terminate this Agreement under this Section 11.2.1(b) within thirty (30) days after the Sunset Date if AstraZeneca had not notified Targacept as of the Sunset Date that AstraZeneca decided to proceed with the Development of Ispronicline in accordance with Section 3.3.1.

11.2.2 **Termination of the Research Program**. AstraZeneca may terminate the Research Program (a) with effect on the third anniversary of the Effective Date on not less than six (6) months' prior written notice to Targacept, for any reason or no reason, or (b) at any time during the Research Program Term, for any material breach by Targacept of this Agreement or the Research Program, with the notice and cure provisions of Sections 11.2.4 applying to this Section 11.2.2 *mutatis mutandis*. Termination of the Research Program under this Section 11.2.2 shall have no effect on the other terms and conditions of this Agreement, except that (x) AstraZeneca shall have no obligation to reimburse Targacept pursuant to Section 6.4.1 or 6.4.2 for costs incurred from and after the effective date of such termination and (y) if AstraZeneca terminates the Research Program pursuant to clause (a) above, notwithstanding any other provision hereof, from and after the effective date of such termination, (i) no Collaboration Candidate or Active+ Compound that has not been designated as a Collaboration Compound as of such date shall become a Collaboration Compound or Candidate Drug and (ii) each Collaboration Candidate, each Active+ Compound and each previously designated Collaboration Compound that had not been designated a Candidate Drug as of the effective date of such termination shall automatically become a Terminated Compound. For purposes of clarity, (A) if

AstraZeneca terminates the Research Program pursuant to Section 11.2.2(a), AstraZeneca's rights, and Targacept's obligations, under this Agreement with respect to Ispronicline, Ispronicline Products, Option Compounds, Option Compound Candidate Drugs, Option Compound Products, Candidate Drugs designated as of the effective date of such termination and Products that contain such Candidate Drugs, and any Licensed Derivatives with respect thereto and all Additional Compounds with respect to any of the foregoing, shall remain in force, and (B) if AstraZeneca terminates the Research Program pursuant to Section 11.2.2(b), the Tail Period shall commence on the date of such termination and AstraZeneca shall retain all rights during such Tail Period, including the right to conduct one or more Additional Research Programs and to select Lead Collaboration Compounds, and AstraZeneca's rights, and Targacept's obligations, under this Agreement with respect to Collaboration Candidates, Active+ Compounds, Collaboration Compounds (including any Collaboration Compounds designated during the Tail Period), Candidate Drugs and Products and all Additional Compounds with respect to any of the foregoing, shall remain in force. For purposes of clarity, termination of the Research Program under this Section 11.2.2 shall have no effect on Targacept's obligations, or AstraZeneca's rights, under Section 5.10.2.

11.2.3 **Termination by AstraZeneca of this Agreement in its Entirety or of a Particular Collaboration Compound, Candidate Drug or Product**. AstraZeneca may terminate this Agreement for any reason or no reason (a) in its entirety, at any time after the earlier of the termination of the Research Program pursuant to Section 11.2.2 and the fourth anniversary of the Effective Date, or (b) with respect to one or more Collaboration Compounds, Candidate Drugs (including Option Compound Candidate Drugs) or Products (including Option Compound Products), at any time, in each case upon not less than ninety (90) days prior written notice to Targacept. Any notice of termination of a Candidate Drug or Product under this Section 11.2.3 shall be delivered in accordance with Section 17.1 and signed by a duly authorized officer of AstraZeneca and shall specifically reference AstraZeneca's intent to terminate such Collaboration Compound, Candidate Drug or Product or this Agreement under this Section 11.2.3. Any notice of termination that does not comply with the preceding sentence shall have no force or effect. For purposes of clarity, notification by AstraZeneca to the JRC, JDC or ESC that AstraZeneca plans to terminate or otherwise cease Development of a Candidate

Drug or Product shall not constitute notice of termination with respect to such Candidate Drug or Product for purposes of this Section 11.2.3.

11.2.4 **Termination of this Agreement for Breach.** In the event that there is a material breach of this Agreement by a Party (other than a material breach by (a) AstraZeneca of its diligence obligations under this Agreement, which breaches shall be governed solely by Section 11.2.5, (b) Targacept of its obligations under Section 5.10.2(b)(4), which breaches shall be governed solely by Sections 5.10.2(b)(4) and 5.10.2(b)(5), (c) AstraZeneca of its obligations to use Commercially Reasonable Efforts to complete an Option Compound Development Plan for an Option Compound assumed and conducted by AstraZeneca pursuant to Section 5.10.2(b)(5), which breaches shall be governed solely by Section 5.10.2(b)(5), (d) AstraZeneca of its obligations under Section 8.6.3 in connection with any merger, consolidation or acquisition (or other Change of Control) pursuant to Section 15.2.2, which breaches shall be governed solely by Section 15.2.2 and (e) either Party in failing to commit resources as provided in any Regulatory Action Plan or otherwise in complying with Section 5.8), the Party not in breach (the "**Non-Defaulting Party**") shall have the right to give the other Party (the "**Defaulting Party**") written notice specifying the nature of the breach, requiring the Defaulting Party to make good or otherwise cure such breach, and stating its intention to terminate this Agreement under this Section 11.2.4 if such breach is not cured. Subject to Section 11.2.8(a), if such breach is not cured within **[********]** (or, in the case of payment breach, **[********]**) (the "**Cure Period**") after the date such notice is delivered (or, if such breach (other than a payment breach) cannot be cured within such **[********]** period, if the Party in breach does not commence actions to cure such breach within the Cure Period and thereafter diligently continue such actions), the Party not in breach shall be entitled, without prejudice to any of its other rights conferred on it by this Agreement and in addition to any other remedies available to it by law or in equity, to terminate this Agreement in its entirety.

11.2.5 **Termination of a Particular Candidate Drug or Product in the Territory or in a Major Market for a Diligence Breach**. In the event that there is a material breach by AstraZeneca of its diligence obligations under this Agreement, Targacept shall have the right to give AstraZeneca written notice specifying the nature of the breach and the specific subclause(s) of this Section 11.2.5 under which it intends to exercise its rights, requiring

AstraZeneca to make good or otherwise cure such breach, and stating its intention, if such breach relates to:

(a) the failure to use Commercially Reasonable Efforts to:

(1) Develop Ispronicline as required in Section 5.5.1(a) in at least one Major Market Country, (A) to terminate in the Territory Ispronicline and all Ispronicline Products, and all Licensed Derivatives (other than Working Licensed Derivatives and products containing Working Licensed Derivatives) with respect to any of the foregoing, in each case as of the effective date of such termination or (B) if such failure occurs prior to the second anniversary of the Effective Date and AstraZeneca is not otherwise satisfying its obligations set forth in Section 5.5.1(b) with respect to the Development of another Candidate Drug, to terminate this Agreement in its entirety;

(2) Develop **[********]** (which, at any time in which there is no Candidate Drug (other than, except as expressly provided in Section 5.5.1(c), Option Compound Candidate Drugs) that has not become a Terminated Compound, shall be satisfied by funding the Research Program as required under Section 2.1.5(a) in accordance with the then-current Annual Research Plan or conducting or, if applicable, funding, any Additional Research Program in accordance with an Additional Research Plan, or, if after the Research Program Term, using Commercially Reasonable Efforts to conduct research or development in support of the selection or development of a Candidate Drug, but not including, except as expressly provided in Section 5.5.1(c), research or Development of an Option Compound Candidate Drug) in at least one Major Market Country as provided in Section 5.5.1(b), to terminate this Agreement in the Territory with respect to all Collaboration Candidates, Active+ Compounds, Collaboration Compounds, Candidate Drugs (other than Option Compound Candidate Drugs as of the effective date of such termination and Option Compound Products that contain any such Option Compound Candidate Drug) and Products (other than any products containing Working Licensed Derivatives), and all Licensed Derivatives (other than Working Licensed Derivatives), with respect to any of the foregoing, in each case as of the effective date of such termination; provided, however, that this Section 11.2.5(a)(2)

shall not apply if AstraZeneca (whether itself or with or through one or more of its Affiliates, Sublicensees or Distributors) is satisfying its obligation to use Commercially Reasonable Efforts to Commercialize **[********]** for which Regulatory Approval is obtained (excluding, except as expressly provided in Section 5.5.1(c), an Option Compound Product) in at least one Major Market Country; or

(3) Develop a particular Option Compound Candidate Drug for a Principal Indication in at least one Major Market Country as provided in Section 5.5.1(c), to terminate in the Territory such Option Compound Candidate Drug and all Option Compound Products that contain such Option Compound Candidate Drug, and all Licensed Derivatives (other than Working Licensed Derivatives and products containing Working Licensed Derivatives) with respect to any of the foregoing, in each case as of the effective date of such termination; provided, however, that this Section 11.2.5(a)(3) shall not apply if AstraZeneca (whether itself or with or through one or more of its Affiliates, Sublicensees or Distributors) is using Commercially Reasonable Efforts to Commercialize a Product that contains such Option Compound Candidate Drug or any Licensed Derivative with respect thereto.

(b) once Regulatory Approval has been obtained in a Major Market Country for a Product for a Primary Indication or for Schizophrenia, failure to use Commercially Reasonable Efforts to Commercialize such Product for such Primary Indication or, if applicable, Schizophrenia, in such Major Market Country as provided in Section 5.5.1, to terminate such Product (including the specific Candidate Drug contained in such Product (provided that such Candidate Drug is not included in any other Product being Developed for use in or Commercialized in such Major Market Country by or on behalf of AstraZeneca as of the date of such termination, which for purposes of clarity, is not intended to limit Targacept's rights to Exploit such first terminated Product in such Major Market Country), all other Products that contain such Candidate Drug and no other Candidate Drug, and all Licensed Derivatives (other than Working Licensed Derivatives and products containing Working Licensed Derivatives) with respect to any of the foregoing) solely in such Major Market Country. For purposes of clarity, Targacept may have rights under both Section 11.2.5(a) and 11.2.5(b) and, in such event, shall be entitled to exercise such rights cumulatively.

(c) once Regulatory Approval has been obtained in a Major Market Country for a Product for a Primary Indication, failure to use Commercially Reasonable Efforts to obtain, and, once obtained, Commercialize, such Product (or another Product containing a Licensed Derivative with respect to the Candidate Drug in such Product) for such Primary Indication in another Major Market Country as provided in Section 5.5.1, to terminate such Product (including the specific Candidate Drug contained in such Product (provided that such Candidate Drug is not included in any other Product being Developed for use in or Commercialized in such Major Market Country by or on behalf of AstraZeneca as of the date of such termination, which for purposes of clarity, is not intended to limit Targacept's rights to Exploit such first terminated Product in such Major Market Country), all other Products that contain such Candidate Drug and no other Candidate Drug and all Licensed Derivatives (other than Working Licensed Derivatives and products containing Working Licensed Derivatives) with respect to any of the foregoing) solely in such other Major Market Country(ies) for which AstraZeneca has not used such Commercially Reasonable Efforts.

Subject to Section 11.2.8(a), if such breach with respect to a Candidate Drug or Product is not cured within **[********]** (or, in the case of payment default, **[********]**, or such other applicable period set forth in Section 11.2.8(a)) (the "**Diligence Cure Period**") after the receipt of such notice (or, if such default cannot be cured within such **[********]** period, if AstraZeneca does not commence actions to cure such breach within the Diligence Cure Period and thereafter diligently continue such actions), Targacept shall be entitled, without prejudice to any of its other rights conferred on it by this Agreement (other than pursuant to Section 11.2.4), and in addition to any other remedies available to it by law or in equity, to exercise its rights pursuant to the subclauses of this Section 11.2.5 specifically referenced in such notice.

11.2.6 **Termination for Insolvency**.

(a) Termination. In the event that either Party files for protection under bankruptcy or insolvency laws, makes an assignment for the benefit of creditors, appoints or suffers appointment of a receiver or trustee over its property that is not discharged within ninety (90) days after such filing, proposes a written agreement of composition or extension of its debts, proposes or is a party to any dissolution or liquidation (other than in connection with a

Change of Control of such Party that does not result in the dissolution or liquidation or other similar event by the successor to such Party), files a petition under any bankruptcy or insolvency act or has any such petition filed against it which involuntary petition is not discharged within sixty (60) days of the filing thereof, then the other Party may terminate this Agreement effective immediately upon written notice to such Party which specifically references this Section 11.2.6.

(b) Rights in Bankruptcy. All rights and licenses granted under or pursuant to this Agreement by AstraZeneca or Targacept are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the United States Bankruptcy Code, licenses of right to "intellectual property" as defined under Section 101 of the United States Bankruptcy Code. The Parties agree that the Parties, as licensees of such rights under this Agreement, shall retain and may fully exercise all of their rights and elections under the United States Bankruptcy Code. The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against either Party under the United States Bankruptcy Code, the Party hereto that is not a Party to such proceeding shall be entitled to a complete duplicate of (or complete access to, as appropriate) any such intellectual property and all embodiments of such intellectual property, which, if not already in the non-subject Party's possession, shall be promptly delivered to it (i) upon any such commencement of a bankruptcy proceeding upon the non-subject Party's written request therefor, unless the Party subject to such proceeding continues to perform all of its obligations under this Agreement or (ii) if not delivered under clause (i) above, following the rejection of this Agreement by or on behalf of the Party subject to such proceeding upon written request therefor by the non-subject Party.

11.2.7 **Terminated Efforts Test**.

(a) Terminated Efforts Test. Without prejudice in any way to Targacept's rights under Sections 11.2.4, 11.2.5 and 11.2.6, if, at any time prior to the expiration of the last royalty obligation pursuant to Section 6.6.1 with respect to the first Product (other than an Option Compound Product that contains an Option Compound Candidate Drug, unless pursuant to Section 5.5.1(c) such Option Compound Candidate Drug is sufficient to satisfy AstraZeneca's diligence obligation set forth in Section 5.5.1(b)) for which the First Commercial Sale occurs (or, if earlier, another Product for which the First Commercial Sale occurs),

AstraZeneca, whether or not in breach of its diligence obligations under Section 5.5.1, has not (whether itself or with or through one or more of its Affiliates, Sublicensees or Distributors), for a period of twelve (12) consecutive months, devoted at least **[********]** work (which shall be satisfied during the Research Program Term by funding the Research Program as required under Section 2.1.5(a) in accordance with the then-current Annual Research Plan or conducting or, if applicable, funding, any Additional Research Program in accordance with an Additional Research Plan) to researching, developing, commercializing or otherwise Exploiting at least one Collaboration Compound, Candidate Drug (including, if after the Research Program Term, research or development in support of the selection or development of a Candidate Drug) or Product for at least one indication in the Field or in Schizophrenia in at least one Major Market Country (the "**Terminated Efforts Test**"), then Targacept shall have the right to provide AstraZeneca written notice specifying its concerns and stating its intention to terminate this Agreement in its entirety under this Section 11.2.7.

(b) Reports. AstraZeneca shall provide, within ten (10) days following any written request of Targacept therefor, but in any event not more than twice per Calendar Year, a written statement in support of the proposition that it is satisfying the Terminated Efforts Test. Such statement shall not be conclusive as to whether AstraZeneca is satisfying the Terminated Efforts Test.

(c) Notice, Termination and Cure. Within thirty (30) days after written notice is delivered to AstraZeneca by Targacept pursuant to Section 11.2.7(a), the Parties shall meet to discuss in good faith Targacept's concerns and AstraZeneca's explanation supporting the proposition that AstraZeneca has not failed to meet the Terminated Efforts Test. In the event that Targacept does not agree with AstraZeneca's explanation and considers AstraZeneca to have failed to meet the Terminated Efforts Test, then Targacept shall have the right, in its sole discretion, to initiate arbitration in accordance with Section 14.2 (full arbitration) and, if it is determined in such arbitration that AstraZeneca had failed to meet the Terminated Efforts Test (or if AstraZeneca does not contest that it had failed to meet the Terminated Efforts Test), Targacept shall have the right to provide AstraZeneca with a notice of termination of this Agreement and if AstraZeneca had contested that it had failed to meet the Terminated Efforts Test and, following the arbitrator's determination, does not resume, or increase, its efforts to

meet the Terminated Efforts Test with **[********]** after the receipt of such notice (or, if such Terminated Efforts Test cannot be achieved within such **[********]** period, if AstraZeneca does not commence actions to meet such Terminated Efforts Test within such period and thereafter diligently continues such actions), Targacept shall have the right to terminate this Agreement. For purposes of clarity, Targacept shall have no right to terminate this Agreement pursuant to this Section 11.2.7 if AstraZeneca had contested that it failed to meet the Terminated Efforts Test and, following the arbitrator's determination, meets the Terminated Efforts Test within **[********]** after the receipt of a termination notice with respect thereto (or, if such Terminated Efforts Test cannot be met within such **[********]** period, if AstraZeneca commences actions to meet such Terminated Efforts Test within such period and thereafter diligently continues such actions).

(d) Relationship to Section 11.2.5. The Parties acknowledge and agree that (i) a failure by AstraZeneca to satisfy the Terminated Efforts Test may or may not constitute a breach by AstraZeneca of its diligence obligations under Section 5.5.1 and (ii) satisfaction by AstraZeneca of the Terminated Efforts Test shall not be conclusive as to whether AstraZeneca is satisfying its diligence obligations under Section 5.5.1. If a failure by AstraZeneca to satisfy the Terminated Efforts Test constitutes a breach by AstraZeneca of any of its diligence obligations under Section 5.5.1 (or if AstraZeneca satisfies the Terminated Efforts Test but is in breach of any of its diligence obligations under Section 5.5.1), Targacept shall have all rights and remedies available under this Agreement and at law or in equity with respect to such breach. If such failure by AstraZeneca to satisfy the Terminated Efforts Test does not constitute a breach by AstraZeneca of any of its diligence obligations under Section 5.5.1, or if notwithstanding any such breach by AstraZeneca, Targacept exercises its rights under this Section 11.2.7 (and not Section 11.2.5), the exclusive right and remedy available to Targacept shall be as provided in this Section 11.2.7 and Targacept shall have no other rights or remedies in law or in equity or under this Agreement with respect to such termination, except as expressly provided in Sections 11.3.3 and 11.3.6.

(e) Exercise of Rights under both Sections 11.2.7 and 11.2.5. If Targacept seeks to exercise its rights both under this Section 11.2.7 and under Section 11.2.5, its notice given pursuant to Section 11.2.7(a) shall also specify the specific subclauses of Section

11.2.5 under which it intends to exercise its rights for breach, require AstraZeneca to make good or otherwise cure such breach, and state its termination intention under Section 11.2.5, as well as this Section 11.2.7.

11.2.8 **Other Provisions Relating to Termination Rights**.

(a) Dispute as to Breach. If a Party shall dispute the existence, extent or nature of any matter underlying a right of termination (whether of this entire Agreement or part of this Agreement, including with respect to the Research Program or to a particular Candidate Drug, Product or Major Market Country, as applicable, in accordance with Section 11.2.2(b), 11.2.4, 11.2.5 or 11.2.7) the matter shall be referred to the ESC and the ESC shall use good faith efforts to resolve the dispute. If the ESC cannot resolve the dispute within **[********]** after the ESC first meets to consider such matter (subject to Section 2.1.5, if applicable), it shall be resolved in accordance with Section 14.2 (full arbitration) and any time period related to such termination right, and termination, shall be tolled during any such ESC review and any arbitration proceeding. For purposes of clarity, with respect to any matter referred to the ESC and, if the ESC cannot resolve the dispute, arbitration pursuant to Section 14.2, the applicable cure period (if any) shall not commence until the ESC or, if applicable, the arbitrator has determined that the alleged Defaulting Party is in breach.

(b) Termination as to a Specific Compound or Product. Except as otherwise expressly set forth this Section 11.2, Section 11.3 or Section 1.309, the termination of a particular Collaboration Compound, Candidate Drug or Product shall not be deemed to be a termination of any Licensed Derivatives with respect to any of the foregoing unless there is an independent basis for such termination of such Licensed Derivatives under this Section 11.2.

11.3 **Consequences of Termination of Agreement**.

11.3.1 **Termination of Agreement in its Entirety by AstraZeneca or Targacept in accordance with Section 11.2.1**. If this Agreement is terminated by either Party pursuant to Section 11.2.1, in addition to the consequences set forth in Sections 3.3.2(a) and 11.3.6:

(a) all Collaboration Candidates, Active+ Compounds, Collaboration Compounds, Candidate Drugs and Products (other than Option Compound Candidate Drugs and any Option Compound Products and any Additional Compounds or Working Licensed Derivatives with respect to any Option Compound Candidate Drugs or Option Compound Products and any products that contain such Additional Compounds or such Working Licensed Derivatives) as of the effective date of termination (if any) shall be Terminated Compounds;

(b) the licenses granted by Targacept pursuant to Sections 8.1.2, 8.1.3 and 8.1.6 shall survive solely with respect to all Option Compound Candidate Drugs and Option Compound Products as of the effective date of such termination, if any, and any Additional Compounds or Working Licensed Derivatives with respect to any Option Compound Candidate Drugs or Option Compound Products (and any products that contain such Additional Compounds or such Working Licensed Derivatives);

(c) provided that Targacept satisfied the obligations set forth in Sections 11.3.1(e) through 11.3.1(g) below, AstraZeneca shall, and does hereby automatically (i) assign to Targacept all of AstraZeneca's and its Affiliates' rights, titles and interests in and to all AstraZeneca Pre-Phase IIb Program Technology, Pre-Phase IIb Program Patent Rights, Joint Technology made, developed or conceived in the conduct of the Pre-Phase IIb Program, Joint Patent Rights with respect to such Joint Technology and all Regulatory Filings Controlled by AstraZeneca or its Affiliates that solely relate to Ispronicline and (ii) duly execute and deliver, or cause to be duly executed and delivered, such instruments and shall do and cause to be done such acts and things, including the filing of such assignments, agreements, documents and instruments as may be necessary for, or as Targacept may reasonably request to carry out more effectively, the purpose of this Section 11.3.1(c);

(d) upon the request of Targacept, and provided that Targacept has (x) obtained insurance coverage in the amounts, and provided AstraZeneca with a certificate of insurance (if requested) as, required under Section 13.4.2, and (y) satisfied the obligations set forth in Sections 11.3.1(e) through 11.3.1(g), AstraZeneca shall, and does hereby automatically, grant to Targacept, subject to the royalty obligations in Section 11.4.1(b), if any, with respect to each Terminated AZ Compound, a worldwide license, with the right to grant sublicenses: (i)

under the Product Trademarks Controlled by AstraZeneca that are solely applicable to such Terminated AZ Compound, which grant shall be exclusive; (ii) under AstraZeneca Patent Rights and AstraZeneca's interest in Joint Patent Rights in a country in the Territory (but, with respect to each Terminated AZ Compound **[********]** (x) **[********]** such Terminated AZ Compound, in each case as of the date **[********]**, or (y) **[********]** such Terminated AZ Compound, to the extent such Technology relates to such Terminated AZ Compound and **[********]**) that would be infringed by the Exploitation in such country of such Terminated AZ Compound in the absence of a license to Exploit such Terminated AZ Compound), which grant shall be non-exclusive (unless, with respect to any Technology, such Technology solely relates to one or more Terminated AZ Compounds, in which case such grant to the Patent Right that covers such Technology shall be exclusive); and (iii) under AstraZeneca Technology and AstraZeneca's interest in Joint Technology (but, with respect to each Terminated AZ Compound, **[********]** (x) **[********]** such Terminated AZ Compound, in each case as of the date **[********]**, or (y) **[********]** such Terminated AZ Compound, to the extent such Technology relates to such Terminated AZ Compound and **[********]** on or prior to the date **[********]**), which grant shall be non-exclusive; in each case ((i), (ii) and (iii)), to Exploit such Terminated AZ Compound in and outside the Field; provided, however, that no AstraZeneca Other Technology or AstraZeneca Other Patent Rights shall be included in the foregoing grants unless and until the Parties agree, or an Expert determines, as applicable, the appropriate royalty rate, if any, pursuant to Section 11.4.1(b);

(e) as consideration for the assignment of rights in and to the AstraZeneca Pre-Phase IIb Program Technology and AstraZeneca Pre-Phase IIb Program Patent Rights pursuant to Section 11.3.1(c) and as partial consideration for the rights in and to the AstraZeneca Technology and AstraZeneca Patent Rights granted pursuant to Section 11.3.1(d), Targacept shall, within thirty (30) days of the date on which this Agreement is terminated pursuant to Section 11.2.1, pay AstraZeneca the sum of Five Million Dollars (US $5,000,000);

(f) to the extent AstraZeneca has paid (i) the milestone in Section 6.5.1(a)(3) in the amount of Twenty Million Dollars (US $20,000,000) or any other milestone payments under Section 6.5 or (ii) any of the aggregate FTE Costs for all FTEs and External Targacept R&D Costs relating to the Research Program incurred by or on behalf of Targacept in

connection with the Research Program as required by Sections 6.4.1 and 6.4.3, Targacept shall, within thirty (30) days of the date on which this Agreement is terminated pursuant to Section 11.2.1, refund such amounts to AstraZeneca; and

(g) if on or prior to the effective date of termination pursuant to Section 11.2.1, AstraZeneca has paid an Option Maintenance Fee with respect to an Option Compound but has not exercised the POC Option for such Option Compound, and such Option Compound has not previously become a Terminated Compound or an Unexercised Option Compound pursuant to Section 5.10.2, then Targacept shall, within thirty (30) days of such effective date of termination, refund the applicable Option Maintenance Fee, whereupon such Option Compound shall become a Terminated Compound.

11.3.2 **Termination of Agreement in its Entirety or as to Particular Collaboration Compounds, Candidate Drugs or Products by AstraZeneca in accordance with Section 11.2.3**. If this Agreement is terminated by AstraZeneca pursuant to Section 11.2.3 (x) in its entirety or (y) with respect to one or more Collaboration Compounds, Candidate Drugs or Products:

(a) if terminated pursuant to clause (x) above, all Collaboration Candidates, Active+ Compounds, Collaboration Compounds, Candidate Drugs (other than Working Licensed Derivatives) and Products (other than products containing Working Licensed Derivatives) as of the effective date of termination (if any) shall be Terminated Compounds, or, if terminated with respect to one or more Collaboration Compounds, Candidate Drugs or Products pursuant to clause (y) above, solely such terminated Collaboration Compound(s), Candidate Drug(s) or Product(s) shall be Terminated Compound(s);

(b) if terminated with respect to one or more Collaboration Compounds, Candidate Drugs or Products pursuant to clause (y) above, the licenses granted pursuant to Sections 8.1.1, 8.1.2, 8.1.3 and 8.1.6 shall survive such termination (provided that, for purposes of clarity, such licenses do not apply to Terminated Compound(s)) in the Territory;

(c) if terminated with respect to one or more Collaboration Compounds, Candidate Drugs or Products pursuant to clause (y) above, the licenses granted by

AstraZeneca to Targacept pursuant to Sections 8.2.1 and 8.2.2 (except with respect to such Terminated Compound(s)) shall survive such termination;

(d) upon the request of Targacept, and provided that Targacept has (1) obtained insurance coverage in the amounts, and provided AstraZeneca with a certificate of insurance (if requested) as, required under Section 13.4.2, and (2) if terminated pursuant to clause (x) above, satisfied the obligations set forth in Section 11.3.2(e), AstraZeneca shall, and does hereby automatically, grant to Targacept, subject to the royalty obligations in Section 11.4.1, if any, with respect to each Terminated AZ Compound, a worldwide license, with the right to grant sublicenses: (i) under the Product Trademarks Controlled by AstraZeneca that are solely applicable to such Terminated AZ Compound, which grant shall be exclusive; (ii) under AstraZeneca Patent Rights and AstraZeneca's interest in Joint Patent Rights in a country in the Territory (but, with respect to each Terminated AZ Compound**[********]** (A) is **[********]** such Terminated AZ Compound, in each case as of the date **[********]**, or (B) **[********]** such Terminated AZ Compound, to the extent such Technology relates to such Terminated AZ Compound and **[********]** on or prior to the date **[********]**) that would be infringed by the Exploitation in such country of such Terminated AZ Compound in the absence of a license to Exploit such Terminated AZ Compounds) that would be infringed by the Exploitation in such country of a Terminated AZ Compound in the absence of a license to Exploit such Terminated AZ Compound, which grant shall be non-exclusive (unless, with respect to any Technology, such Technology solely relates to one or more Terminated AZ Compounds, in which case such grant to the Patent Right that covers such Technology shall be exclusive); and (iii) under AstraZeneca Technology and AstraZeneca's interest in Joint Technology (but, with respect to each Terminated AZ Compound**[********]** (A) **[********]** such Terminated AZ Compound, in each case as of the date **[********]**, or (B) **[********]** such Terminated AZ Compound, to the extent such Technology relates to such Terminated AZ Compound and **[********]** on or prior to the date **[********]**), which grant shall be non-exclusive; in each case ((i), (ii) and (iii)), to Exploit such Terminated AZ Compound in and outside the Field; provided, however, that no AstraZeneca Other Technology or AstraZeneca Other Patent Rights shall be included in the foregoing grants unless and until the Parties agree, or an Expert determines, as applicable, the appropriate royalty rate, if any, pursuant to Section 11.4.1(b);

(e) if terminated with respect to one or more Collaboration Compounds, Candidate Drugs or Products pursuant to clause (y) above, Sections 8.6 and 8.9 shall survive.

11.3.3 **Termination of Agreement by Targacept in its Entirety in accordance with Section 11.2.4, 11.2.5(a), 11.2.6 or 11.2.7 or as to a Particular Candidate Drug or Product in the Territory in accordance with Section 11.2.5(a)**. If this Agreement is terminated by Targacept (x) in its entirety pursuant to Section 11.2.4, 11.2.5(a), 11.2.6 or 11.2.7 or (y) as to one or more Candidate Drugs or Products in the entire Territory pursuant to Section 11.2.5(a):

(a) if terminated pursuant to clause (x) above, all Collaboration Candidates, Active+ Compounds, Collaboration Compounds, Candidate Drugs (other than Working Licensed Derivatives) and Products (other than products containing Working Licensed Derivatives) shall be Terminated Compounds, or if terminated with respect to one or more Candidate Drugs or Products pursuant to clause (y) above, solely (i) such terminated Candidate Drug(s) or Product(s), (ii) if a Candidate Drug is terminated, all Products (other than products containing Candidate Drugs that are not Terminated Compounds or Working Licensed Derivatives) that contain such Candidate Drug and (iii) if a Product is terminated, all Products (other than products containing Candidate Drugs that are not Terminated Compounds or Working Licensed Derivatives) that contain the same Candidate Drug as is contained in such Product, in each case ((i), (ii) and (iii)), shall be Terminated Compounds;

(b) if terminated with respect to one or more Candidate Drugs or Products pursuant to clause (y) above, the licenses granted by Targacept to AstraZeneca pursuant to Sections 8.1.1, 8.1.2, 8.1.3 and 8.1.6 shall survive such termination (but, for purposes of clarity, such licenses do not apply to Terminated Compound(s));

(c) if terminated with respect to one or more Candidate Drugs or Products pursuant to clause (y) above, the licenses granted by AstraZeneca to Targacept pursuant to Sections 8.2.1 and 8.2.2 (except with respect to such Terminated Compound(s)) shall survive such termination;

(d) upon the request of Targacept, and provided that Targacept has obtained insurance coverage in the amounts, and provided AstraZeneca with a certificate of insurance (if requested) as, required under Section 13.4.2, AstraZeneca shall, and does hereby automatically, grant to Targacept, subject to the royalty obligations in Section 11.4.1, if any, with respect to each Terminated AZ Compound, a worldwide license, with the right to grant sublicenses: (i) under the Product Trademarks Controlled by AstraZeneca that are solely applicable to such Terminated AZ Compound, which grant shall be exclusive; (ii) under AstraZeneca Patent Rights and AstraZeneca's interest in Joint Patent Rights in a country in the Territory (but, with respect to each Terminated AZ Compound, **[********]** (x) **[********]** such Terminated AZ Compound, in each case as of the date **[********]**, or (y) **[********]** such Terminated AZ Compound, to the extent such Technology relates to such Terminated AZ Compound and **[********]** on or prior to the date **[********]**) that would be infringed by the Exploitation in such country of a Terminated AZ Compound in the absence of a license to Exploit such Terminated AZ Compound, which grant shall be non-exclusive (unless, with respect to any Technology, such Technology solely relates to one or more Terminated AZ Compounds, in which case such grant to the Patent Right that covers such Technology shall be exclusive); and (iii) under AstraZeneca Technology and AstraZeneca's interest in Joint Technology (but, with respect to each Terminated AZ Compound, **[********]** (x) **[********]** such Terminated AZ Compound, in each case as of the date **[********]**, or (y) **[********]**, to the extent such Technology relates to such Terminated AZ Compound and **[********]** on or prior to the date **[********]**), which grant shall be non-exclusive; in each case ((i), (ii) and (iii)), to Exploit such Terminated AZ Compound in and outside the Field; provided, however, that no AstraZeneca Other Technology or AstraZeneca Other Patent Rights shall be included in the foregoing grants unless and until the Parties agree, or an Expert determines, as applicable, the appropriate royalty rate, if any, pursuant to Section 11.4.1(b); and

(e) if terminated with respect to one or more Candidate Drugs or Products pursuant to clause (y), Sections 8.6 and 8.9 shall survive such termination.

11.3.4 **Termination of Agreement by Targacept with respect to one or more Candidate Drugs or Products in one or more Major Market Countries in accordance with Section 11.2.5(b) or 11.2.5(c)**. If this Agreement is terminated by Targacept as to one or more

Candidate Drugs or Products in one or more Major Market Countries, but not with respect to the entire Territory, pursuant to Section 11.2.5(b) or 11.2.5(c):

(a) (i) such terminated Candidate Drug(s) (other than Working Licensed Derivatives) or Product(s) (other than products containing Candidate Drugs that are not Terminated Compounds or Working Licensed Derivatives), (ii) if a Candidate Drug is terminated, all Products (other than products containing Candidate Drugs that are not Terminated Compounds or Working Licensed Derivatives) that contain such Candidate Drug and (iii) if a Product is terminated, all Products (other than products containing Candidate Drugs that are not Terminated Compounds or Working Licensed Derivatives) that contain the same Candidate Drug as is contained in such Product, in each case ((i), (ii) and (iii)), shall be Partially-Terminated Products;

(b) subject to Section 11.3.4(e), the licenses granted by Targacept to AstraZeneca pursuant to Sections 8.1.1, 8.1.2, 8.1.3 and 8.1.6 shall survive such termination, but with respect to each Partially-Terminated Product in such terminated Major Market Country(ies), such licenses shall be converted to a non-exclusive license to Exploit (but shall exclude the right to file Drug Approval Applications for, or obtain or maintain Regulatory Approvals for, or promote, market or commercially sell, offer for sale, or have sold (other than to an Affiliate in an intra-company transfer or to a Sublicensee or Distributor for sale in the Territory) each such Partially-Terminated Product in such terminated Major Market Country(ies);

(c) the licenses granted by AstraZeneca to Targacept pursuant to Sections 8.2.1 and 8.2.2 shall survive such termination, but, with respect to each Partially-Terminated Product, such licenses shall survive only with respect to non-terminated Major Market Country(ies);

(d) upon the request of Targacept, and provided that Targacept has (x) obtained insurance coverage in the amounts, and provided AstraZeneca with a certificate of insurance (if requested) as, required under Section 13.4.2, and (y) executed a safety agreement with respect to each such Partially-Terminated Product pursuant to Section 5.9.3(a), AstraZeneca shall, and does hereby automatically, grant to Targacept a license, subject to the royalty obligations in Section 11.4.1, if any, with the right to grant sublicenses, solely in such terminated

Major Market Country(ies) (i) under the Product Trademarks Controlled by AstraZeneca that are solely applicable to such Partially-Terminated Product, which grant shall be exclusive; (ii) under AstraZeneca Patent Rights and AstraZeneca's interest in Joint Patent Rights in a country in the Territory (but, with respect to each Partially-Terminated Product, **[********]** (x) **[********]** such Partially-Terminated Product, in each case as of the date **[********]**, or (y) **[********]** such Partially-Terminated Product, to the extent such Technology relates to such Partially-Terminated Product and **[********]** on or prior to the date **[********]**) that would be infringed by the Exploitation in such country of a Partially-Terminated Product in the absence of a license to Exploit such Partially-Terminated Product, which grant shall be non-exclusive (unless, with respect to any Technology, such Technology solely relates to one or more Partially-Terminated Products, in which case such grant to the Patent Right that covers such Technology shall be exclusive); and (iii) under AstraZeneca Technology and AstraZeneca's interest in Joint Technology (but, with respect to each Partially-Terminated Product, **[********]** (x) **[********]** such Partially-Terminated Product, in each case as of the date **[********]**, or (y) **[********]** such Partially-Terminated Product, to the extent such Technology relates to such Partially-Terminated Product, and **[********]** on or prior to the date **[********]**), which grant shall be non-exclusive; in each case ((i), (ii) and (iii)), to Exploit such Partially-Terminated Product in and outside the Field; provided, however, that in any event, AstraZeneca, its Affiliates and its Sublicensees shall retain a non-exclusive right to Exploit, but not to file Drug Approval Applications for, or obtain or maintain Regulatory Approvals for, or promote, market or commercially sell, offer for sale, or have sold (other than to an Affiliate in an intra-company transfer or to a Sublicensee or Distributor for sale in the Territory) any such Partially-Terminated Product(s) in such terminated Major Market Country(ies), as necessary or useful to exercise its rights under this Agreement in the Partially-Terminated Product Territory; and provided further that no AstraZeneca Other Technology or AstraZeneca Other Patent Rights shall be included in the foregoing grants unless and until the Parties agree, or an Expert determines, as applicable, the appropriate royalty rate, if any, pursuant to Section 11.4.1(b); and

(e) Sections 8.6 and 8.9 shall survive.

11.3.5 **Termination of Agreement in its Entirety by AstraZeneca in accordance with Section 11.2.4 or 11.2.6**. If this Agreement is terminated in its entirety (x) by

AstraZeneca pursuant to Section 11.2.4 or 11.2.6 or (y) for any other reason (other than by Targacept pursuant to Section 11.2.1, 11.2.4, 11.2.5, 11.2.6 or 11.2.7, by AstraZeneca pursuant to Section 11.2.1, 11.2.3 or 15.2.1, by mutual agreement or, for purposes of clarity, upon expiration of the Term pursuant to Section 11.1); provided that, for purposes of clarity, this Section 11.3.5 shall not expand the rights of AstraZeneca to terminate this Agreement beyond that expressly set forth in Sections 11.2.1, 11.2.3, 11.2.4 and 11.2.6 and, for purposes of clarity, the termination of the Research Program pursuant to Section 11.2.2 shall not trigger application of this Section 11.3.5:

(a) unless designated as a Terminated Compound prior to the effective date of such termination, (i) none of the Collaboration Compounds, Candidate Drugs and Products shall be Terminated Compounds and (ii) if such termination occurs prior to the end of the Tail Period, none of the Collaboration Candidates or Active+ Compounds shall be Terminated Compounds until designated as such pursuant to Section 2.2.4 or until they otherwise become such in accordance with Section 1.309(d);

(b) subject to Section 11.3.5(c), the licenses granted by Targacept to AstraZeneca pursuant to Sections 8.1.2, 8.1.3, 8.1.4 and 8.1.5 shall survive;

(c) (x) the royalty rates set forth in Section 6.6.1 shall be reduced by **[********]** and (y) the milestone obligations set forth in Section 6.5 shall be reduced by **[********]**; provided that if such termination results from a material breach by Targacept of (i) a representation or warranty with respect to any Targacept Technology or Targacept Patents claiming or covering (A) Ispronicline, such royalty rates and milestones shall be so reduced only with respect to **[********]** with respect thereto; (B) an Option Compound, such royalty rates and milestones shall be so reduced only with respect to **[********]** with respect thereto; or (C) a Collaboration Compound or, except as provided in clause (A) or (B) above, Candidate Drug, such royalty rates and milestones shall be so reduced only with respect to **[********]** with respect thereto; (ii) an obligation to use Commercially Reasonable Efforts in connection with a Targacept Development Activity relating to a Candidate Drug or Product, such royalty rates and milestones shall be so reduced only with respect to such Candidate Drug (including any Products that contain the same Candidate Drug) or Product (including any other Products that include the

same Candidate Drug as such Product); or (iii) an obligation to use Commercially Reasonable Efforts in connection with the Research Program, such royalty rates and milestones shall be so reduced only with respect to Collaboration Compounds, Candidate Drugs (other than Ispronicline and Option Compound Candidate Drugs) and Products (other than Ispronicline Products and Option Compound Products); for purposes of clarity, nothing in this Section 11.3.5 shall constitute an acknowledgement or agreement of Targacept that a material breach of any (1) particular representation or warranty or (2) obligation to use Commercially Reasonable Efforts in connection with a Targacept Development Activity constitutes a material breach of this Agreement giving rise to a right of termination by AstraZeneca under Section 11.2.4.

(d) for purposes of clarity, AstraZeneca shall retain all rights set forth hereunder with respect to all Option Compound Candidate Drugs and Option Compound Products designated as such as of the effective date of such termination and any Licensed Derivatives with respect thereto and any Additional Compounds with respect to any of the foregoing, provided that AstraZeneca shall not have any further option rights described in Section 5.10.2 with respect to any other Option Compounds; provided, however, that notwithstanding the foregoing, with respect to any Option Compound for which AstraZeneca has paid an Option Maintenance Fee pursuant to Section 5.10.2(b)(3), but which has not become a Terminated Compound or an Unexercised Option Compound prior to the effective date of such termination, AstraZeneca shall have the right, at its election, to treat such termination as a failure by Targacept to meet its diligence obligations with respect to an Option Compound as set forth in Section 5.10.2(b)(4), such that Targacept shall refund the applicable Option Maintenance Fee and AstraZeneca shall have the right, but not the obligation, to complete the relevant Option Compound Development Plan in accordance with Section 5.10.2(b)(5) and Section 5.10.2 shall survive solely for purposes thereof;

(e) the ESC, JDC, JRC and CCC shall be disbanded and, except in relation to royalty and milestone payments pursuant to Section 6.6.1(e), AstraZeneca shall have no obligation to provide information or reports, or to participate in meetings with Targacept with respect to the Development and Commercialization of Candidate Drugs or Products under this Agreement, including under Section 5.9, except with respect to royalty reports as provided in Section 6.6.1(e);

(f) Targacept's rights with respect to any AZ Co-Promotion Opportunity or any unexercised Co-Promotion Option pursuant to Section 5.11 shall, at AstraZeneca's discretion, terminate and AstraZeneca shall be entitled to terminate any co-promotion agreement with respect to any AZ Co-Promotion Opportunity or Co-Promotion Option entered into by the Parties prior to termination, including any Co-Promotion Agreement; and

(g) Sections 8.6.1, 8.6.2 and 8.9 shall survive.

11.3.6 **Additional Consequences in the Event of Termination**.

(a) AstraZeneca Obligations.

(1) In the event of any termination of this Agreement in whole or in part in accordance with Section 11.2 (other than pursuant to Section 11.2.5(b) or 11.2.5(c)), except as expressly provided in this Article 11, AstraZeneca (i) shall have no obligation to Exploit in any way Terminated Compounds or Products that contain Terminated Compounds anywhere in the world following the date, with respect to each such Terminated Compound, on which such Terminated Compound became a Terminated Compound, (ii) shall not be responsible for any amounts otherwise payable under Section 6.4 with respect to such Terminated Compound(s) or Products that contain Terminated Compounds incurred following the date, with respect to each such Terminated Compound, on which such Terminated Compound became a Terminated Compound and (iii) shall not be responsible for any milestone payments for milestone events that are achieved under Section 6.5 with respect to such Terminated Compound(s) or Products that contain Terminated Compounds anywhere in the world following the date, with respect to each such Terminated Compound, on which such Terminated Compound became a Terminated Compound; provided, however, that in the event of any termination of this Agreement by AstraZeneca pursuant to Section 11.2.4, AstraZeneca shall not be responsible for any milestone payments for milestone events that are achieved but not yet due as of the date, with respect to each such Terminated Compound, on which such Terminated Compound became a Terminated Compound.

(2) In the event of the termination of this Agreement with respect to a Partially-Terminated Product in one or more terminated Major Market Countries pursuant to Section 11.2.5(b) or 11.2.5(c), except as expressly provided in this Article 11, AstraZeneca (i) shall have no obligation to Exploit such Partially-Terminated Product in any way in such terminated Major Market Country(ies) following the effective date of such termination, (ii) shall not be responsible for any amounts otherwise payable under Section 6.4 with respect to such Partially-Terminated Product in such terminated Major Market Country(ies) incurred following the effective date of such termination and (iii) shall not be responsible for any milestone payments for milestone events that are achieved under Section 6.5 with respect to such Partially-Terminated Product in such terminated Major Market Country(ies) following the effective date of such termination.

(b) Confidential Information and Data. Each Party shall promptly return all Confidential Information and Proprietary Materials of the other Party that are not subject to a continuing license hereunder; provided that each Party may retain one copy of the Confidential Information of the other Party in its archives solely for the purpose of establishing the contents thereof and ensuring compliance with its obligations hereunder.

(c) Regulatory Filings.

(1) In the event of any termination of this Agreement in whole or in part in accordance with Section 11.2 (other than pursuant to Section 11.2.5(b) or 11.2.5(c) or by AstraZeneca pursuant to Section 11.2.4), to the extent requested in writing by Targacept, provided that Targacept has (x) obtained insurance coverage in the amounts, and provided AstraZeneca with a certificate of insurance (if requested) as, required under Section 13.4.2, and (y) if this Agreement is terminated in its entirety by either Party pursuant to Section 11.2.1, paid all amounts due under Sections 11.3.1(e), (f) and (g) (if applicable), AstraZeneca shall promptly: (i) where permitted by law, transfer to Targacept all of its right, title and interest in all Regulatory Filings (including Drug Approval Applications and Regulatory Approvals) then in its name applicable to each Terminated AZ Compound in the Territory, and all material aspects of Confidential Information Controlled by it as of the date of termination relating to such Regulatory

Filings (including Drug Approval Applications and Regulatory Approvals); (ii) notify the applicable Regulatory Authorities and take any other action reasonably necessary to effect such transfer; (iii) provide Targacept with copies all correspondence between AstraZeneca and such Regulatory Authorities relating to such Regulatory Filings, Drug Approval Applications and Regulatory Approvals; (iv) unless expressly prohibited by any Regulatory Authority, transfer control to Targacept of all Clinical Trials of each such Terminated AZ Compound being conducted as of the effective date of termination and continue to conduct such trials, at Targacept's cost, for up to six (6) months to enable such transfer to be completed without interruption of any such trial; provided that AstraZeneca shall not have any obligation to continue any Clinical Trial if, AstraZeneca believes, in its sole discretion, that to do so would raise safety concerns or violate Applicable Laws; (v) assign (or cause its Affiliates to assign) to Targacept all agreements with any Third Party with respect to the conduct of Clinical Trials for each such Terminated AZ Compound including agreements with contract research organizations, clinical sites and investigators, unless expressly prohibited by any such agreement (in which case AstraZeneca shall cooperate with Targacept in all reasonable respects to secure the consent of such Third Party to such assignment); (vi) provide Targacept with all supplies of each such Terminated AZ Compound in the possession and Control of AstraZeneca or any Affiliate or contractor of AstraZeneca; and (vii) subject to any Third Party agreement, provide Targacept with copies of all reports and data generated or obtained by AstraZeneca or its Affiliates pursuant to this Agreement that relate to each such Terminated AZ Compound in the Major Market Countries that have not previously been provided to Targacept. For purposes of clarity, nothing in this subsection (c) shall require AstraZeneca to make any payments or provide any other consideration to any Third Party.

(2) In the event of any termination of this Agreement with respect to one or more Partially-Terminated Products in one or more terminated Major Market Countries pursuant to Section 11.2.5(b) or 11.2.5(c), to the extent requested by Targacept, provided that Targacept has (x) obtained insurance coverage in the amounts, and provided AstraZeneca with a certificate of insurance (if requested) as, required under Section 13.4.2, and (y) executed a safety agreement with respect to such Partially-

Terminated Product(s) in accordance with Section 5.9.3(a), AstraZeneca shall promptly (i) where permitted by Applicable Laws, provide Targacept with access to, and grant Targacept the right and license to use and to reference, all Regulatory Filings (including Drug Approval Applications and Regulatory Approvals) then in its name applicable to the Commercialization (or other Exploitation as necessary to support such Commercialization) of such Partially-Terminated Product in any such terminated Major Market Country(ies) and all material aspects of Confidential Information relating to such Regulatory Filings (including Drug Approval Applications and Regulatory Approvals) with respect to such Partially-Terminated Product Controlled by it, in each case solely as of the date such terminated Major Market Country(ies) are terminated from the Territory; (ii) provide Targacept with copies of all correspondence between AstraZeneca and such Regulatory Authorities relating to such Regulatory Filings and Regulatory Approvals that relate to such terminated Major Market Country(ies) as of the date such terminated Major Market Country(ies) are terminated from the Territory; (iii) assign to Targacept all agreements between AstraZeneca and any Third Party with respect to the conduct of clinical trials for such Partially-Terminated Product(s) that relate solely to obtaining or maintaining Regulatory Approvals in such terminated Major Market Country(ies), including agreements or contracts with contract research organizations, clinical sites and investigators, unless expressly prohibited by any such agreement (in which case AstraZeneca shall cooperate with Targacept in all reasonable respects to secure the consent of such Third Party to such assignment); and (iv) subject to any Third Party agreements, provide Targacept with copies of all reports and data obtained by AstraZeneca or its Affiliates pursuant to this Agreement that relate specifically to, or are otherwise necessary for, the Commercialization of such Partially-Terminated Product in any such terminated Major Market Country(ies) as of the date such terminated Major Market Country(ies) are terminated from the Territory.

(d) Manufacturing.

(1) In the event of any termination of this Agreement in whole or in part in accordance with Section 11.2 (other than pursuant to Section 11.2.5(b) or 11.2.5(c) or by AstraZeneca pursuant to Section 11.2.4), if AstraZeneca is manufacturing

or having manufactured any Terminated AZ Compound or any intermediate thereof for use in any country in the Territory as of the effective date of termination, to the extent requested by Targacept, provided that Targacept has (x) obtained insurance coverage in the amounts, and provided AstraZeneca with a certificate of insurance (if requested) as, required under Section 13.4.2, and (y) if this Agreement is terminated in its entirety by either Party pursuant to Section 11.2.1, paid all amounts due under Sections 11.3.1(e) through (g) (if applicable), (i) AstraZeneca shall supply Targacept with its requirements for each such Terminated AZ Compound (which amounts shall be consistent with AstraZeneca's historical usage of each such Terminated AZ Compound) for **[********]** following such termination at a transfer price equal to **[********]** supply of such Terminated AZ Compound(s) or intermediate, plus **[********]**, and (ii) promptly after Targacept's request, AstraZeneca shall provide to Targacept or its designee all information in its possession with respect to the manufacture of each such Terminated AZ Compound or intermediate as of the effective date of such termination.

(2) In the event of any termination of this Agreement with respect to one or more Partially-Terminated Products in one or more terminated Major Market Countries pursuant to Section 11.2.5(b) or 11.2.5(c), if AstraZeneca is manufacturing or having manufactured any Partially-Terminated Product or any intermediate thereof for use in a terminated Major Market Country as of the effective date of termination, to the extent requested by Targacept, provided that Targacept has (x) obtained insurance coverage in the amounts, and provided AstraZeneca with a certificate of insurance (if requested) as, required under Section 13.4.2, and (y) executed a safety agreement with respect to each such Partially-Terminated Product in accordance with Section 5.9.3(a), (i) AstraZeneca shall supply Targacept with its requirements for each such Partially-Terminated Product in such terminated Major Market Country (which amounts shall be consistent with AstraZeneca's historical usage of each such Partially-Terminated Product in such Major Market Country(ies)) for **[********]** following such termination at a transfer price equal to **[********]** supply of such Partially-Terminated Product or intermediate, plus **[********]**, and (ii) promptly after Targacept's request, AstraZeneca shall provide to Targacept or its designee all information in its possession

with respect to the manufacture of each such Partially-Terminated Product or intermediate as of the effective date of such termination.

11.4 **AstraZeneca Royalties**.

11.4.1 **Royalty Rates**.

(a) For each Royalty-Bearing Product, Targacept shall pay AstraZeneca a royalty based on Targacept Net Sales of such Royalty-Bearing Product in each Calendar Year (or partial Calendar Year) at the rate of **[********]** of Targacept Net Sales. A "**Royalty-Bearing Product**" is a product that contains an Active+ Compound, Collaboration Compound or Candidate Drug that has become a Terminated Compound (other than as a result of a termination by Targacept under Section 11.2.4 or 11.2.5 or by either Party under Section 11.2.1) (a "**Royalty-Bearing Terminated Compound**") as an active ingredient.

(b) If for any Terminated AZ Compound (including any Royalty-Bearing Product) or any Partially-Terminated Product, Targacept wishes to use or otherwise obtain rights under the AstraZeneca Other Technology or AstraZeneca Other Patent Rights under the grants set forth in Section 11.3.1(d), 11.3.2(d), 11.3.3(d) or 11.3.4(d) (each, a "**Royalty-Bearing Terminated AZ Product**"), Targacept shall deliver a written notice to AstraZeneca, whereupon the Parties shall negotiate in good faith an appropriate royalty rate under the applicable license grants, giving good faith consideration to the value derived from such AstraZeneca Other Patent Right(s) and AstraZeneca Other Technology based on such rates as are customary in the industry for such rights and, if and to the extent that such AstraZeneca Other Patent Rights provide exclusivity with respect to such Royalty-Bearing Terminated AZ Product, the value of such exclusivity, which royalties shall be in addition to any payments due under Section 11.4.1(a); provided that in the event the Parties are unable to agree, such matter shall be referred to an Expert for resolution in accordance with Section 14.4 (expedited arbitration). For purposes of clarity, upon the effective date of any such termination, any Targacept Net Sales with respect to any Partially-Terminated Product(s) shall be included in the royalty calculations set forth in this Section 11.4.

11.4.2 **Royalty Term**. Targacept's obligation to pay royalties shall commence, on a country-by-country basis, with respect to each separate Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product, on the later of (a) the date on which the Royalty-Bearing Terminated Compound, Terminated AZ Compound or Partially-Terminated Product, as applicable, contained in such product becomes a Terminated Compound, and (b) the date of First Commercial Sale of such Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product in such country by Targacept, its Affiliates or Sublicensees (but, for purposes of clarity, not AstraZeneca or its Affiliates or Sublicensees). The obligation shall expire, on a country-by-country basis, with respect to each separate Royalty-Bearing Product and Royalty-Bearing Terminated AZ Product, on the later to occur of (i) the twelfth (12th) anniversary of the First Commercial Sale by Targacept, its Affiliates or Sublicensees of such Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product in such country and (ii) the expiration date in such country of the last to expire of (A) with respect to a Royalty-Bearing Product, any AstraZeneca Patent Right or (B) with respect to a Royalty-Bearing Terminated AZ Product, any AstraZeneca Other Patent Right, in each case ((A) and (B)), that includes at least one Valid Claim covering the composition of matter of such Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product, a pharmaceutical preparation comprising such Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product or a method of use of such Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product for the indication(s) for which Commercialization Regulatory Approval is obtained or that is otherwise capable of providing market exclusivity with respect to such Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product for the indication(s) for which such Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product has received Commercialization Regulatory Approval in such country.

11.4.3 **Other Applicable Terms**. During such period (if any) as Targacept is required to pay royalties to AstraZeneca pursuant to Section 11.4.2, the provisions of Sections 6.6.1(e) and 6.6.2 through 6.6.6 shall apply *mutatis mutandis* to the calculation, payment and recording of Targacept's obligations to pay royalties under this Section 11.4 as they apply to AstraZeneca pursuant to, and for such purpose each reference, in such Sections (a) to AstraZeneca shall be deemed to be to Targacept and vice versa and (b) to AZ Net Sales shall be deemed to be Targacept Net Sales.

11.4.4 **Third Party Payments**.

(a) Terminated Compounds. From and after the date on which each Terminated Compound becomes a Terminated Compound, Targacept shall be solely responsible for all (i) up-front fees (including any fees paid in installments) and milestones (including any royalties or other payments that are not tied to sales of a product containing a Terminated Compound (including any Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product)) payable to a Third Party in consideration for rights necessary or useful for the Exploitation of a Terminated Compound (including any Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product) or a product that contains such Terminated Compound and (ii) royalties (but excluding any royalties or other payments that are not tied to sales of a product containing a Terminated Compound (including any Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product)) payable to a Third Party in consideration for rights necessary or useful for the Exploitation of a Terminated Compound (including any Royalty-Bearing Product or Royalty-Bearing Terminated AZ Product) or a product that contains such Terminated Compound, in each case ((i) and (ii)), irrespective of the Party that has entered into the applicable agreement with, or first made a payment to, such Third Party). For purposes of clarity, Targacept shall not have any obligation under this Section to reimburse AstraZeneca for payments with respect to a Terminated Compound prior to the date such Terminated Compound becomes a Terminated Compound.

(b) Breach of Section 11.4.4(a). In the event AstraZeneca believes that Targacept is in breach of Section 11.4.4(a), it shall have the right to give Targacept written notice specifying the nature of the breach, requiring Targacept to make good or otherwise cure such breach, and stating its intention to terminate the licenses granted under Section 8.2.3, 11.3.1(d), 11.3.2(d), 11.3.3(d) or 11.3.4(d) or its obligations under Section 11.3.1(c), 11.3.6(c)(1), 11.3.6(c)(2), 11.3.6(d)(1) or 11.3.6(d)(2), as applicable to the Terminated Compound with respect to which the breach applies. If such breach is not cured within **[********]** after the date such notice is delivered (or, if such breach cannot be cured within such **[********]** period, if Targacept does not commence actions to cure such breach within the cure period and thereafter diligently continue such actions), AstraZeneca shall be entitled, without prejudice to any of its other rights conferred on it by this Agreement, to terminate such

applicable licenses or obligations. If Targacept shall dispute the existence, extent or nature of such breach, the matter shall be referred to the ESC and the ESC shall use good faith efforts to resolve the dispute. If the ESC cannot resolve the dispute within thirty (30) days after the ESC first meets to consider such matter (subject to Section 2.1.5, if applicable), it shall be resolved in accordance with Section 14.4 (expedited arbitration) and any time period related to such termination right, and termination, shall be tolled during any such ESC review and any arbitration proceeding.

(c) Partially-Terminated Products. From and after the date on which each Partially-Terminated Product becomes a Partially-Terminated Product, Targacept shall be solely responsible for all (i) up-front fees (including any fees paid in installments) and milestones (including any royalties or other payments that are not tied to sales of a product containing a Partially-Terminated Product) payable to a Third Party in consideration for rights necessary or useful for the Exploitation of a Partially-Terminated Product outside of such Partially-Terminated Product's Partially-Terminated Product Territory and (ii) royalties (but excluding any royalties or other payments that are not tied to sales of a Partially-Terminated Product) payable to a Third Party in consideration for rights necessary or useful for the Exploitation of a Partially-Terminated Product outside of such Partially-Terminated Product's Partially-Terminated Product Territory, in each case ((i) and (ii)), irrespective of the Party that has entered into the applicable agreement with, or made a prior payment to, such Third Party). For purposes of clarity, Targacept shall not have any obligation under this Section to reimburse AstraZeneca for payments with respect to a Partially-Terminated Product prior to the date such Partially-Terminated Product becomes a Partially-Terminated Product.

11.4.5 **Acknowledgment**. Targacept recognizes and acknowledges that each of the following, separately and together, has substantial economic benefit to Targacept: (i) the licenses granted to Targacept hereunder with respect to AstraZeneca Technology; (ii) the licenses granted to Targacept under Patent Rights Controlled by AstraZeneca; (iii) the restrictions on AstraZeneca pursuant to Section 8.6.3; and (iv) the exclusivity afforded to Targacept by each of the foregoing. The Parties agree that the royalty rates set forth in Section 11.4.1 reflect an efficient and reasonable blended allocation of the values provided by AstraZeneca to Targacept.

11.5 **Unauthorized Sales**.

11.5.1 Outside the Field and Schizophrenia. To the extent that Targacept has the right to Exploit products that contain Terminated Compound(s) outside the Field and Schizophrenia or outside the Field, as applicable, and to the extent permitted by law, Targacept, during the Term, (a) shall, and shall cause its Affiliates and Sublicensees to, market or promote only outside the Field and Schizophrenia or outside the Field, as applicable, and (b) shall not, and shall not permit its Affiliates and Sublicensees to, market or promote such product(s) directly or indirectly (i) to any Person in the Field or Schizophrenia or in the Field, as applicable, or (ii) to any Person that (A) is reasonably likely to directly or indirectly market or promote such product (or the Terminated Compound contained therein) for use in the Field or Schizophrenia or in the Field, as applicable, or assist another Person to do so, or (B) has directly or indirectly marketed or promoted such product (or the Terminated Compound contained therein) for use in the Field or Schizophrenia or in the Field, as applicable, or assisted another Person to do so.

11.5.2 Outside the Territory.

(a) With respect to each Partially-Terminated Product and to the extent permitted by law, AstraZeneca (i) shall, and shall cause its Affiliates and Sublicensees to, distribute, market, promote, offer for sale and sell such Partially-Terminated Product only in the applicable Partially-Terminated Product Territory with respect to such Partially-Terminated Product and (ii) shall not, and shall not permit its Affiliates and Sublicensees to, distribute, market, promote, offer for sale or sell such Partially-Terminated Product directly or indirectly (A) to any Person outside such Partially-Terminated Product Territory or (B) to any Person in such Partially-Terminated Product Territory that (1) is reasonably likely to directly or indirectly distribute, market, promote, offer for sale or sell such Partially-Terminated Product outside such Partially-Terminated Product Territory or assist another Person to do so or (2) has directly or indirectly distributed, marketed, promoted, offered for sale or sold the Partially-Terminated Product outside such Partially-Terminated Product Territory or assisted another Person to do so, except in each case ((i) and (ii)), to the extent AstraZeneca has retained such rights pursuant to Section 11.3.4(d).

(b) With respect to each Partially-Terminated Product and to the extent permitted by law, Targacept (i) shall, and shall cause its Affiliates and Sublicensees to, distribute, market, promote, offer for sale and sell such Partially-Terminated Product only in the applicable terminated Major Market Country(ies) with respect to such Partially-Terminated Product and (ii) shall not, and shall not permit its Affiliates and Sublicensees to, distribute, market, promote, offer for sale or sell such Partially-Terminated Product directly or indirectly (A) to any Person outside such terminated Major Market Country(ies) or (B) to any Person in such terminated Major Market Country(ies) that (1) is reasonably likely to directly or indirectly distribute, market, promote, offer for sale or sell such Partially-Terminated Product outside such terminated Major Market Country(ies) or assist another Person to do so or (2) has directly or indirectly distributed, marketed, promoted, offered for sale or sold such Partially-Terminated Product outside such terminated Major Market Country(ies) or assisted another Person to do so.

11.6 **Surviving Provisions**.

11.6.1 Accrued Rights. Termination or expiration of this Agreement (in its entirety or with respect to one or more Collaboration Compounds, Candidate Drugs or Products, or with respect to one or more Collaboration Compounds, Candidate Drugs or Products in one or more Major Market Countries) for any reason shall be without prejudice to any rights that shall have accrued to the benefit of a Party prior to such termination or expiration. Such termination or expiration shall not relieve a Party from obligations that are expressly indicated to survive the termination of expiration of this Agreement.

11.6.2 Surviving Provisions. Without limiting the foregoing, in addition to the provisions of this Agreement that survive termination pursuant to Section 11.3.1 through 11.3.5, expiration or termination of this Agreement (in its entirety or with respect to one or more Collaboration Compounds, Candidate Drugs or Products, or with respect to one or more Collaboration Compounds, Candidate Drugs or Products in one or more Major Market Countries) for any reason shall be without prejudice to:

(a) the rights and obligations of the Parties provided in Sections 4.5.1, 4.10, 4.11.1, 5.9.3, 5.12, 7.1.1, 7.1.2, 7.4, 7.5, 8.1.4, 8.1.5, 8.2.3, 8.2.4, 8.3 (to the extent the license grants in Section 8.1 and 8.2, as applicable, survive), 8.5, 8.9.1 (to the extent the license

grant in Section 8.1.3 survives), 9.1, 9.3, 11.3, 11.4 (to the extent incurred prior to expiration or earlier termination), 16.11 (to the extent relating to Materials delivered prior to expiration or termination) and 16.15 and Articles 6 (solely with respect to Section 6.4, to the extent costs and expenses are incurred prior to expiration or earlier termination), 13, 14 and 17 (other than Sections 17.14 and 17.15) (including, for purposes of interpreting any such Section or Article, all other Sections or Articles referenced in any such Section or Article and including Article 1), and this Section 11.6, all of which shall survive such termination or expiration;

(b) any other rights or remedies provided at law or equity that either Party may otherwise have.

12. REPRESENTATIONS AND WARRANTIES

12.1 **Mutual Representations and Warranties**. Targacept and AstraZeneca each represents and warrants to the other, as of the Execution Date, as follows:

12.1.1 **Organization**. It is a corporation duly organized, validly existing and in good standing under the laws of the jurisdiction of its organization, and has all requisite power and authority, corporate or otherwise, to execute, deliver and perform this Agreement.

12.1.2 **Authorization**. The execution and delivery of this Agreement and the performance by it of the transactions contemplated hereby have been duly authorized by all necessary corporate action and will not violate (a) such Party's certificate of incorporation or bylaws, (b) any agreement, instrument or contractual obligation to which such Party is bound in any material respect, (c) any requirement of any Applicable Laws, or (d) any order, writ, judgment, injunction, decree, determination or award of any court or governmental agency presently in effect applicable to such Party.

12.1.3 **Binding Agreement**. This Agreement is a legal, valid and binding obligation of such Party enforceable against it in accordance with its terms and conditions, subject to the effects of bankruptcy, insolvency or other laws of general application affecting the enforcement of creditor rights, to judicial principles affecting the availability of specific

performance and to general principles of equity, whether enforceability is considered a proceeding at law or equity.

12.1.4 **Consents**. Except as may be required pursuant to Section 17.14, all necessary consents, approvals and authorizations of all regulatory and governmental authorities and other Persons required to be obtained by it in connection with the execution and delivery of this Agreement and the performance of its obligations hereunder have been obtained.

12.1.5 **No Inconsistent Obligation**. It is not under any obligation, contractual or otherwise, to any Person that conflicts with or is inconsistent in any respect with the terms of this Agreement or that would impede the diligent and complete fulfillment of its obligations hereunder.

12.2 **Additional Representations of Targacept**. Targacept further represents, warrants to AstraZeneca, as of the Execution Date, and covenants as follows:

12.2.1 Except as set forth in Part A of Schedule 12.2, Targacept is the sole and exclusive owner of the entire right, title and interest in the Patent Rights listed on Schedule 12.2, Part A (the "**Owned Patent Rights**") and is entitled to grant the licenses specified herein. Except as provided in Part A of Schedule 12.2, such rights are not subject to any encumbrance, lien or claim of ownership by any Third Party. If any Patent Rights are listed on Part B of Schedule 12.2 (the "**In-Licensed Patent Rights**"), Targacept is the sole and exclusive licensee of and Controls all right, title and interest in and to such Patent Rights and is entitled to grant the licenses specified herein. There are no Targacept Patent Rights with respect to which Targacept is a non-exclusive licensee. Except as provided in Part B of Schedule 12.2, such rights, if any, are not subject to any encumbrance, lien or claim of ownership by, or any obligation, financial or otherwise, to, a Third Party. Targacept owns or has a license or other right to use all Targacept Other Technology and is entitled to grant the licenses thereto specified herein and has not granted rights to a Third Party under any Targacept Patent Rights or Targacept Other Technology that are inconsistent or conflict with the rights granted to AstraZeneca, or that would otherwise prevent or impair AstraZeneca from realizing its expected benefits under, this Agreement. True, complete and correct copies of the complete file wrapper and other documents and materials relating to the prosecution, defense, maintenance, validity and enforceability of the

Owned Patent Rights and the In-Licensed Patent Rights (if any) and all license agreements regarding, and other agreements relating to Targacept's Control of (including any financial or other obligations with respect thereto), the In-Licensed Targacept Patent Rights (if any) and the Targacept Other Technology (the "**In-License Agreements**"), as amended to the date hereof, have been provided or made available to AstraZeneca prior to the Execution Date (with financial terms redacted). AstraZeneca will not have any financial obligations under any In-License Agreement. The Owned Patent Rights and the In-Licensed Patent Rights (if any) constitute all of the Targacept Patent Rights other than Targacept Excluded Patent Rights. True, complete and correct copies of all other license and other agreements, if any, to which Targacept is a party that would impose any obligations on AstraZeneca's Exploitation in the Field or Schizophrenia of any Collaboration Candidates, Active+ Compounds, Collaboration Compounds, Candidate Drugs or Products have been provided to AstraZeneca at Targacept's offices in the due diligence data room in connection with AstraZeneca's due diligence prior to the Execution Date (each of which shall be deemed to be In-License Agreements). Each In-License Agreement is listed on Part C of Schedule 12.2. Targacept nor, to its Knowledge, any Third Party is in breach of any In-License Agreement and to the Knowledge of Targacept each In-License Agreement is in full force and effect.

12.2.2 To Targacept's Knowledge, the Targacept Patent Rights are being diligently prosecuted in the respective Patent Offices in accordance with all applicable laws and regulations. The Targacept Patent Rights have been filed and maintained properly and correctly in all material respects and all applicable fees have been paid on or before the deadline for payment.

12.2.3 To Targacept's Knowledge, no Person is infringing or threatening to infringe Targacept Patent Rights or misappropriating or threatening to misappropriate the Targacept Other Technology.

12.2.4 All Targacept Patent Rights are existing and, to the Knowledge of Targacept, no Targacept Patent Rights are invalid or unenforceable. Targacept has the right to enforce the Targacept Patent Rights. The conception, development and reduction to practice of Targacept Other Technology, including the research and development of Ispronicline and the

preparation of the Regulatory Filings, have not constituted or involved the misappropriation of trade secrets or other rights or property of any Person. There are no claims, judgments or settlements against, or amounts with respect thereto, owed by Targacept or any of its Affiliates relating to the Regulatory Filings, the Targacept Patent Rights or the Targacept Other Technology and to Targacept's Knowledge the conduct of the Research Program and AstraZeneca's Exploitation of Candidate Drugs and Products under this Agreement will not infringe the Patent Rights or other intellectual property rights of any Third Party. No claim or litigation has been brought or threatened by any Person alleging, and Targacept has no Knowledge of any claim, whether or not asserted, that (a) the Targacept Patent Rights are invalid or unenforceable or (b) the Regulatory Filings, the Targacept Patent Rights or the Targacept Other Technology or the disclosing, copying, making, assigning or licensing of the Regulatory Filings, the Targacept Patent Rights or the Targacept Other Technology, or Exploiting as set forth herein the products that are the subject of the Regulatory Filings or the Targacept Patent Rights or that otherwise comprise the Targacept Other Technology, including Ispronicline, violates, infringes or otherwise conflicts or interferes with any intellectual property or proprietary right of any Person. To Targacept's Knowledge, Targacept has the right to use all Technology, Proprietary Materials and Patent Rights necessary to conduct the Research Program and the Exploitation of any Collaboration Compound, Candidate Drug or Product will not be subject to any other license or agreement of Targacept or any of its Affiliates other than an In-License Agreement.

12.2.5 Targacept has not previously assigned, transferred, licensed, conveyed or otherwise encumbered its right, title or interest in or to the Targacept Patent Rights, Targacept Technology, Regulatory Filings or Ispronicline (including by granting any covenant not to sue with respect thereto) or any Patent Rights or Technology that would be Targacept Patent Rights or Targacept Technology but for such assignment, transfer, license, conveyance or encumbrance, except in each case where such assignment, transfer, license, conveyance or encumbrance is terminated and no longer in force or effect.

12.2.6 In respect of the pending United States patent applications included in the Targacept Patent Rights, Targacept has presented all relevant prior art of which it and, to its

Knowledge, the inventors have knowledge to the relevant Patent Examiner at the United States Patent and Trademark Office.

12.2.7 The Targacept Patent Rights listed on Part D of Schedule 12.2 represent all Patent Rights within Targacept's Control relating to Ispronicline and its Exploitation in or outside the Field.

12.2.8 The Targacept Other Technology that will, upon execution of this Agreement, be subject to the confidentiality obligations of AstraZeneca hereunder has been kept confidential or has been disclosed to Third Parties only under terms of confidentiality.

12.2.9 Targacept has provided to AstraZeneca at Targacept's offices in the due diligence data room in connection with AstraZeneca's due diligence prior to the Execution Date true, complete and correct copies of all Regulatory Filings and Targacept Other Technology and other information in its possession or Control regarding or related to Ispronicline. Targacept has prepared, maintained and retained all Regulatory Filings that are required to be maintained or reported pursuant to and in accordance with Applicable Laws and in accordance, in all material respects, with GLP and Good Clinical Practices.

12.2.10 Targacept has provided to AstraZeneca at Targacept's offices in the due diligence data room in connection with AstraZeneca's due diligence prior to the Execution Date all material adverse information with respect to the safety and efficacy of Ispronicline Known to Targacept.

12.2.11 No rights or licenses are required under Targacept Other Technology, Targacept Patent Rights or, to Targacept's Knowledge, under any Third Party Patent Rights or Third Party Technology for AstraZeneca or its Affiliates or Sublicensees to Exploit Ispronicline other than those granted under Section 8.1.

12.2.12 All works of authorship and all other materials subject to copyright protection included in Targacept Other Technology are original and were either created by Targacept employees within the scope of their employment or are otherwise works made for hire, or all right, title and interest in and to such materials have been legally and fully assigned and transferred to Targacept, and all rights in all inventions and discoveries, made, developed or

conceived by any employee or independent contractor of Targacept during the course of their employment (or other retention) by Targacept, and relating to or included in Targacept Other Technology or that are the subject of one or more Targacept Patent Rights have been or will be assigned in writing to Targacept.

12.2.13 Targacept has obtained the right (including under any Patent Rights and other intellectual property rights) to Exploit all Technology, Proprietary Materials and all other materials (including any formulations and manufacturing processes and procedures) developed or delivered by any Third Party under any agreements between Targacept and any such Third Party with respect to Ispronicline, and Targacept has the rights under each such agreement to transfer such Technology, Proprietary Materials or other materials to AstraZeneca and its designees and to grant AstraZeneca the right to use such Technology, Proprietary Materials and other materials in the manufacture and other Exploitation of Ispronicline and any Ispronicline Product without restriction.

12.2.14 All information, documentation and other materials furnished or made available by Targacept upon the request of AstraZeneca during AstraZeneca's period of diligence prior to the Execution Date or otherwise related to the Collaboration are true, complete and correct copies of what they purport to be.

12.2.15 Upon termination of the SMRI Agreement in accordance with Section 5.10.4, neither The Stanley Medical Research Institute nor any other Third Party will have any rights to, and Targacept does not have and will not have any obligations to The Stanley Medical Research Institute (or any obligations to any Third Party arising under the SMRI Agreement) with respect to, TC-1827 or any other Compounds. As of the Execution Date, Targacept has satisfied all of its debts and obligations under the note held by The Stanley Medical Research Institute in connection with the SMRI Agreement, which note has been cancelled and is of no further force and effect.

12.2.16 No Targacept Patent Rights or Targacept Other Technology is Controlled by Targacept under the **[********]**. All Targacept Patent Rights or Targacept Other Technology covered by the **[********]** have been validly assigned to Targacept and Targacept is the sole and exclusive owner of all right, title and interest therein.

12.2.17 **[********]** does not own or control, and Targacept does not license from **[********]**, in each case under the **[********]**, any (i) Patent Rights that are necessary or useful to Exploit Ispronicline (except as set forth on Schedule 12.2) or (ii) Technology or proprietary materials that are incorporated in or have been used in the Exploitation of Ispronicline.

12.2.18 **[********]**. In addition, (a) no Development Compounds, Back-Up Compounds or Licensed Products (as each such term is defined in the **[********]**) existed during the term of, or as of the termination of, the **[********]**, (b) neither **[********]** nor any of its Affiliates has any rights, and Targacept has no obligations, with respect to any Terminated Compounds (as such term is defined in the **[********]**) under or in connection with the **[********]** or the termination thereof and (c) Targacept did not object to any compounds pursuant to **[********]**. In addition, (x) no Materials or Confidential Information **[********]** (as each such term is defined in the **[********]**) shall be used under the Research Program, any Additional Research Program or otherwise in connection with this Agreement and (y) neither Aventis nor any of its Affiliates owns or controls any (i) Patent Rights that are necessary or useful to Exploit Ispronicline or (ii) Technology or proprietary materials that are incorporated in or have been used in the Exploitation of Ispronicline.

12.2.19 **[********]** and neither **[********]** nor any of its Affiliates has any rights, and Targacept has no obligations, under or in connection with **[********]** with respect to the Targacept Patent Rights or the Targacept Technology or any Compounds, including Ispronicline. In addition, (a) only **[********]** were designated under the **[********]** and there were and are no **[********]** and (b) no Materials or Confidential Information of **[********]**, including any **[********]** shall be used under the Research Program, any Additional Research Program or otherwise in connection with this Agreement.

12.2.20 None of the Licensed Products (as such term is defined in the **[********]** shall be used under the Research Program, any Additional Research Program, any Development Program or otherwise in connection with this Agreement.

12.2.21 This Agreement, and the transactions contemplated hereby, constitute an **[********]**, for purposes of the **[********]**.

12.2.22 The representations and warranties of Targacept in this Agreement, and the information, documents and materials furnished to AstraZeneca in connection with its period of diligence prior to the Execution Date of this Agreement, do not, taken as a whole, (a) contain any untrue statement of a material fact or (b) omit to state any material fact necessary to make the statements or facts contained therein, in light of the circumstances under which they were made, not misleading.

For purposes of clarity, all references to Targacept Other Technology or Regulatory Filings in this Section 12.2 shall mean Targacept Other Technology that is Targacept Other Technology, or Regulatory Filings that are Regulatory Filings, as of the Execution Date.

12.3 **Representations of Targacept with respect to Option Compound Candidate Drugs**. Together with any IND-Ready Notice or POC Notice with respect to an Option Compound, Targacept shall provide AstraZeneca with a written statement containing (a) any exceptions to the representations and warranties set forth in Section 12.2 (other than Sections 12.2.14 and 12.2.15 and, in the case of an IND-Ready Notice, all representations and warranties set forth in Section 12.2 to the extent relating to Regulatory Filings), then Known to Targacept as they relate specifically to such Option Compound, (b) a list of any Targacept Patent Rights covering such Option Compound, identified as Owned Patent Rights or In-Licensed Patent Rights, as applicable, and (c) a list of all license or other agreements to which Targacept or any of its Affiliates is a party and either by which Targacept Controls such Option Compound or that would impose any obligations, financial or otherwise, on AstraZeneca's Exploitation thereof, which shall be deemed to be In-License Agreements. Together with such statement, Targacept shall provide AstraZeneca with true, complete and correct copies of any such In-License Agreement to the extent not previously provided to AstraZeneca. If AstraZeneca designates an Option Compound as an Option Compound Candidate Drug, Targacept shall be deemed to have made each of the representations and warranties set forth in Section 12.2 (other than Sections 12.2.14 and 12.2.15 and, in the case of an IND-Ready Option Candidate Drug, all representations and warranties set forth in Section 12.2 to the extent relating to Regulatory Filings) with respect to such Option Compound Candidate Drug only, as of the date of the written statement delivered pursuant to the first sentence of this Section 12.3 (or, if AstraZeneca provided notice pursuant to

the last sentence of this Section 12.3, the date that AstraZeneca exercises such IND-Ready Option or POC Option), subject only to the exceptions set forth on Schedule 12.2 as of the Effective Date (as updated by each written statement provided pursuant to this Section 12.3 or pursuant to Section 12.4) and with any references in Section 12.2 to (i) the Execution Date or the Effective Date being instead to the date of such statement, (ii) Ispronicline being instead to such Option Compound, (iii) Targacept Patent Rights being instead to Targacept Patent Rights that contain one or more claims that cover such Option Compound or the Exploitation thereof, (iv) Targacept Other Technology being instead to Targacept Other Technology that is necessary or reasonably useful for AstraZeneca to Exploit such Option Compound, (v) In-License Agreement being instead to In-License Agreements relating to such Option Compound, (vi) Schedule 12.2 (or any Part thereof) being instead to such statement and (vii) Targacept being instead to Targacept and its Affiliates, if any. For purposes of clarity, this Section 12.3 applies only to each Option Compound for which Targacept provides AstraZeneca with an IND-Ready Notice or POC Notice, has no application to any other compound or product or any Patent Right, Technology or Regulatory Filing not addressed above and does not require any update, supplement to or superseding of any representation, warranty or covenant made by Targacept pursuant to Section 12.2. If AstraZeneca notifies Targacept in writing, with at least **[********]** advance notice, as to the date it intends (which notice shall not be binding on AstraZeneca) to exercise an IND-Ready Option or POC Option, Targacept shall update the written statement provided in accordance with the first sentence of this Section 12.3 as of such exercise date.

12.4 **Representations of Targacept with respect to Lead Collaboration Compounds**. Within **[********]** (or such greater number of days as the Parties may agree in writing) after the JRC designates a Lead Collaboration Compound or after delivery of written notice to Targacept by AstraZeneca that AstraZeneca has designated a Lead Collaboration Compound, Targacept shall provide AstraZeneca with a written statement containing (a) any exceptions to the representations and warranties set forth in Section 12.2 (other than Sections 12.2.14 and 12.2.15 and all representations and warranties set forth in Section 12.2 to the extent relating to Regulatory Filings), then Known to Targacept as they relate specifically to such Lead Collaboration Compound, (b) a list of any Targacept Patent Rights covering such Lead Collaboration Compound, identified as Owned Patent Rights or In-Licensed Patent Rights, as applicable, and (c) a list of all license or other agreements to which Targacept or any of its

Affiliates is a party and either by which Targacept Controls such Lead Collaboration Compound or that would impose any obligations, financial or otherwise, on AstraZeneca's Exploitation thereof, which shall be deemed to be In-License Agreements. Together with such statement, Targacept shall provide AstraZeneca with true, complete and correct copies of any such In-License Agreement to the extent not previously provided to AstraZeneca. Targacept shall be deemed to have made each of the representations and warranties set forth in Section 12.2 (other than Sections 12.2.14 and 12.2.15 and all representations and warranties set forth in Section 12.2 to the extent relating to Regulatory Filings) with respect to such Lead Collaboration Compound only, as of the date of the written statement delivered pursuant to the first sentence of this Section 12.4, subject only to the exceptions set forth on Schedule 12.2 as of the Effective Date (as updated by each statement provided pursuant to this Section 12.4 or pursuant to Section 12.3) and with any references in Section 12.2 to (i) the Execution Date or the Effective Date being instead to the date of such statement, (ii) Ispronicline being instead to such Lead Collaboration Compound, (iii) Targacept Patent Rights being instead to Targacept Patent Rights that contain one or more claims that cover such Lead Collaboration Compound or the Exploitation thereof, (iv) Targacept Other Technology being instead to Targacept Technology that is necessary or reasonably useful for AstraZeneca to Exploit such Lead Collaboration Compound, (v) In-License Agreement being instead to In-License Agreements relating to such Lead Collaboration Compound, (vi) Schedule 12.2 (or any Part thereof) being instead to such statement, (vii) Targacept being instead to Targacept and its Affiliates, if any and (viii) Technology, information, materials and agreements provided to AstraZeneca at Targacept's offices in a due diligence data room being instead to such Technology, information, materials and agreements furnished or made available to AstraZeneca prior to the date of such statement. For purposes of clarity, this Section 12.4 applies only to each Lead Collaboration Compound that is in the Collaboration Compound Pool as of the end of the Tail Period (or, if later, the resolution of any dispute pursuant to Section 4.3.2 or as provided in Section 4.9), has no application to any other compound or product or any Patent Right, Technology or Regulatory Filing not addressed above and does not require any update, supplement to or superseding of any representation, warranty or covenant made by Targacept pursuant to Section 12.2. If a Lead Collaboration Compound is designated as, or otherwise becomes, a Terminated Compound during the Research Program

Term or the Tail Period other than as a result of a breach by Targacept, any representations and warranties made by Targacept pursuant to this Section 12.4 shall cease to be effective.

12.5 **Consequences of a Material Breach of a Representation or Warranty**. Notwithstanding anything in this Agreement to the contrary, in the event of a material breach of a representation and warranty under this Article 12 by Targacept, such that the Exploitation of Candidate Drugs or Products by AstraZeneca, its Affiliates or any of their Sublicensees infringes or misappropriates any Patent Rights, trade secret or other intellectual property right of a Third Party in any country in the Territory, then Targacept shall, notwithstanding Sections 6.6.1(d)(2), 10.2.4 and 10.2.6, be solely responsible for any damages or liabilities of either Party or their respective Affiliates or Sublicensees with respect thereto, including the cost of litigation and any license fees, milestones or royalties under any license, settlement or other agreement with such Third Party resulting therefrom; provided, however, that if Targacept obtains a license from such Third Party as necessary for AstraZeneca and its Affiliates and Sublicensees to Exploit the Collaboration Compounds, Candidate Drugs and Products in such country, and fully indemnifies and holds harmless AstraZeneca for any such damages, liabilities, costs, license fees, milestones and royalties, AstraZeneca shall have no right to terminate this Agreement for breach of such representation and warranty under Section 11.2.4.

13. INDEMNIFICATION AND INSURANCE

13.1 **Indemnification of AstraZeneca by Targacept**. Targacept shall indemnify, defend and hold harmless AstraZeneca, its Affiliates, their respective directors, officers, employees and agents, and their respective successors, heirs and assigns (collectively, the "**AstraZeneca Indemnitees**"), against all liabilities, damages, losses, costs and expenses (including reasonable attorneys' fees and expenses of litigation) (collectively, "**Losses**") incurred by or imposed upon the AstraZeneca Indemnitees, or any one of them, as a direct result of claims, suits, actions, written demands or judgments of Third Parties, including personal injury and product liability claims and claims of suppliers and Targacept employees (collectively, "**Claims**") arising out of (a) any breach by Targacept of this Agreement, (b) any negligence or willful misconduct on the part of Targacept or its Affiliates, (c) the Exploitation, whether before or after termination of this Agreement and whether or not such Exploitation is permitted

hereunder, of any Terminated Compound or Option Compound (but for clarity, not with respect to any such Exploitation after such Option Compound has become an Option Compound Candidate Drug) by Targacept or any of its Affiliates, Sublicensees (other than AstraZeneca), distributors or agents, (d) the Ongoing Ispronicline Trial, or (e) the termination of the SMRI Agreement (or any surviving obligations thereunder), except in each case with respect to any Claim or Losses if and to the extent resulting from a breach of this Agreement or any Co-Promotion Agreement by, or the gross negligence or willful misconduct of, AstraZeneca or its Affiliates; provided that, with respect to any Claim for which Targacept has an obligation to any AstraZeneca Indemnitee pursuant to this Section 13.1 and AstraZeneca has an obligation to any Targacept Indemnitee pursuant to Section 13.2, each Party shall indemnify each of the other Party's Indemnitees for its Losses to the extent of its responsibility, relative to the other Party, for such Losses.

13.2 **Indemnification of Targacept by AstraZeneca**. AstraZeneca shall indemnify, defend and hold harmless Targacept, its Affiliates, their respective directors, officers, employees and agents, and their respective successors, heirs and assigns (the "**Targacept Indemnitees**"), against any Losses incurred by or imposed upon the Targacept Indemnitees, or any one of them, as a direct result of Claims arising out of (a) any breach by AstraZeneca of this Agreement, (b) any negligence or willful misconduct on the part of AstraZeneca or its Affiliates, (c) the Exploitation, whether before or after termination of this Agreement and whether or not such Exploitation is permitted hereunder, of any Collaboration Compound or Candidate Drug (after its designation as such) or Product by AstraZeneca or any of its Affiliates, Sublicensees, distributors or agents (other than Targacept), except in each case with respect to any Claim or Loss if and to the extent resulting from a breach of this Agreement or any Co-Promotion Agreement by, or the gross negligence or willful misconduct of, Targacept or its Affiliates; provided that with respect to any Claim for which Targacept has an obligation to any AstraZeneca Indemnitee pursuant to Section 13.1 and AstraZeneca has an obligation to any Targacept Indemnitee pursuant to this Section 13.2, each Party shall indemnify each of the other Party's Indemnitees for its Losses to the extent of its responsibility, relative to the other Party, for such Losses.

13.3 **Conditions to Indemnification**.

13.3.1 **Notice of Claim**. A Party seeking recovery under this Article 13 (the "**Indemnified Party**") in respect of any Losses incurred by it or, in the case of AstraZeneca, an AstraZeneca Indemnitee or, in the case of Targacept, a Targacept Indemnitee (in either case, the "**Indemnitees**"), shall give prompt notice of such Claim (an "**Indemnification Claim Notice**") to the Party from which recovery is sought (the "**Indemnifying Party**"), but in no event shall the Indemnifying Party be liable for any Losses to the extent resulting from any delay in providing such notice. Each Indemnification Claim Notice must contain a description of the claim and the nature and amount of such Loss (to the extent that the nature and amount of such Loss is known at such time). The Indemnified Party shall furnish promptly to the Indemnifying Party copies of all papers and official documents received in respect of any Losses. All indemnification claims in respect of a Party or its Indemnitees shall be made solely by such Party.

13.3.2 **Third Party Claims**. The obligations of an Indemnifying Party under this Article 13 with respect to Losses arising from Claims of any Third Party that are subject to indemnification as provided for in Section 13.1 or 13.2 (a "**Third Party Claim**") shall be governed by and be contingent upon the following additional terms and conditions:

(a) Control of Defense. At its option, the Indemnifying Party may assume the defense of any Third Party Claim by giving written notice to the Indemnified Party within thirty (30) days after the applicable Indemnification Claim Notice is delivered to the Indemnifying Party. The assumption of the defense of a Third Party Claim by the Indemnifying Party shall not be construed as an acknowledgment that the Indemnifying Party is liable to indemnify the Indemnified Party or any of its Indemnitees in respect of the Third Party Claim, nor shall it constitute a waiver by the Indemnifying Party of any defenses it may assert against the Indemnified Party's, or its Indemnitee's, claim for indemnification. Upon assuming the defense of a Third Party Claim, the Indemnifying Party may appoint as lead counsel in the defense of the Third Party Claim any legal counsel reasonably selected by the Indemnifying Party. In the event the Indemnifying Party assumes the defense of a Third Party Claim, the Indemnified Party shall immediately deliver to the Indemnifying Party all original notices and documents (including court papers) received by the Indemnified Party or any of its Indemnitees in connection with the Third Party Claim. Should the Indemnifying Party assume the defense of a Third Party Claim, except as provided in Section 13.3.2(b), the Indemnifying Party shall not be

liable to the Indemnified Party or any of its Indemnitees for any legal expenses subsequently incurred by such Indemnified Party or Indemnitee(s) in connection with the analysis, defense or settlement of the Third Party Claim. In the event that it is judicially determined (in a final, non-appealable decision) or otherwise agreed by the Parties, that the Indemnifying Party is not obligated to indemnify, defend or hold harmless an Indemnified Party or any of its Indemnitee(s) from and against the Third Party Claim, the Indemnified Party shall reimburse the Indemnifying Party for any and all actual costs and expenses (including reasonable attorneys' fees and costs of suit) and any Losses actually paid by the Indemnifying Party in its defense of the Third Party Claim with respect to such Indemnified Party or such Indemnitee(s).

(b) Right to Participate in Defense. Without limiting Section 13.3.2(a), the Indemnified Party or its Indemnitee shall be entitled to participate in, but not control, the defense of such Third Party Claim and to employ counsel of its choice for such purpose; provided, however, that such employment shall be at the Indemnified Party's, or its Indemnitee's own expense unless (i) the employment thereof has been specifically authorized by the Indemnifying Party in writing, (ii) the Indemnifying Party has failed to assume the defense and employ counsel in accordance with Section 13.3.2(a) (in which case the Indemnified Party shall control the defense) or (iii) the named parties to such Third Party Claim include both the Indemnifying Party and the Indemnified Party and the Indemnified Party reasonably concludes, based on advice from counsel, that the Indemnifying Party and the Indemnified Party have conflicting interests with respect to such Third Party Claim.

(c) Settlement. With respect to any Losses relating solely to the payment of money damages in connection with a Third Party Claim and that will not result in the Indemnified Party or its Indemnitee becoming subject to injunctive or other relief or would not otherwise reasonably be expected to adversely affect the business of the Indemnified Party or its Indemnitee in any manner, and as to which the Indemnifying Party shall have acknowledged in writing the obligation to indemnify the Indemnified Party hereunder, the Indemnifying Party shall have the sole right to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Loss, on such terms as the Indemnifying Party, in its sole discretion, shall deem appropriate. With respect to all other Losses in connection with Third Party Claims, where the Indemnifying Party has assumed the defense of the Third Party Claim in accordance

with Section 13.3.2(a), the Indemnifying Party shall have authority to consent to the entry of any judgment, enter into any settlement or otherwise dispose of such Loss provided it obtains the prior written consent of the Indemnified Party (which consent shall not be unreasonably withheld, conditioned or delayed). The Indemnifying Party shall not be liable for any settlement or other disposition of a Loss by the Indemnified Party or any of its Indemnitees that is reached without the written consent of the Indemnifying Party. Regardless of whether the Indemnifying Party chooses to defend or prosecute any Third Party Claim, neither the Indemnified Party or its Indemnitees shall admit any liability with respect to, or settle, compromise or discharge (other than as a result of a court-imposed judgment), any Third Party Claim without the prior written consent of the Indemnifying Party.

(d) Cooperation. Regardless of whether the Indemnifying Party chooses to defend any Third Party Claim, the Indemnified Party shall, and shall cause each of its Indemnitees, to cooperate in the defense or prosecution thereof and shall furnish such records, information and testimony, provide such witnesses and attend such conferences, discovery proceedings, hearings, trials and appeals as may be reasonably requested in connection therewith. Such cooperation shall include access during normal business hours afforded to Indemnifying Party to, and reasonable retention by the Indemnified Party of, records and information that would reasonably be expected to be relevant to such Third Party Claim or its defense, and making the Indemnified Party and its Indemnitees and other employees and agents available on a mutually convenient basis to provide additional information and explanation of any material provided hereunder, and the Indemnifying Party shall reimburse the Indemnified Party for all its reasonable out-of-pocket expenses in connection therewith.

13.4 **Insurance**.

13.4.1 **General**. AstraZeneca and Targacept shall have and maintain such type and amounts of liability insurance covering the manufacture, supply, use and sale of the Products or Terminated Products as is normal and customary in the pharmaceutical industry generally, in each case for a similarly situated party.

13.4.2 **Targacept**. Notwithstanding Section 13.4.1, at a minimum, Targacept shall maintain (a) commercial general liability insurance covering bodily injury and third party

property damage with minimum limits of One Million Dollars (US $1,000,000) per occurrence and Two Million Dollars (US $2,000,000) general aggregate and (b) products liability/completed operations coverage with minimum limits of Ten Million Dollars (US $10,000,000) each occurrence and Ten Million Dollars (US $10,000,000) general aggregate (provided that AstraZeneca acknowledges that, as of the Execution Date, Targacept maintains products liability/completed operations coverage with minimum limits of Eight Million Dollars (US $8,000,000) per occurrence and general aggregate and agrees that, notwithstanding the foregoing, Targacept shall not be required to obtain any additional coverage until such policies are due for renewal) or, if Targacept has received Commercialization Regulatory Approval for, and is Commercializing, a Terminated Compound, Twenty Million Dollars (US $20,000,000) per occurrence and Fifty Million Dollars (US $50,000,000) general aggregate. Each of the above policies of insurance (x) shall cover claims arising out of Targacept's performance of this Agreement that are made within a period of at least **[********]** after the Term and claims arising out of Targacept's Exploitation of any Royalty-Bearing Terminated Compound or Royalty-Bearing Terminated AZ Product that are made within a period of at least **[********]** after the end of any such period in which Targacept is Exploiting any such Royalty-Bearing Terminated Compound or Royalty-Bearing Terminated AZ Product, and (y) shall be primary to any liability insurance carried by AstraZeneca, which insurance shall be excess and non-contributory for claims and losses arising out of Targacept's performance of this Agreement. The general and product liability policies shall be specifically endorsed to list AstraZeneca as an additional insured. In addition, Targacept shall maintain worker's compensation insurance as required by all applicable laws and employers liability coverage of not less than Five Hundred Thousand Dollars (US $500,000). Prior to the Effective Date and upon each renewal or replacement of a policy and at such times as AstraZeneca may reasonably request in writing, Targacept shall provide AstraZeneca with a certificate of insurance evidencing the insurance coverage required under this Section 13.4.2, which certificate shall provide at least **[********]** notice of cancellation or termination of such insurance coverage. Such policies shall remain in effect throughout the Term and for **[********]** thereafter and throughout any period during which Targacept is Exploiting any Royalty-Bearing Terminated Compound or Royalty-Bearing Terminated AZ Product and for **[********]** thereafter, and shall not be canceled, if not replaced, without the prior written authorization of AstraZeneca. Maintenance of such insurance coverage

shall not relieve Targacept of any responsibility under this Agreement for damages in excess of insurance limits or otherwise. This Section 13.4.2 shall apply during the Term and for [********] thereafter, and thereafter shall continue to apply during any period in which Targacept is Exploiting any Royalty-Bearing Terminated Compound or Royalty-Bearing Terminated AZ Product and for [********] thereafter.

13.5 **Warranty Disclaimer**. EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN THIS AGREEMENT (INCLUDING SECTION 16.13), NEITHER PARTY MAKES ANY WARRANTY WITH RESPECT TO ANY TECHNOLOGY, GOODS, SERVICES, RIGHTS OR OTHER SUBJECT MATTER OF THIS AGREEMENT AND EACH PARTY HEREBY DISCLAIMS ALL WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE AND NONINFRINGEMENT.

13.5.1 **No Warranty of Success**. Nothing contained in this Agreement shall be construed as a warranty on the part of either Party that (a) the Research Program or any Additional Research Program will yield any Collaboration Compound or Candidate Drug or otherwise be successful, (b) any Development Program will yield a Product or otherwise be successful or (c) the outcome of the Research Program, any Additional Research Program or any Development Program will be commercially exploitable in any respect. In addition, nothing contained in this Agreement shall be construed as a warranty on the part of Targacept that it will provide any Option Compounds or ROFN Indication Opportunities to AstraZeneca.

13.6 **Limited Liability**. NOTWITHSTANDING ANYTHING TO THE CONTRARY IN THIS AGREEMENT (BUT WITHOUT LIMITING THE PARTIES' RIGHTS UNDER SECTIONS 13.1, 13.2 AND 13.3), NEITHER PARTY SHALL BE LIABLE TO THE OTHER PARTY OR ANY OF ITS AFFILIATES FOR (I) ANY SPECIAL, PUNITIVE, INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES, INCLUDING LOST PROFITS OR LOST REVENUES, OR (II) EXCEPT WITH RESPECT TO TARGACEPT'S OBLIGATIONS UNDER ARTICLE 16 AND ASTRAZENECA'S OBLIGATIONS UNDER SECTION 11.3.6(d), COST OF PROCUREMENT OF SUBSTITUTE GOODS, TECHNOLOGY OR SERVICES, WHETHER UNDER ANY CONTRACT, WARRANTY, NEGLIGENCE, STRICT LIABILITY OR OTHER LEGAL OR EQUITABLE THEORY.

14. DISPUTE RESOLUTION

14.1 **Arbitration**. In the event of any dispute, difference or question arising between the Parties in connection with this Agreement, the construction thereof, or the rights, duties or liabilities of either Party hereunder (including any Disputed Matter with respect to an Excepted Decision that is submitted for arbitration as provided in Section 2.1.5) (each, an "**Arbitration Matter**"), the arbitration proceeding shall be conducted in accordance with the Commercial Arbitration Rules and Supplementary Procedures for Large Complex Disputes of the AAA and otherwise as described in this Article 14.

14.2 **Full Arbitration**. Unless Section 14.3 or 14.4 is applicable, the following procedures shall apply:

14.2.1 The arbitration shall be conducted by a panel of three (3) persons experienced in the pharmaceutical business who are independent of both Parties and conflict-free. Within thirty (30) days after initiation of arbitration, each Party shall select one person to act as arbitrator and the two Party-selected arbitrators shall select a third arbitrator within thirty (30) days of their appointment. If the arbitrators selected by the Parties are unable or fail to agree upon the third arbitrator, the third arbitrator shall be appointed by the AAA. The place of arbitration shall be **[********]**, and all proceedings and communications shall be in English.

14.2.2 Either Party may apply to the arbitrators for interim injunctive relief until the arbitration decision is rendered or the Arbitration Matter is otherwise resolved. Either Party also may, without waiving any right or remedy under this Agreement, seek from any court having jurisdiction any injunctive or provisional relief necessary to protect the rights or property of that Party pending resolution of the Arbitration Matter pursuant to this Section 14.2. The arbitrators shall have no authority to award punitive or any other type of damages not measured by a Party's compensatory damages. Each Party shall bear its own costs and expenses and attorneys' fees, and the Party that does not prevail in the arbitration proceeding shall pay the arbitrators' fees and any administrative fees of arbitration.

14.2.3 Except to the extent necessary to confirm an award or decision or as may be required by Applicable Laws, neither a Party nor an arbitrator may disclose the existence,

content, or results of an arbitration without the prior written consent of both Parties. In no event shall an arbitration be initiated after the date when commencement of a legal or equitable proceeding based on the Arbitration Matter would be barred by the applicable New York statute of limitations.

14.2.4 The Parties agree that, in the event of an Arbitration Matter involving the alleged breach of this Agreement (including whether a Party has satisfied its diligence obligations hereunder) or AstraZeneca's failure to meet the Terminated Efforts Test, neither Party may terminate this Agreement under Section 11.2.4 or 11.2.5 (or, if Targacept is alleging a failure by AstraZeneca to meet the Terminated Efforts Test under Section 11.2.7, take action under Section 11.2.7) and AstraZeneca may not terminate the Research Program under Section 11.2.2(b) until resolution of the Arbitration Matter pursuant to this Section 14.2.

14.2.5 The Parties hereby agree that any disputed performance or suspended performance pending the resolution of an Arbitration Matter that the arbitrators determine to be required to be performed by a Party must be completed within a reasonable time period following the final decision of the arbitrators.

14.2.6 The Parties hereby agree that any monetary payment to be made by a Party pursuant to a decision of the arbitrators shall be made in United States dollars, free of any tax or other deduction. The Parties further agree that the decision of the arbitrators shall be the sole, exclusive and binding remedy between them regarding determination of Arbitration Matters presented.

14.3 **Accelerated Arbitration**. To the extent the Arbitration Matter involves an Excepted Decision that is submitted to arbitration by a Party under Section 2.1.5(c), (d), (e) or (f) or any other matter that is expressly referred to accelerated arbitration elsewhere in this Agreement, the following procedures shall apply:

14.3.1 The Parties shall mutually select a single independent, conflict-free arbitrator (the "**Expert**"), who shall have sufficient scientific background and experience to resolve the Arbitration Matter. If the Parties are unable to reach agreement on the selection of an Expert within fifteen (15) Business Days after submission to arbitration, then either or both

Parties shall immediately request the AAA of **[********]** to select an arbitrator with the requisite scientific background, experience and expertise (which arbitrator shall also be deemed the Expert for purposes of this Section 14.3). The place of arbitration shall be **[********]**, and all proceedings and communications shall be in English.

14.3.2 Each Party shall prepare and submit a written summary of such Party's position and any relevant evidence in support thereof to the Expert within **[********]** of the selection of the Expert. Upon receipt of such summaries from each Party, the Expert shall provide copies of the same to the other Party. Within **[********]** of the delivery of such summaries by the Expert, each Party shall submit a written rebuttal of the other Party's summary and may also amend and re-submit its original summary. Oral presentations shall not be permitted unless otherwise requested by the Expert. The Expert shall make a final decision with respect to the Arbitration Matter within **[********]** following receipt of the last of such rebuttal statements submitted by the Parties.

14.3.3 Either Party may apply to the Expert for interim injunctive relief until the arbitration decision is rendered or the Arbitration Matter is otherwise resolved. Either Party also may, without waiving any right or remedy under this Agreement, seek from any court having jurisdiction any injunctive or provisional relief necessary to protect the rights or property of that Party pending resolution of the Arbitration Matter pursuant to this Section 14.3. Each Party shall bear its own costs and expenses and attorneys' fees, and the Party that does not prevail in the arbitration proceeding shall pay the Expert's fees and any administrative fees of arbitration.

14.3.4 Except to the extent necessary to confirm an award or decision or as may be required by Applicable Laws, neither Party may, and the Parties shall instruct the Expert not to, disclose the existence, content, or results of an arbitration without the prior written consent of both Parties. In no event shall an arbitration be initiated after the date when commencement of a legal or equitable proceeding based on the Arbitration Matter would be barred by the applicable New York statute of limitations.

14.3.5 The Parties hereby agree that, with respect to a disputed milestone event, if the Expert determines that the milestone event has in fact occurred, AstraZeneca shall make the applicable milestone payment within **[********]** of the Expert's determination.

14.3.6 The Parties hereby agree that any payment to be made by a Party pursuant to a decision of the Expert shall be made in United States dollars, free of any tax or other deduction. The Parties further agree that, subject to Sections 5.10.2(e)(2) and 5.10.2(e)(3), the decision of the Expert shall be the sole, exclusive and binding remedy between them regarding determination of the Arbitration Matters presented.

14.4 **Expedited Arbitration**. To the extent the Arbitration Matter involves a dispute that any provision of this Agreement provides to be referred for expedited arbitration pursuant to Section 14.4, the procedures set forth in Section 14.3 shall apply except that the Expert shall make a determination by selecting the resolution proposed by one of the Parties that as a whole is the most fair and reasonable to the Parties in light of the totality of the circumstances and shall provide the Parties with a written statement setting forth the basis of the determination in connection therewith. For purposes of clarity, the Expert shall only have the right to select a resolution proposed by one of the Parties in its entirety and without modification.

15. CHANGE OF CONTROL

15.1 **Targacept Change of Control**.

15.1.1 **Notice**. If Targacept enters into an agreement that results or, if the transaction contemplated thereby is completed, would result, in a Change of Control, Targacept shall provide AstraZeneca with prompt written notice describing such Change of Control in reasonable detail (the "**Targacept Change of Control Notice**"). The Targacept Change of Control Notice shall be provided by Targacept prior to execution of such agreement, if permitted under Applicable Laws and not prohibited by the terms of any written agreement between Targacept and any Third Party, and otherwise as soon as practicable thereafter and, in any event, not later than promptly following the consummation of the transaction contemplated by such agreement.

15.1.2 **Change of Control Involving Competitive Entity or Competitive Program that is Outside the Collaboration**. If the Change of Control that is described in the Targacept Change of Control Notice results or, if completed, would result in a Competitive Entity merging with or becoming an Affiliate of Targacept, or involves a Third Party that has a

Competitive Program that Targacept elects to continue outside the Collaboration as provided in Section 15.1.3(a), then unless otherwise agreed by in writing AstraZeneca the following shall apply:

(a) Research Program and JRC. If the Targacept Change of Control Notice is delivered prior to expiration of the Research Program Term, AstraZeneca may elect, by giving written notice to Targacept within one (1) year after the later of the date the Targacept Change of Control Notice is delivered to AstraZeneca and the consummation of the Change of Control transaction (the "**Election Period**"), to terminate the Research Program, which shall be treated in the same manner as a termination of the Research Program pursuant to Section 11.2.2(b), or the Agreement, which shall be deemed to be a termination of the Agreement pursuant to Section 11.2.3. If AstraZeneca does not terminate the Research Program, it may thereafter amend the Research Plan or any Annual Research Plan (including AstraZeneca's obligation to fund all or part of the FTEs pursuant to Section 6.4) and can undertake any research activities previously allocated to Targacept in the Research Plan or any Annual Research Plan, in its sole discretion, with any such activities being AstraZeneca Research Activities. From and after the Change of Control, if the JRC is unable to agree on any matter properly before the JRC, AstraZeneca shall be entitled to resolve such dispute in the JRC without referring such dispute to the ESC, except that AstraZeneca shall not be entitled to resolve any Excepted Decision (i) that involves the approval of an Annual Research Plan or of an amendment to the Research Plan or any Annual Research Plan to amend the criteria for Minimum Binding Affinity or the Active+ Criteria or (ii) described in Section 2.1.5(b)).

(b) Development Program. AstraZeneca may elect, by delivering written notice to Targacept within the Election Period, to terminate Targacept's participation in any Development Program pursuant to Article 4 (including Targacept's right to participate in the JDC, CCC and ESC which committees shall, if AstraZeneca elects, in its sole discretion, be disbanded). Any dispute arising in the JDC, CCC or ESC shall be resolved by **[********]** in such committee and, if AstraZeneca elects to disband any of the JDC, CCC or ESC, any activities and decisions which would otherwise have been performed or made by such committee shall be performed or made by AstraZeneca acting unilaterally, in each case, except with respect

to any dispute or decision that would have been an Excepted Decision pursuant to Section 2.1.5(b), (c), (d), (e) or (f).

(c) Co-Promotion. AstraZeneca may elect, by delivering written notice to Targacept within the Election Period, to terminate Targacept's rights under Section 5.11 with respect to any Co-Promotion Opportunity or Co-Promotion Option that has already been executed and any agreement with respect thereto, including a Co-Promotion Agreement. AstraZeneca shall not have any obligation to offer any new Co-Promotion Opportunities or Co-Promotion Options to Targacept under Section 5.11.

(d) Reporting Obligations. AstraZeneca shall have no obligations to provide information or reports, or to participate in meeting with Targacept with respect to the Development and Commercialization of Candidate Drugs and Products under this Agreement, including under Section 5.9, except to provide royalty reports as provided in Section 6.6.1(e).

(e) Options. With respect to any Option Compound which is subject to an Option Compound Development Plan at the date of the Targacept Change of Control, AstraZeneca may elect, by delivering written notice to Targacept within the Election Period, to treat such Targacept Change of Control in the same manner as a breach of the Option Compound Development Plan under Section 5.10.2(b)(4), provided that (i) notwithstanding Section 5.10.2(b)(5), the milestones, royalties and other payments with respect to such Option Compound shall be referred to expedited arbitration as provided in Section 5.10.2(e), even if such Option Compound achieves Option Compound Proof of Concept, for the arbitrator to consider downward adjustments in such payments to reflect not only any failure of such Option Compound to Achieve Proof of Concept, but the additional funds and risk that AstraZeneca incurred in determining whether such Option Compound achieved Option Compound Proof of Concept (as opposed to what it would have incurred (i.e., no funds beyond the Option Maintenance Fee) had Targacept completed such activities (without any fault attributed to either Party) and (ii) for purposes of clarity, in no event shall this Agreement be deemed breached solely as a result of an election by AstraZeneca pursuant to this Section 15.1.2(e) as a result of such Change of Control; provided that the terms of this Agreement (including Section 8.6) shall continue to apply to Targacept and Targacept's acquiror or successor in the Change of Control.

Notwithstanding Section 5.10.2(e)(3) and (4), Targacept shall be required to accept the decision of the Expert, even if the AZ Proposal prevails.

In each case, other than as expressly set forth in the applicable subsection ((a) through (e)) of this Section 15.1.2, this Agreement shall remain in full force and effect in all respects (including with respect to AstraZeneca's rights under Section 5.10.2 and the Parties' rights under Article 11).

15.1.3 **Change of Control Involving Competitive Program**. If the Change of Control that is described in the Targacept Change of Control Notice involves a Third Party that is not a Competitive Entity but that has a Competitive Program, then (a) Targacept shall have the right, on written notice to AstraZeneca within **[********]** after the Change of Control, to elect to continue such program outside of the Collaboration, in which case such Change of Control shall be subject to Section 15.1.2 and, notwithstanding Section 8.6, the existence and continuation of such Competitive Program in any respect following the Change of Control shall not be deemed to be a breach of this Agreement, and (b) if Targacept does not provide such notice within such **[********]** period, any such Competitive Program shall be and remain subject to this Agreement, including Section 8.6.

15.2 **AstraZeneca Change of Control**.

15.2.1 **Notice**. If AstraZeneca or any of its Affiliates merges or consolidates with, is otherwise acquired by, or acquires, a Third Party (including through a Change of Control), after the Execution Date and during the Term, AstraZeneca shall provide Targacept with prompt written notice describing such merger, consolidation or acquisition (or other Change of Control) in reasonable detail (the "**AstraZeneca Change of Control Notice**"). The AstraZeneca Change of Control Notice shall be provided by AstraZeneca prior to execution of any operative agreement, if permitted under Applicable Laws and not prohibited by the terms of any agreement between AstraZeneca and any Third Party, and otherwise as soon as practicable thereafter and, in any event, not later than promptly following the consummation of the transaction contemplated by such agreement.

15.2.2 **Change of Control Involving Competitive Program**. If the merger, consolidation or acquisition (or other Change of Control) that is described in the AstraZeneca

Change of Control Notice involves a Third Party that has a Competitive Program, then, notwithstanding any provision hereof, the existence and continuation of such Competitive Program in any respect following such merger, consolidation or acquisition (or other Change of Control) shall not be deemed to be a breach of this Agreement or result in any termination or limitation of any of Targacept's exclusivity obligations under Sections 8.6.1 and 8.6.2, provided that, unless the Parties agree otherwise in writing, AstraZeneca shall, within **[********]** after the date of the merger, consolidation or acquisition (or other Change of Control), notify Targacept whether it intends to: (x) cease, or cause its relevant Affiliate to cease, the Competitive Program; (y) divest, or cause its relevant Affiliate to divest, whether by license or otherwise, the Competitive Program; or (z) terminate this Agreement pursuant to Section 11.2.3.

(a) If AstraZeneca notifies Targacept in writing within such **[********]** period that it intends to cease, or cause its relevant Affiliate or its acquiror or acquiree (as applicable) to cease the Competitive Program, AstraZeneca or its Affiliate, acquiror or acquiree, as the case may be, shall (i) promptly cease the Competitive Program with due regard for patient safety and the rights of any subjects that are participants in any clinical studies or post-approval studies relating to the Competitive Program and Applicable Laws; and (ii) keep Targacept reasonably informed of its efforts and progress in effecting such cessation of activities and shall provide a written summary of such efforts to Targacept each Calendar Quarter until completed.

(b) If AstraZeneca notifies Targacept in writing within such **[********]** period that it intends to divest such Competitive Program, AstraZeneca or its Affiliate, acquiror or acquiree (as the case may be) shall use reasonable efforts to effect such divestiture as quickly as possible and shall keep Targacept reasonably informed of its efforts and progress in effecting such divestiture and shall provide a written summary of such efforts each Calendar Quarter until completed. If AstraZeneca or its Affiliate, acquiror or acquiree effects such divestiture by way of one or more sublicenses, the licensor shall be entitled to receive license fees, milestones and royalties on sales of any products developed pursuant to the Competitive Program so divested, provided that neither AstraZeneca nor any of its Affiliates (or its acquiror or acquiree, as applicable) funds or continues to conduct any development or commercialization of such products. For purposes of clarity, such retained financial interest

shall not be deemed to be a "relevant factor" (but the existence or continuation by the acquiror of the Competitive Program shall continue to be deemed to be a "relevant factor") for purposes of determining AstraZeneca's Commercially Reasonable Efforts obligations under this Agreement. In addition, such licensor shall have the right to take back rights to such product if the licensee materially breaches its obligations under its license agreement with AstraZeneca or its Affiliate, acquiror or acquiree, in which event such product, if it continues to be a Competitive Program, shall again become subject to the terms of this Section 15.2.2. If, notwithstanding such reasonable efforts, AstraZeneca is not able to effect such a divestiture, it shall have the right to cease such Competitive Program as provided in Section 15.2.2(a).

If AstraZeneca fails to provide the notice under this Section 15.2.2 within such **[********]** period, or having provided such notice, fails to carry out the designated actions, subject to Sections 15.2.2(a) and 15.2.2(b), then, unless the Parties agree otherwise, AstraZeneca shall be deemed to be in breach of its exclusivity obligations under Section 8.6.3, if applicable, and **[********]** shall, if applicable, be limited or terminated as provided therein (provided that for purposes of this Section 15.2.2, the filing of a Drug Approval Application or the commercial sale of (i) an Alpha4Beta2 Agonist that is not a Collaboration Compound, Candidate Drug or Product in the Field or in Schizophrenia, or (ii) a Secondary Pharmacology Compound or an Other NNR Compound in the Field or, prior to the Schizophrenia Expiration Date, in Schizophrenia, in each case ((i) and (ii)), shall be deemed to be Initiation of a Clinical Trial for purposes of Section 8.6.1(a) or (b), as applicable) and Targacept shall thereafter have no further obligations under Section 5.10.3; provided, however, that, notwithstanding anything in this Agreement to the contrary, in no event shall a determination that AstraZeneca has breached its exclusivity obligations as a result of a merger, consolidation or acquisition (or other Change of Control) with a Third Party that has a Competitive Program give rise to a right to terminate this Agreement and the exclusive right and remedy available to Targacept with respect to such breach shall be as provided in this Section 15.2.2, provided that during the period in which the obligations set forth in Section 8.6.3 are in force, if AstraZeneca or any of its Affiliates merges or consolidates with, is otherwise acquired by, or acquires, a Third Party (including through a Change of Control) that has a Competitive Program, and AstraZeneca does not cease or divest such Competitive Program as provided in Section 15.2.2(a) or 15.2.2(b), then, solely with respect to the Development of any Candidate Drug or Product, and without expanding AstraZeneca's obligations under Section

5.5.1, the effect of diverting effort or resources to such Candidate Drug or Product on such Competitive Program shall not be taken into account when determining whether AstraZeneca is exercising Commercially Reasonable Efforts with respect to such Development as and if required under Section 5.5.1.

16. MATERIAL SUPPLY

16.1 **Supplies of Ispronicline Capsules**.

16.1.1 Subject to the terms and conditions of this Article 16, except as set forth in Section 16.7, Targacept shall supply to AstraZeneca, and AstraZeneca shall purchase from Targacept, all of the Ispronicline Capsules and capsule placebos required by AstraZeneca to conduct the Pre-Phase IIb Program in accordance with the Pre-Phase IIb Plan and any Development Program prior to and including Achievement of Proof of Concept with respect to Ispronicline in accordance with the applicable Product Development Plan.

16.1.2 Subject to the terms and conditions of this Article 16, Targacept shall supply to AstraZeneca such quantities of Ispronicline Capsules (including such dosage strengths) and capsule placebos, in each case as AstraZeneca from time to time may order from Targacept; provided that in no event shall Targacept be required to supply a quantity of Ispronicline Capsules or capsule placebos in excess of (a) (i) **[********]** Ispronicline Capsules, (ii) **[********]** Ispronicline Capsules, (iii) **[********]** Ispronicline Capsules, and (iv) **[********]** placebos, less (b) in each case, the quantities thereof supplied to AstraZeneca pursuant to Section 16.1.1 and quantities required for scheduled stability testing and other customary holdbacks.

16.2 **Supplies of Bulk Ispronicline API**. Subject to the terms and conditions of this Article 16, Targacept shall supply to AstraZeneca such quantities of Ispronicline API in bulk form as AstraZeneca from time to time may order from Targacept; provided that in no event shall Targacept be required to supply a quantity of Ispronicline API in excess of **[********]**thereof.

16.3 **Inventory of Ispronicline Capsules and API**. Targacept represents and warrants to AstraZeneca that, as of the Effective Date, Targacept owns (a) **[********]**

Ispronicline Capsules, (b) 1**[********]** Ispronicline Capsules, (c) **[********]** Ispronicline Capsules, (d) **[********]** capsule placebos, and (e) **[********]** of Ispronicline API.

16.4 **Supplies of Active+ Compounds and Collaboration Candidates**. Subject to the terms and conditions of this Article 16, Targacept shall supply to AstraZeneca such quantities of each Active+ Compound and Collaboration Candidate (but excluding Active+ Compounds and Collaboration Candidates that have become Collaboration Compounds, Candidate Drugs or Terminated Compounds and excluding Collaboration Candidates that are Licensed Derivatives made by or on behalf of AstraZeneca) as AstraZeneca from time to time may order from Targacept during the Research Term or Tail Period to conduct AstraZeneca Research Activities.

16.5 **Supplies of [********] Option Compounds and IND-Ready Option Candidate Drugs**. Subject to the terms and conditions of this Article 16, Targacept shall supply to AstraZeneca such quantities of (a) each **[********]** as may be necessary for AstraZeneca to conduct, or have conducted, any **[********]**; (b) each Option Compound that is the subject of an Option Compound Development Plan that AstraZeneca has elected to complete pursuant to Section 5.10.2(b)(5) and (c) each IND-Ready Option Candidate Drug, in each case ((a), (b) and (c)), as AstraZeneca from time to time may order from Targacept.

16.6 **Supplies of POC Option Candidate Drugs**. Subject to the terms and conditions of this Article 16, Targacept shall supply to AstraZeneca such quantities of each POC Option Candidate Drug as AstraZeneca from time to time may order from Targacept.

16.7 **Changes in Pre-Phase IIb Plan; Failure to Supply**.

16.7.1 If, as a result of any amendment or modification of the Pre-Phase IIb Plan, AstraZeneca requires materials (the "**Substitute Materials**") different from Ispronicline Capsules or capsule placebos to complete the Pre-Phase IIb Program in accordance with the Pre-Phase IIb Plan or the Development Program with respect to Ispronicline up to and including Achievement of Proof of Concept in accordance with the relevant Product Development Plan, in each case as amended or modified, then AstraZeneca, at its option, may (a) obtain such Substitute Materials from Targacept, which shall be obligated to supply such Substitute Materials in accordance with the terms hereof, (b) Manufacture such Substitute Materials itself

or have such Substitute Materials Manufactured by an Affiliate, or (c) obtain such Substitute Materials from one or more Third Parties.

16.7.2 If at any time Targacept fails to supply Ispronicline Capsules or capsule placebos in accordance with the terms of this Article 16, AstraZeneca may (a) Manufacture such Ispronicline Capsules or capsule placebos itself or have such Ispronicline Capsules or capsule placebos Manufactured by an Affiliate, or (b) obtain such Ispronicline Capsules or capsule placebos from one or more Third Parties.

16.8 **AstraZeneca Manufacturing; Supply Strategy**.

16.8.1 Targacept acknowledges and agrees that (a) AstraZeneca shall have no obligation to order from Targacept any quantity of Ispronicline API or any Active+ Compound, Collaboration Candidate, Collaboration Compound, **[********]**, Option Compound (solely for purposes of conducting an Option Compound Development Plan that AstraZeneca has elected to complete pursuant to Section 5.10.2(b)(5)), IND-Ready Option Candidate Drug or POC Option Candidate Drug and (b) AstraZeneca shall have the exclusive right to Manufacture or have Manufactured (including by Targacept pursuant to Sections 16.2, 16.5 and 16.6) all quantities of Materials (other than Ispronicline Capsules and capsule placebos supplied by Targacept pursuant to Section 16.1.1, **[********]** supplied by Targacept pursuant to Section 16.5, and Research Compound Materials).

16.8.2 AstraZeneca shall have the exclusive right and obligation to Manufacture or have Manufactured (including by Targacept pursuant to Sections 16.2, 16.5 and 16.6) (a) clinical supplies necessary for Clinical Trials with respect to Candidate Drugs and Products conducted by or on behalf of AstraZeneca under this Agreement (other than Ispronicline Capsules and capsule placebos supplied by Targacept pursuant to Section 16.1.1) but, for clarity, not the Ongoing Ispronicline Trial, and (b) commercial supplies of Candidate Drugs and Products.

16.8.3 Targacept shall, from time to time at the request of AstraZeneca, meet with AstraZeneca to discuss and establish a global strategy for the non-clinical and clinical supply of all Materials.

16.9 **Ordering and Delivery of Materials**.

16.9.1 Subject to the limitations set forth in Sections 16.1.2, 16.2 and 16.9.7, Targacept shall supply Materials pursuant to written purchase orders submitted by AstraZeneca ("**Purchase Orders**") in accordance with this Section 16.9.

16.9.2 Each Purchase Order shall set forth (a) the quantity of each type of Material required by AstraZeneca, (b) the required delivery date thereof (subject to Section 16.9.3 and 16.9.4), (c) the required place of delivery thereof, (d) whether AstraZeneca requires release of such Materials in accordance with Section 16.9.4(a) or (b).

16.9.3 Targacept shall, with respect to Ispronicline Capsules and Ispronicline API, and, if and to the extent Targacept has the requested quantities in its possession (*i.e.,* in stock), Research Compound Materials, **[********]**, Option Compounds (solely for purposes of conducting an Option Compound Development Plan that AstraZeneca has elected to complete pursuant to Section 5.10.2(b)(5)), IND-Ready Option Candidate Drugs and POC Option Candidate Drugs, deliver the quantities set forth on the applicable AstraZeneca Purchase Order to the location(s) and on the date(s) set forth therein, provided that with respect to any such location outside the United States or any such date that is less than **[********]** after the date Targacept received such Purchase Order, Targacept will be deemed to have satisfied its obligations under this Section 16.9.3 with respect to a Purchase Order if it ships the requested quantities within **[********]** of receipt of such Purchase Order using the carrier and method of shipment (*e.g.,* overnight delivery) specified therein and takes all steps necessary to expedite the delivery of such shipment to AstraZeneca.

16.9.4 Prior to submitting any Purchase Order to Targacept for **[********]**, Option Compounds (solely for purposes of conducting an Option Compound Development Plan that AstraZeneca has elected to complete pursuant to Section 5.10.2(b)(5)), IND-Ready Option Candidate Drugs, POC Option Candidate Drugs or Research Compound Materials, the Parties shall discuss AstraZeneca's needs and Targacept's ability to meet such needs, and the estimated cost therefor. After such discussion, AstraZeneca may then submit the applicable Purchase Order, and Targacept shall use Commercially Reasonable Efforts to satisfy AstraZeneca's supply

requirements set forth therein in the time set forth therein, and when the requested Materials are available, deliver such Materials in accordance with Section 16.9.3.

16.9.5 Each Purchase Order submitted by AstraZeneca in accordance with this Section 16.9 shall constitute a binding obligation of AstraZeneca to purchase the quantity of Material set forth therein and a binding obligation of Targacept to deliver the quantity of Materials set forth therein at the required place of delivery set forth therein by the required delivery date set forth therein. To the extent that any Purchase Order contains terms that are inconsistent with, or in addition to, the terms of this Agreement, the terms of this Agreement shall govern and such inconsistent or additional terms shall have no force or effect.

16.9.6 Notwithstanding anything in this Article 16 to the contrary, Targacept shall deliver all Materials ordered pursuant to each Purchase Order DDP (as defined in Incoterms 2000) the required place of delivery specified in such Purchase Order. Title to such Materials shall pass to AstraZeneca at the time of delivery.

16.9.7 Notwithstanding anything in this Article 16 to the contrary, except as provided in Sections 16.9.3 and 16.9.4, Targacept's supply obligations under this Article 16 shall be to use Commercially Reasonable Efforts to supply and shall be limited to non-commercial quantities.

16.10 **Documentation and Release**.

16.10.1 Targacept shall maintain, or cause any Third Party that Manufactures Materials to maintain, all records necessary to comply with all Applicable Laws relating to the Manufacture of the Materials, including Manufacturing records, standard operating procedures, equipment log books, batch records, laboratory notebooks and all raw data relating to the Manufacturing of such Materials. All such records shall be retained for such period as may be required by Applicable Laws. Prior to destruction of any such records, Targacept shall offer custody of such records to AstraZeneca.

16.10.2 Each delivery of Materials shall be accompanied by (a) a certificate of analysis setting forth the tests conducted and the results thereof with respect to such Materials (other than Research Compound Materials) and (b) a certificate of compliance stating

that such Materials comply with the applicable Specifications and have been Manufactured and tested in accordance with Applicable Laws.

16.10.3 In addition, Targacept shall provide, or cause any Third Party that Manufactures any Materials to provide, as applicable, to AstraZeneca such other records and documentation in its possession or control relating to each delivery of Materials as AstraZeneca reasonably may request, including completed batch records, deviation reports, out-of-specification reports, and investigation reports.

16.10.4 If required by AstraZeneca pursuant to any Purchase Order, Targacept shall, or shall cause the Third Party that Manufactures the applicable Materials to, (a) perform release as required by Applicable Law for each delivery of Materials and (b) if so requested by AstraZeneca, cause a Qualified Person as described in Articles 48 and 49 of Directive 2001/83/EC to release each delivery of Materials to be distributed in Europe as described in Article 13 of Directive 2001/20 /EC.

16.11 **Invoicing and Payment**.

16.11.1 The purchase price payable by AstraZeneca for all Materials delivered hereunder (the "**Purchase Price**") shall be an amount equal to (a) if such Materials are Manufactured by Targacept, **[********]** supply of such Materials plus **[********]** plus **[********]**, and (b) if such Materials are Manufactured by a Third Party, **[********]**.

16.11.2 Targacept shall invoice AstraZeneca for all Materials delivered hereunder promptly after delivery thereof. AstraZeneca shall pay all such invoices within **[********]** after receipt thereof; provided that if AstraZeneca disagrees for any reason with the amount of any invoice submitted by Targacept, AstraZeneca shall notify Targacept in writing of such disagreement within **[********]** after the date of such invoice, and the Parties promptly shall attempt in good faith to resolve the difference and any portion of the invoiced amount that is not in dispute shall be paid by AstraZeneca within **[********]** after receipt of such invoice.

16.11.3 The parties shall cooperate in accordance with Applicable Laws to ensure that where permissible no import duties are paid on imported Materials. Where import duties are payable, the parties shall cooperate to ensure that Targacept values the Materials in

accordance with Applicable Laws and minimizes where permissible any such duties and any related import taxes that are not reclaimable from the relevant authorities.

16.12 **Materials Acceptance**.

16.12.1 In the event that AstraZeneca determines that any Materials delivered hereunder do not comply with the warranty set forth in Section 16.13, AstraZeneca shall give Targacept written notice of such noncompliance and the reasons therefor (including sufficient samples for confirmatory testing, if applicable) (a) within **[********]** after delivery, in the case of noncompliance readily discoverable by a customary inspection of such Materials upon delivery thereof, or (b) within **[********]** after discovery, in the case of noncompliance not readily discoverable by a customary inspection of such Materials upon receipt thereof. Targacept shall evaluate, or cause to be evaluated, such Materials (including appropriate testing of the samples provided by AstraZeneca, if applicable) and notify AstraZeneca within **[********]** after receipt of AstraZeneca's notice whether it has confirmed such noncompliance. If Targacept notifies AstraZeneca that it has not confirmed such noncompliance and AstraZeneca continues to believe such Materials are noncompliant, Targacept and AstraZeneca promptly shall submit the dispute to an independent testing laboratory or other applicable expert of recognized standing in the industry mutually acceptable to AstraZeneca and Targacept. Each Party shall cooperate with the laboratory or other expert in its evaluation. The findings of the laboratory or other expert shall be binding on the Parties. The expenses for such laboratory or other expert shall be borne by the Party whose analysis was not substantiated by the findings of such laboratory or other expert.

16.12.2 If, pursuant to Section 16.12.1, any Materials are determined not to comply with the warranty set forth in Section 16.13, then:

(a) if AstraZeneca has made payment for such Materials, Targacept, at AstraZeneca's option, promptly shall: (i) refund the Purchase Price paid by AstraZeneca for such noncompliant Materials; (ii) offset the Purchase Price paid by AstraZeneca against other amounts due to Targacept hereunder; or (iii) replace such noncompliant Materials with compliant Materials at no additional cost to AstraZeneca.

(b) if AstraZeneca has not made payment for such Materials, Targacept, at AstraZeneca's option, promptly shall: (i) cancel the applicable invoice or (ii) replace such noncompliant Materials with compliant Materials at the original Purchase Price invoiced for such noncompliant Materials.

(c) Targacept promptly shall reimburse AstraZeneca for all out-of-pocket costs incurred by AstraZeneca with respect to such noncompliant Materials, including costs of return, recall and destruction.

16.12.3 Targacept shall promptly notify AstraZeneca if it discovers that any Materials delivered hereunder do not comply with the warranty set forth in Section 16.13.

16.13 **Warranty**. Targacept warrants that (a) at the time of delivery, all quantities of Materials or other related clinical materials (including placebos) delivered by it hereunder (i) have been Manufactured in accordance with the applicable Specifications and all Applicable Laws; (ii) are not adulterated or misbranded under the FDCA, or under any other Applicable Laws; and (iii) may be introduced into interstate commerce pursuant to the FDCA; and (b) that the processes, procedures and materials used in the Manufacture of all Materials delivered hereunder do not infringe the intellectual property or other proprietary rights of a Third Party at the time of delivery. Targacept also warrants and covenants that Targacept has not been debarred and is not subject to debarment and that it will not use in any capacity, in connection with the Manufacture of any Materials or any other clinical materials (including placebos), any person who has been debarred pursuant to Section 306 of the FDCA, 21 U.S.C. § 335a, or who is the subject of a conviction described in such section (or under any analogous provisions of Applicable Laws outside the United States).

16.14 **Access and Inspection**.

16.14.1 Targacept shall, and shall cause any Third Party that Manufactures Materials to, give access to any Regulatory Authority to observe and inspect the Manufacturing facilities of Targacept or such Third Party and the procedures and records used for the Manufacture of the Materials and to audit such facilities, procedures and records for compliance with Applicable Laws.

16.14.2 Targacept shall, and shall use reasonable efforts to cause any Third Party that Manufactures Materials to, notify AstraZeneca by telephone within **[********]**, after learning of any proposed or announced visit or inspection of the Manufacturing facilities of Targacept or such Third Party by any Regulatory Authority, and Targacept shall, and shall use reasonable efforts to cause any Third Party that Manufactures Materials to, permit AstraZeneca or its agents to be present and participate in such visit or inspection (if such visit or inspection relates specifically to the Manufacture of Materials). Targacept shall, and shall use reasonable efforts to cause any Third Party that Manufactures Materials to, provide to AstraZeneca a copy of any report and other written communications received from such Regulatory Authority in connection with such visit or inspection (if such visit or inspection relates specifically to the Manufacture of Materials), and any written communications received from such Regulatory Authority relating to Materials or any equipment or Manufacturing process used in connection with the Manufacture of Materials, within **[********]** after receipt thereof, and Targacept shall, and shall use reasonable efforts to cause any Third Party that Manufactures Materials to, consult with AstraZeneca concerning the response of Targacept or such Third Party to each such communication. Targacept shall, and shall use reasonable efforts to cause any Third Party that Manufactures Materials to, provide AstraZeneca with a copy of all draft responses for comment as soon as practicable and all final responses for review and approval by AstraZeneca, which shall not be unreasonably withheld, conditioned or delayed, within **[********]** prior to submission thereof.

16.14.3 Targacept shall, and shall use reasonable efforts to cause any Third Party that Manufactures Materials to, give access to AstraZeneca and its agents, from time to time upon reasonable prior notice, to observe and inspect the Manufacturing facilities of Targacept or such Third Party and the procedures and records used for the Manufacture of the Materials (subject, in the case of any Third Party, to AstraZeneca's execution of a confidentiality agreement in a form reasonably acceptable to such Third Party). Following such audit, AstraZeneca shall discuss its observations and conclusions with Targacept or such Third Party, as applicable, and Targacept shall, or shall use reasonable efforts to cause such Third Party to, implement any corrective action reasonably required by AstraZeneca within **[********]**.

16.15 **Tech Transfer**. Upon AstraZeneca's request, Targacept shall, and shall cause any Third Party that Manufactures Ispronicline Capsules, Ispronicline API, any Collaboration Compound or any Candidate Drug under contract with Targacept to, provide AstraZeneca with all reasonable assistance required by AstraZeneca in order to transfer the Manufacturing process for Ispronicline Capsules, Ispronicline API, such Collaboration Compound or such Candidate Drug to AstraZeneca or its designee. Without limiting the generality of the foregoing, Targacept shall, and shall cause such Third Parties to:

16.15.1 from time to time upon AstraZeneca's request, make available to AstraZeneca or its designee all documentation, records, and know-how owned or controlled by Targacept and such Third Parties relating to the Manufacturing process for Ispronicline Capsules, Ispronicline API, such Collaboration Compound or such Candidate Drug, including documentation constituting material support, performance advice, shop practice, specifications as to materials to be used, control methods and any other material that is necessary or useful to enable AstraZeneca or such designee to use and practice the Manufacturing process for Ispronicline Capsules, Ispronicline API, such Collaboration Compound or such Candidate Drug;

16.15.2 cause all appropriate employees and representatives of Targacept and such Third Parties to meet with employees or representatives of AstraZeneca or its designee at the Manufacturing facility of AstraZeneca or its designee, from time to time at mutually convenient times, to assist with the working up and use of the Manufacturing process for Ispronicline Capsules, Ispronicline API, such Collaboration Compound or such Candidate Drug and with the training of AstraZeneca's or its designee's personnel to the extent necessary or useful to enable AstraZeneca or such designee to use and practice the Manufacturing process for Ispronicline Capsules, Ispronicline API, such Collaboration Compound or such Candidate Drug;

16.15.3 take such steps as are necessary or useful to assist in reasonable respects AstraZeneca or its designee in obtaining any necessary license, permit or approval from any Regulatory Authority with respect to AstraZeneca's or its designee's Manufacture of Ispronicline Capsules, Ispronicline API, such Collaboration Compound or such Candidate Drug; and

16.15.4 provide such other assistance as AstraZeneca may reasonably request to enable AstraZeneca or its designee to use and practice the Manufacturing process for Ispronicline Capsules, Ispronicline API, such Collaboration Compound or such Candidate Drug(s).

16.15.5 AstraZeneca shall promptly reimburse Targacept for all reasonable costs and expenses incurred by Targacept in performing the technology transfer services and activities specified in this Section 16.15 against reasonable documentation therefor.

16.15.6 The foregoing Sections 16.15.1 through 16.15.5 shall apply *mutatis mutandis* to AstraZeneca with respect to Terminated Compounds to the extent that, and in such quantities as, AstraZeneca was Manufacturing such Terminated Compound immediately prior to such termination.

16.16 **Third Party Suppliers**.

16.16.1 Without the prior written consent of AstraZeneca, Targacept shall not obtain any Ispronicline Capsules, capsule placebos, or Ispronicline API supplied to AstraZeneca hereunder from any Third Party other than (a) Siegfried Ltd. or (b) AAI Development Services, Inc., in each case or any Affiliate thereof.

16.16.2 Targacept shall provide to AstraZeneca a complete and correct copy of each agreement between Targacept and a Third Party pursuant to which Targacept obtains any Materials that it supplies to AstraZeneca hereunder promptly following AstraZeneca's request.

16.17 **Ancillary Agreements**.

16.17.1 Targacept has made available to AstraZeneca complete and correct copies of each agreement identified on Schedule 16.17 (the "**Ancillary Agreements**"). Each of the Ancillary Agreements is in full force and effect and constitutes a legal, valid and binding agreement of Targacept, enforceable in accordance with its terms (subject to the effects of bankruptcy, insolvency or other laws of general application affecting the enforcement of creditor rights, to judicial principles affecting the availability of specific performance and to general

principles of equity, whether enforceability is considered a proceeding at law or equity), and Targacept has performed all of its obligations under, and is not in violation or breach of or default under, each such Ancillary Agreement. To the Knowledge of Targacept, the other party to each Ancillary Agreement is not in violation or breach of or default under such Ancillary Agreement.

16.17.2 During the Term, Targacept shall:

(a) duly and punctually perform all of its obligations under each of the Ancillary Agreements in accordance with its terms;

(b) not amend, modify or terminate, or consent to any amendment, modification, or termination of, any Ancillary Agreement without the prior written consent of AstraZeneca; and

(c) promptly notify AstraZeneca of any Known violation or breach of or default under any Ancillary Agreement by any party thereto.

16.17.3 AstraZeneca promptly shall reimburse Targacept for all amounts paid by Targacept pursuant to and in accordance with the Ancillary Agreements from and after the date of this Agreement against reasonable documentation of such paid amounts; provided that AstraZeneca shall not be required to reimburse Targacept for an aggregate amount with respect to any Ancillary Agreement in excess of the maximum reimbursement amount for such Ancillary Agreement set forth on Schedule 16.17.

16.18 **Definitions**.

16.18.1 For purposes of this Article 16, the following terms shall have the following meanings.

(a) “Ancillary Agreements” has the meaning set forth in Section 16.17.1.

(b) “API Specifications” means the standards and specifications for Ispronicline API set forth on Schedule 16.18.1.

(c) “Capsule Specifications” means the standards and specifications for each dosage strength of Ispronicline Capsules set forth on Schedule 16.18.1.

(d) “Ispronicline Capsules” means capsules containing **[********]**, as applicable, of Ispronicline API, in bulk packaging.

(e) “Ispronicline API” means Ispronicline, in bulk packaging.

(f) “Manufacture” means manufacture, including activities relating to processing, formulating, packaging, labeling, holding, storing and quality control testing.

(g) “Materials” means, collectively, Ispronicline Capsules, Ispronicline API, Active+ Compounds, Collaboration Candidates, Collaboration Compounds, [********] Option Compounds (solely for purposes of conducting an Option Compound Development Plan that AstraZeneca has elected to complete pursuant to Section 5.10.2(b)(5)), IND-Ready Option Candidate Drugs, POC Option Candidate Drugs and any Substitute Materials.

(h) “Purchase Order” has the meaning set forth in Section 16.9.1.

(i) “Purchase Price” has the meaning set forth in Section 16.11.1.

(j) “Research Compound Materials” means, collectively, Active+ Compounds and Collaboration Candidates, in each case that have not become Collaboration Compounds, Candidate Drugs or Terminated Compounds and are not Licensed Derivatives made by or on behalf of AstraZeneca.

(k) “Specifications” means, collectively, (i) the Capsule Specifications, (ii) the API Specifications, and (iii) the standards and specifications for each (A) Active+ Compound and Collaboration Candidate, as agreed by the Parties from time to time, (B) Collaboration Compound, Option Compound (solely for purposes of conducting an Option Compound Development Plan that AstraZeneca has elected to complete pursuant to Section 5.10.2(b)(5)), IND-Ready Option Candidate Drug, POC Option Candidate Drug or Substitute Material, as applicable, as determined by AstraZeneca in writing and **[********]** as determined by Targacept in writing, in each case as amended from time to time in accordance with the terms hereof.

(l) “Substitute Materials” has the meaning set forth in Section 16.7.1.

17. MISCELLANEOUS

17.1 **Notices**. All notices and communications shall be in writing and delivered personally or by courier or mailed via certified mail, return receipt requested, addressed as follows, or to such other address as may be designated from time to time:

If to AstraZeneca:
V-Malarehamnen 9
S-151 85 Södertälje
Sweden
Tel: 46-8553-27713
Fax: 46-8553-28812
Attention: Johannes Linde
Secretary

With copies to:
AstraZeneca UK Ltd.
London, W1K 1LN
England
Tel: 44-20-7304-5188
Fax: 44-20-7304-5196
Attention: Graeme HR Musker
Company Solicitor

Covington & Burling
1201 Pennsylvania Ave., NW
Washington, DC 20004
Tel: 202-662-6000
Fax: 202-662-6261
Attention: John A. Hurvitz

If to Targacept:
200 East First Street
Suite 300
Winston-Salem, NC 27101-4165
Tel: 336-480-2100
Fax: 336-480-2103
Attention: Chief Executive Officer
Attention: General Counsel

With a copy to:
Mintz, Levin, Cohn, Ferris, Glovsky
and Popeo, PC
One Financial Center
Boston, Massachusetts 02111
Tel: (617) 542-6000
Fax: (617) 542-2241
Attention: Jeffrey M. Wiesen

In addition, all notices to the JRC, JDC, ESC or CCC shall be sent to each Party’s designees at such Party’s address stated above or to such other address as such Party may designate by written notice given in accordance with this Section 17.1.

Except as otherwise expressly provided in this Agreement or agreed in writing by the Parties, any notice, communication or document (excluding payment) required to be given, delivered or made shall be deemed given, delivered or made and effective upon actual receipt or, if earlier, (a) three (3) Business Days after deposit with an internationally-recognized overnight express courier with changes prepaid, or (b) five (5) Business Days after mailed by certified, registered or regular mail, postage prepaid, in each case addressed to a Parties at its address stated above or to such other address as such Party may designate by written notice given in accordance with this Section 17.1.

Notwithstanding the foregoing, all notices required or permitted to be sent pursuant to Sections 2.1.3(a), 2.2.3(a), 2.3.3(a), 2.4.3(a) and 4.3.1 may be sent by electronic transmission with receipt confirmed by telephone.

17.2 **Governing Law**. This Agreement shall be governed by and construed in accordance with the laws of the State of New York (USA), excluding any conflicts or choice of law rule or principle that might otherwise refer construction or interpretation of this Agreement to the substantive law of another jurisdiction. The Parties agree to exclude the application to this Agreement of the United Nations Convention on Contracts for the International Sale of Goods.

17.3 **Binding Effect**. This Agreement shall be binding upon and inure to the benefit of the Parties and their respective legal representatives, successors and permitted assigns.

17.4 **Headings**. Section and subsection headings are inserted for convenience of reference only and do not form a part of this Agreement.

17.5 **Counterparts**. This Agreement may be executed simultaneously in two or more counterparts, each of which shall be deemed an original and both of which, together, shall constitute a single agreement.

17.6 **Amendment; Waiver**. This Agreement may be amended, modified, superseded or canceled, and any of the terms of this Agreement may be waived, only by a written instrument executed by each Party or, in the case of waiver, by the Party or Parties waiving compliance. Except as expressly provided in this Agreement (including Section 2.1.5(e) and Section 5.4), (a) the delay or failure of either Party at any time or times to require performance of any provisions

shall in no manner affect the rights at a later time to enforce the same, and (b) no waiver by either Party of any condition or of the breach of any term contained in this Agreement, whether by conduct, or otherwise, in any one or more instances, shall be deemed to be, or considered as, a further or continuing waiver of any such condition or of the breach of such term or any other term of this Agreement.

17.7 **No Third Party Beneficiaries**. Except as set forth in Sections 13.1 and 13.2, no Third Party (including employees of either Party) shall have or acquire any rights by reason of this Agreement.

17.8 **Purposes and Scope**. The Parties hereto understand and agree that this Collaboration is limited to the activities, rights and obligations as set forth in this Agreement. Nothing in this Agreement shall be construed (a) to create or imply a general partnership between the Parties, (b) to make either Party the agent of the other for any purpose, (c) to alter, amend, supersede or vitiate any other arrangements between the Parties with respect to any subject matters not covered hereunder, (d) to give either Party the right to bind the other, (e) to create any duties or obligations between the Parties except as expressly set forth herein, or (f) to grant any direct or implied licenses or any other right other than as expressly set forth herein. In addition, (i) AstraZeneca shall have no duty or obligation, fiduciary or otherwise, (x) to Exploit any Collaboration Compound, Candidate Drug, Product, Additional Compound or other compound or product except as expressly set forth in Section 5.5.1 or (y) not to Exploit any other compound or product in or outside the Field, except as set forth in Section 8.6.3 or, solely with respect to Terminated Compounds, as otherwise expressly provided in this Agreement, and (ii) Targacept shall have no duty or obligation, fiduciary or otherwise, not to Exploit any compound or product in or outside the Field, except as set forth in Sections 8.6.1 and 8.6.2 or as otherwise expressly provided in this Agreement. Nothing in this Section 17.8 is intended to expand the rights granted by either Party to the other Party under this Agreement.

17.9 **Assignment and Successors**. Neither this Agreement nor any obligation of a Party hereunder may be assigned by either Party without the consent of the other which shall not be unreasonably withheld, conditioned or delayed, except that each Party may assign this Agreement and the rights, obligations and interests of such Party, in whole or in part, to any of

its Affiliates, to any purchaser of all of its assets or all of its assets to which this Agreement relates or to any successor corporation resulting from any merger, consolidation, share exchange or other similar transaction.

17.10 **Force Majeure**. Neither AstraZeneca nor Targacept shall be liable for failure of or delay in performing obligations set forth in this Agreement, and neither shall be deemed in breach of its obligations, if such failure or delay is due to a Force Majeure. In event of such Force Majeure, the Party affected shall use reasonable efforts to cure or overcome the same and resume performance of its obligations hereunder.

17.11 **Interpretation**. The Parties hereto acknowledge and agree that: (a) each Party and its counsel reviewed and negotiated the terms and provisions of this Agreement and have contributed to its revision; (b) the rule of construction to the effect that any ambiguities are resolved against the drafting Party shall not be employed in the interpretation of this Agreement; and (c) the terms and provisions of this Agreement shall be construed fairly as to each Party and not in a favor of or against either Party, regardless of which Party was generally responsible for the preparation of this Agreement. In addition, unless a context otherwise requires, wherever used, the singular shall include the plural, the plural the singular, the use of any gender shall be applicable to all genders and the word "or" is used in the inclusive sense (and/or) and the use of the term "including" shall mean including, without limiting the generality of any description preceding such term.

17.12 **Integration; Severability**. This Agreement is the entire agreement with respect to the subject matter hereof and supersedes all other agreements and understandings between the Parties with respect to such subject matter. If any provision of this Agreement is held to be illegal, invalid or unenforceable under any present or future law applicable to the Parties or the performance by either Party of its obligations hereunder, and if the rights or obligations of either Party under this Agreement will not be materially and adversely affected thereby, (a) such provision shall be fully severable, (b) this Agreement shall be construed and enforced as if such illegal, invalid or unenforceable provision had never compromised a part hereof, (c) the remaining provisions of this Agreement shall remain in full force and effect and shall not be affected by the illegal, invalid or unenforceable provision or by its severance herefrom, and (d)

in lieu of such illegal, invalid or unenforceable provision, there shall be added automatically as a part of this Agreement a legal, valid and enforceable provision as similar in terms to such illegal, invalid or unenforceable provision as may be possible and reasonably acceptable to the Parties. To the fullest extent permitted by applicable law, each Party hereby waives any provision of law that would render any provision hereof prohibited or unenforceable in any respect.

17.13 **Further Assurances**. Each of Targacept and AstraZeneca agrees to duly execute and deliver, or cause to be duly executed and delivered, such further instruments and do and cause to be done such further acts and things, including the filing of such additional assignments, agreements, documents and instruments, as the other Party may at any time and from time to time reasonably request, to carry out more effectively the provisions and purposes of this Agreement.

17.14 **HSR Filing**. The Parties shall each, as promptly as practicable after the date of this Agreement, file or cause to be filed with the U.S. Federal Trade Commission and the U.S. Department of Justice and any relevant foreign governmental authority any notifications required to be filed under the HSR Act with respect to the transactions contemplated hereby; provided that the Parties shall each file the notifications required to be filed under the HSR Act within five (5) Business Days after the date of this Agreement. The Parties shall use reasonable efforts to respond promptly to any requests for additional information made by either of such agencies and to cause the waiting period (and any extension thereof) under the HSR Act to terminate or expire at the earliest possible date after the date of filing. Notwithstanding anything in this Agreement to the contrary, this Agreement (other than this Section 17.14) shall not become effective until the expiration or earlier termination of the waiting period (or any extension thereof) under the HSR Act in the United States. If within ninety (90) days after the date of filing under the HSR Act, the Parties have failed to obtain the necessary clearances required under the HSR Act, either Party shall have the right, on written notice to the other Party, to terminate this Agreement.

17.15 **Effective Date Representations**. Targacept shall conduct its business, including with respect to Ispronicline, in the ordinary course, consistent with past practices, during the period from the Execution Date until the Effective Date. Each Party shall use its reasonable efforts to ensure that its representations and warranties set forth in this Agreement remain true

and correct at and as of the Effective Date as if such representations and warranties were made at and as of the Effective Date.

[Remainder of page intentionally left blank.]

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their duly authorized representatives.

TARGACEPT, INC.

By: /s/ J. Donald deBethizy
Name: J. Donald deBethizy
Title: President and Chief Executive Officer

ASTRAZENECA AB (PUBL)

By: /s/ Martin Nicklasson
Name: Martin Nicklasson
Title: President and Chief Executive Officer

EXHIBIT A

Form of Safety Agreement

[********]

[*Entire 17-page document is redacted*]

SCHEDULE 1.134

Definition of a Chemical Framework

Structural Guidelines

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SCHEDULE 1.148
Description of IND-Ready Studies

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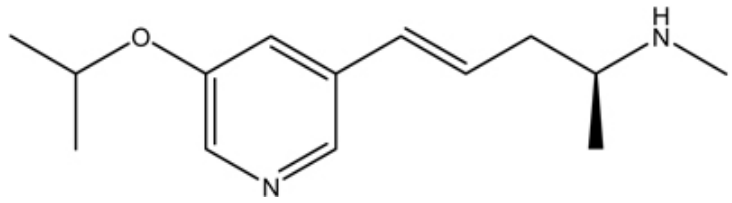
SCHEDULE 1.164

Structure of Ispronicline



SCHEDULE 4.4.2

Specified Personnel

[********]

SCHEDULE 5.11.2

Material Terms to be Included in
Form of Co-Promotion Agreement

Reference is made to the Collaborative Research and License Agreement by and between Targacept, Inc. ("**Targacept**") and AstraZeneca AB ("**AstraZeneca**"), dated as of December __, 2005, as may be amended from time to time, (the "**Master Agreement**"). Capitalized terms used in this Schedule 5.11.2 and not otherwise defined shall have the meanings given to them in the Master Agreement.

The Co-Promotion Agreement to be negotiated by the Parties upon exercise by Targacept of a Co-Promotion Option pursuant to Section 5.11.2 of the Master Agreement shall contain the following material terms.

1. Co-Promotion Rights and Obligations.

(a) Subject to the terms and conditions herein, AstraZeneca shall grant to Targacept the right to Co-Promote each Co-Promoted Product in the Co-Promotion Territory; *provided*, *however*, that Targacept shall be required to provide at least **[********]** (but without its consent, not more than **[********]** sales representatives to Detail the Co-Promoted Product(s).

(b) Targacept shall use Commercially Reasonable Efforts to execute its obligations under each Plan (as defined in Section 12), consistent with each applicable budget, and to cooperate diligently with AstraZeneca in carrying out such Plan. Targacept shall perform its activities under this Agreement in accordance with Applicable Laws and AstraZeneca's then-current standard operating procedures of which Targacept may be notified in writing from time to time.

(c) AstraZeneca shall enter into an agreement with a contract sales organization ("**CSO**") (the "**CSO Agreement**") to recruit and train a CSO sales force to Detail each Co-Promoted Product, at AstraZeneca's sole cost and expense. AstraZeneca shall provide a copy of any proposed CSO Agreement to Targacept for its review at least **[********]** prior to execution by AstraZeneca, and shall consider in good faith any comments provided by Targacept to AstraZeneca in writing within **[********]** after Targacept's receipt of such CSO Agreement. Prior to the First Commercial Sale with respect to a Co-Promoted Product, AstraZeneca shall assign to Targacept, and Targacept shall assume, the applicable CSO Agreement. Each CSO Agreement shall provide that Targacept may offer employment on terms determined by Targacept to the sales representatives and sales managers hired by the CSO. Except as provided in this Section 1(c), or as otherwise agreed in writing by the Parties, Targacept shall not have the right to use a CSO to Co-Promote a Co-Promoted Product.

2. Sales Force Composition.

(a) Designated Sales Forces. During the term of the Co-Promotion Agreement ("**Term**"), each of AstraZeneca and Targacept shall use the number of sales forces assigned to the promotion of a Co-Promoted Product ("**Designated Sales Force**") as set forth in the applicable Plan then in effect to Detail such Co-Promoted Product. Except as provided in Section 1(c), Targacept shall not use a contract sales force to satisfy its sales representative requirement and minimum PDE (as defined in Section 5) requirement for any period without the prior written consent of AstraZeneca.

(b) Minimum Qualifications. Except as may be set forth to the contrary in the applicable Plan, each of Targacept's sales representatives and sales managers shall (i) have graduated from an accredited four-year college and (ii) have satisfactorily completed the sales training program specified in Section 4(b). In addition, at least **[********]** of Targacept's sales representatives and sales managers engaged in the Co-Promotion of a Co-Promoted Product at any time during the Term must have been promoting branded pharmaceutical products in the Co-Promotion Territory for **[********]** prior to the date that such person commences Co-Promoting such Co-Promoted Product.

(c) Turnover and Vacancies. During the Term and after the launch of the first Co-Promoted Product, Targacept shall use commercially reasonable efforts to ensure that (i) turnover on any of its Designated Sales Force in any Calendar Year does not exceed standards customary in the United States contract sales organization industry at the time as determined by the CCC and set forth in the applicable Plan and (ii) each Designated Sales Force has a maximum vacancy rate for any Calendar Period during the Term that does not exceed standards customary in the United States contract sales organization industry at the time as determined by the CCC and set forth in the applicable Plan.

(d) Sales Force Incentives. The incentive compensation structure for a Party's Designated Sales Forces shall be solely determined by such Party, *provided* that each such incentive program shall provide that the weighting for sales performance of the Co-Promoted Products shall be at least **[********]** of such Party's Designated Sales Forces' total incentive compensation.

(e) Sales Meetings and Review. Each Party shall permit the other Party's sales and marketing management personnel (at reasonable levels), upon the request of such other Party, to attend and participate in those portions of its sales meetings that relate solely to the Co-Promoted Products; *provided* that each Party shall ensure that significant portions of any sales meeting with respect to the Co-Promoted Products shall relate solely to the Co-Promoted Products; *provided further* that each Party shall bear the costs of travel and attendance at such meetings for its own sales and marketing management personnel. Further, Targacept shall permit AstraZeneca's sales and marketing management personnel, upon request of AstraZeneca, to spend time in the field (ride-alongs) with Targacept's sales representatives to assess their performance under the Co-Promotion Agreement (*e.g.*, messaging, quality, sales direction).

(f) Non-Solicitation. During the Term and for a period of **[********]** thereafter, neither Party shall actively recruit or solicit any member of any Designated Sales Force or any other staff of the other Party engaged in the marketing, promotion or Detailing of any Co-

Promoted Product. For the avoidance of doubt, this provision shall not restrict either Party or its Affiliates from advertising employment opportunities, engaging head-hunters or engaging in any other activity directed towards recruitment, in each case if and to the extent that such advertising or activities do not directly target the other Party or its Affiliates.

(g) Managed Care. AstraZeneca shall be responsible for managing necessary responsibilities with respect to the Co-Promoted Products across all managed care market segments in the Co-Promotion Territory and shall have exclusive responsibility for: (i) contract strategy, (ii) contract creation; (iii) government reporting, rebate processing, FSS calculations and pricing schedules; (iv) contract compliance, monitoring and audits; (v) contract administration and claims processing; and (vi) all other matters related to managed care.

3. Promotional Materials.

(a) During the Term, AstraZeneca, in consultation with Targacept, shall develop and produce all written, printed or graphic material, other than product labels and inserts, intended for use by sales representatives in promoting Co-Promoted Products in the Co-Promoted Territory, including visual aids, file cards, premium items, clinical study reports, reprints, drug information updates, and any other promotional support items (collectively, the "**Promotional Materials**") to be used by the Parties in connection with the Co-Promotion of Co-Promoted Products in accordance with the terms of the applicable Plan. In the event of any dispute between the Parties with respect to the content of any Promotional Materials, AstraZeneca's determination shall be final. The quantities of Promotional Materials for each Co-Promoted Product produced by AstraZeneca shall be allocated to the Parties in proportion to the number of representatives engaged by each Party to Co-Promote such Co-Promoted Product.

(b) Targacept shall, and shall cause its sales representatives to, use only the Promotional Materials provided by AstraZeneca in connection with the Co-Promotion of Co-Promoted Products. Targacept shall ensure that the Promotional Materials are used only in the form provided and not changed in any way (including by underlining or otherwise highlighting any text or graphics or adding any notes thereto) by any members of its Designated Sales Forces.

(c) Targacept shall, and shall cause its sales representatives to, immediately cease the use of any Promotional Materials when instructed to do so by AstraZeneca. Targacept shall, and shall cause its sales representatives to, use the Promotional Materials only for the purposes contemplated by the Co-Promotion Agreement. All Promotional Materials in the possession of Targacept or its sales representatives shall be returned to AstraZeneca upon termination of the Co-Promotion Agreement or as earlier requested by AstraZeneca.

(d) Targacept shall, and shall cause its sales representatives to, make only such statements and claims regarding the Co-Promoted Products, including as to efficacy and safety, as are consistent with the applicable product labels and inserts and Promotional Materials. Targacept shall not, and Targacept shall cause its sales representatives not to, make any untrue or misleading statements or comments about the Co-Promoted Products.

4. Training.

(a) Training Materials. AstraZeneca, in consultation with Targacept, shall (i) establish training objectives and training plans for members of the Parties' Designated Sales Forces who are hired or assigned to Co-Promote Co-Promoted Products and (ii) develop and produce all training programs and materials (including Co-Promoted Product sales orientation assessment tests and refresher tests) to be used by each of the Parties for initial and refresher training of the members of its Designated Sales Forces; it being understood and agreed by the Parties that in the event of any dispute between the Parties with respect to such objectives or plans or the content of any such programs or materials, AstraZeneca's determination shall be final. AstraZeneca shall bear the cost of all initial training materials and Targacept shall bear the cost of any refresher or additional training materials produced for Targacept, *provided* that AstraZeneca shall only produce such refresher or additional materials at Targacept's request.

(b) Training Programs. Prior to the launch of a Co-Promoted Product, AstraZeneca shall provide training materials to, and hold in-person meetings or webcasts for, each member of Targacept's Designated Sales Force(s) prior to his or her commencement of Co-Promotion of such Co-Promoted Product to ensure that he or she is appropriately trained in proper marketing and sales techniques and properly trained and able to satisfy his or her responsibilities under the Co-Promotion Agreement. In addition, AstraZeneca shall reasonably train Targacept's sales force trainers with respect to such Co-Promoted Product. Such training may be provided by AstraZeneca in connection with the CSO Agreement. Following the launch of a Co-Promoted Product, each Party shall be responsible for training its sales force trainers with respect to such Co-Promoted Product.

5. PDE Requirements. For purposes hereof, "**PDE**" means a primary Detail equivalent where (i) a Primary Product Presentation (a Detail during a sales call in which a Co-Promoted Product receives **[********]** of the total call time and emphasis) has a value of **[********]** primary Detail equivalent, (ii) a Secondary Product Presentation (a Detail during a sales call in which a Co-Promoted Product receives **[********]** of the total call time and emphasis) has the value of **[********]** primary Detail equivalents and (iii) a Product Presentation in third position has **[********]**. In any event, no more than **[********]** products may be presented during any sales call.

(a) Performance of PDEs. In each calendar trimester, or such other period as AstraZeneca may designate from time to time (each, a "**Calendar Period**") during the Term, Targacept shall perform the number of PDEs for each Co-Promoted Product required to be performed by Targacept as set forth in the applicable Plan for such Calendar Period. During each Calendar Period, Targacept shall be required to perform **[********]** of the aggregate number PDEs for such Calendar Period. In addition, in each Calendar Period during the Term, Targacept shall ensure that at least **[********]** of the number of PDEs it actually performed were made to targeted prescribers or target purchasers, if any. Targacept may deliver up to **[********]** of its required PDEs to non-target prescribers or target purchasers, if any, if it reasonably believes in good faith that such PDEs are likely to result in increased sales of Co-Promoted Products.

(b) Shortfalls. In the event that Targacept believes in good faith that, notwithstanding diligent efforts, it will be unable to perform the number of required PDEs for any Calendar Period, it shall promptly give written notice to AstraZeneca and the CCC that it shall not be able

to meet its PDE obligations and the projected shortfall in PDEs. Upon receipt of such notice, AstraZeneca shall have the option, exercisable in its sole discretion, to perform additional PDEs to make up for the projected shortfall, which it may perform through its Designated Sales Forces or through a contract sales force.

(c) Permissible PDEs. For purposes of determining compliance by Targacept with any of its annual PDE performance requirements set forth in the Co-Promotion Agreement, except as provided in the last sentence of Section 5(a), PDEs that are not performed by Targacept as set forth in the applicable Plan for the applicable Calendar Period, in each case shall not be taken into account.

6. Failure to Perform Required Number of PDEs; Consequences.

(a) Subject to Section 6(b) and Section 6(d), if, during any Calendar Period, Targacept fails to perform at least **[********]** of its required PDEs for each Co-Promoted Product as set forth in the applicable Plan for such Calendar Period, then Targacept's Co-Promotion compensation for the subsequent Calendar Period shall be reduced by an amount equal to the product of (i) the PDE Cost (as defined in Section 10), multiplied by (ii) the total of (A) **[********]** for such Co-Promoted Product for such Calendar Period, less (B) **[********]** for such Co-Promoted Product **[********]** during such Calendar Period, multiplied by (C) the applicable Value Loss Factor (which shall be (x) **[********]** such Co-Promoted Product, (y) **[********]** and (z) **[********]**.

(b) Subject to Section 6(d), if, during any **[********]** Calendar Periods occurring during **[********]** during the Term, Targacept fails to perform at least **[********]** of its required PDEs for each Co-Promoted Product as set forth in the applicable Plan for each such Calendar Period, then the reduction in the amount otherwise payable to Targacept pursuant to Section 6(a) above with respect to the second and, if applicable, third such Calendar Periods shall be **[********]**.

(c) Subject to Section 6(d), in addition to any amounts payable pursuant to Sections 6(a) and (b), if during any Calendar Year Targacept performs less than **[********]** of the aggregate number of its required PDEs for each Co-Promoted Product to be performed during such Calendar Year as set forth in the applicable Plan for such Calendar Year, then AstraZeneca may terminate the Co-Promotion Agreement by giving notice to Targacept not later than **[********]** after the end of Calendar Year during which the termination right arises, and such termination shall become effective ninety (90) days after delivery of such notice.

(d) Notwithstanding anything herein to the contrary, in no event shall the amount payable to Targacept under the Co-Promotion Agreement be reduced as set forth in this Section 6, and in no event shall AstraZeneca have the right to terminate the Co-Promotion Agreement, due to a failure of Targacept to provide a particular percentage of PDEs for a particular Calendar Period or Calendar Year unless AstraZeneca has itself satisfied the same percentage standard and provides Targacept with reasonable documentation thereof.

7. Samples. AstraZeneca may, in its sole and absolute discretion and at its expense, make Co-Promoted Product samples available to Targacept for use by Targacept's sales representatives in Detailing Co-Promoted Products. AstraZeneca in its sole and absolute discretion will determine the number of samples, if any, to be distributed and sampling strategy for such samples. If AstraZeneca makes samples available to Targacept, Targacept shall comply with Applicable Laws and AstraZeneca's sample distribution policies.

8. Promotion of Other Products. During the Term, members of any Targacept Designated Sales Force shall be permitted to promote products in addition to Co-Promoted Products; *provided* that (i) such other products have not received Regulatory Approval for any indication for which any product that is then being promoted by AstraZeneca's Designated Sales Force that is aligned with the Targacept Designated Sales Force has received Regulatory Approval, and (ii) the Targacept Designated Sales Force shall not, directly or indirectly, promote, respond to or refer medical inquiries or otherwise encourage the use of any such product for any indication other than the indication(s) set forth in the approved labeling for such product.

9. Reporting and Auditing.

(a) Recordkeeping. Targacept shall keep complete and accurate books and records (financial and otherwise) pertaining to the performance of its obligations under the Co-Promotion Agreement, including records of PDEs performed by its sales representatives, in sufficient detail to calculate all fees and expenses payable pursuant to the Co-Promotion Agreement and to prepare all reports required thereunder. All financial books and records maintained by the Parties shall be maintained in accordance with GAAP.

(b) Detail Reporting. Each Party shall cause each of its sales representatives to report his or her Detailing activity in accordance with the procedures specified from time to time in the applicable Plan. Each Party, at its sole expense, shall ensure that each of its sale representatives on its Designated Sales Forces is properly equipped with all necessary hardware, software and other information technology required from time to time by the applicable Plan to perform his or her recordkeeping and reporting obligations under this Section.

(c) Tracking Reports. Targacept shall provide to AstraZeneca such additional information and reports concerning Detail activity under the Co-Promotion Agreement at the times and in the manner specified in the applicable Plan; *provided* that (a) no less often than **[********]** after the launch of each Co-Promoted Product and (b) no less often than **[********]** thereafter, Targacept shall submit to AstraZeneca a written report containing the following information with respect to such month or Calendar Period, as the case may be: **[********]**.

(d) PDE Audits. No more than once during any **[********]** period during the Term, AstraZeneca shall have the right to engage a disinterested third party auditor (an "**Auditor**") to conduct an audit of Targacept's Detailing activities to confirm the accuracy of the Detail and PDE related-information contained in the reports delivered by Targacept. Any such audit shall be at AstraZeneca's sole expense; *provided*, *however*, that if the results of such audit identify an overstatement of PDEs in such reports by **[********]** more in any Calendar Period, then

Targacept shall bear the expense of such audit and shall implement promptly corrective actions reasonably acceptable to AstraZeneca to ensure accurate reporting thereafter. At any time within twelve (12) months after the completion of an audit that identifies an overstatement of PDEs by **[********]** or more in any Calendar Period, AstraZeneca shall have the right to engage an Auditor to conduct, at Targacept's expense, a subsequent audit of Targacept's Detailing activities, to ensure that Targacept has corrected its reporting deficiencies.

(e) Detail Message Audits. AstraZeneca shall have the right, at its sole expense, to engage an Auditor to conduct market research in order to evaluate the effectiveness of the Details performed by Targacept and the content of the "**Product Message**" (the principal promotional messages with respect to a Co-Promoted Product set forth in the applicable Plan, that a sales representative is required to convey to a prescriber or purchaser during a Detail of such product) delivered by the Targacept's sales representatives. If such market research indicates that (i) AstraZeneca is delivering the appropriate Product Message and (ii) Targacept is not delivering the appropriate Product Message, then AstraZeneca may deliver written notice of such failure to Targacept. Within ten (10) Business Days after receipt of such notice, Targacept shall develop and deliver to AstraZeneca a plan of action designed to correct such failure that is reasonably satisfactory to AstraZeneca (a "**Corrective Plan**"). Targacept shall implement the Corrective Plan within thirty (30) days after approval thereof by AstraZeneca. AstraZeneca shall have the right, at the expense of Targacept, to engage an Auditor to conduct independent market research in order to evaluate whether Targacept has corrected such failure in accordance with the Corrective Plan. If such market research indicates that Targacept has not corrected such failure, then AstraZeneca may deliver written notice of such failure to Targacept. Within fifteen (15) Business Days after receipt of such notice, Targacept (at its sole expense) will develop and deliver to AstraZeneca a comprehensive re-training program for its Designated Sales Forces reasonably satisfactory to AstraZeneca (the "**Retraining Program**"). Targacept shall implement the Retraining Program within sixty (60) days. AstraZeneca shall have the right, at the expense of Targacept, to engage an Auditor to conduct independent market research in order to evaluate whether Targacept has corrected such failure as a result of the Retraining Program.

10. Co-Promotion Fees and Expenses.

(a) Promotion Fee Payment. Not later than **[********]** after the end of each Calendar Period during the Term (commencing with the Calendar Period in which the launch of the first Co-Promoted Product occurs), AstraZeneca shall pay to Targacept a fee in an amount equal to (i) **[********]** during such Calendar Period, multiplied by (ii) the PDE Cost for such Calendar Period. Each Party shall bear and be solely responsible for all costs and expenses incurred by it in connection with the Co-Promotion of Co-Promoted Products and the performance of its obligations under the Co-Promotion Agreement that are not PDE Costs. For purposes hereof, "**PDE Cost**," means (A) with respect to the first twelve (12)-month period following the launch of the first Co-Promoted Product, the arithmetic mean of the good faith quotes obtained jointly by AstraZeneca and Targacept not less than twelve (12) months prior to such launch from each of **[********]** reputable third party CSOs in the Co-Promotion Territory for the price that would be charged by such CSOs for performing a PDE on the terms and conditions of the quote specified in the then-current applicable Plan, or, if obtaining such quotes is not reasonably practicable, such other method as may be agreed by the Parties, and (B) with

respect to each successive twelve (12)-month period thereafter, (1) the PDE Cost for the immediately preceding twelve (12)-month period, multiplied by (2) the sum of **[********]**, determined as follows:

[********].

(b) Cap on AstraZeneca Payments. In no event shall the aggregate amounts payable by AstraZeneca pursuant to the Co-Promotion Agreement exceed **[********]** Dollars (US $**[********]**) per year without AstraZeneca's consent, in its sole discretion.

11. Commercial Coordination Committee. The Parties shall establish a Commercial Coordination Committee ("**CCC**") that shall have responsibility for the development and implementation of marketing strategies for Co-Promoted Products in the Co-Promotion Territory and shall supervise, guide and coordinate the Parties' promotional activities in the Co-Promotion Territory. The CCC shall have such membership requirements, procedures and responsibilities as set forth in Section 2.4 of the Master Agreement.

12. Plan. For each Co-Promoted Product, there shall be a Co-Promotion plan (each, a "**Plan**"), that sets forth, with respect to the applicable annual period, a description of strategy and positioning implementation for such Co-Promoted Product in the Co-Promotion Territory and the key marketing issues for such Co-Promoted Product in the Co-Promotion Territory including:

(a) a "Promotional Plan" that specifies the Promotional Materials to be used by the Parties in conducting promotional activities with respect to such Co-Promoted Products and the applicable Product Message;

(b) a "Sales Force Management Plan" that specifies, per region or local market within the Co-Promotion Territory, (i) the number of specialty Designated Sales Forces to be provided by each of Targacept and AstraZeneca and the alignment thereof; (ii) the minimum number of sales representatives and other members of the Designated Sales Forces to be provided by each of Targacept and AstraZeneca; (iii) the minimum qualifications for sales representatives (to the extent that such minimum represents a change from the minimum set forth in Section 2(b)); (iv) the minimum number of PDEs that each sales representative will perform in each Calendar Period, (v) standards for turnover and vacancies for the Parties' Designated Sales Forces, and (vi) the manner in which each Party will use medical information scientists, market development specialists and other members of the Parties' respective Designated Sales Forces;

(c) a "Strategic Targeting Plan" that specifies Detailing strategy and obligations of the Parties on a Calendar Period basis, including (i) the "call plan" size (i.e., the number of targeted prescribers and targeted purchasers, if any, to be called on by each sales representative); (ii) identification and prioritization of targeted prescribers by deciles and targeted purchasers (if any); *provided* that if both Parties are fielding a Designated Sales Force(s) with respect to a class of target prescribers or target purchasers, then the number of Details to be allocated to each Party's Designated Sales Force(s) **[********]** each Party's respective Designated Sales Force(s), and their territories; (iii) reach and frequency expectations for the targeted prescribers and targeted purchasers (if any) in each Calendar Period; and (iv) the number of PDEs for each Co-Promoted Product to be performed in each Calendar Period;

(d) a reporting plan that specifies the reporting obligations of the Parties and their sales representatives with respect to the performance of their promotional activities under the Co-Promotion Agreement, including the recording of Detailing activity by sales representatives, the synchronizing and transfer of Detail information to AstraZeneca's databases, the review by sales representatives of the activities of their counterparts on the other Party's Designated Sales Force(s), and the hardware, software and other information technology to be used therefor;

(e) sales forecasts for such Co-Promoted Product on a quarterly basis (or more frequently if determined by the CCC; and

(f) such other plans relating to the marketing and promotion of such Co-Promoted Product in the Co-Promotion Territory as the CCC deems necessary or appropriate.

The initial Plan shall be prepared by the CCC and included in the Co-Promotion Agreement for each Co-Promoted Product. Each subsequent Plan shall be prepared by the CCC at least **[********]** prior to the beginning of the annual period to be covered by any such Plan.

13. Product Supply.

(a) Orders for Products; Terms of Sale. AstraZeneca shall have the sole responsibility and right to fill orders with respect to Co-Promoted Products. Targacept shall not take orders for Co-Promoted Products, but if for any reason Targacept should receive sales orders for Co-Promoted Products, Targacept shall promptly forward such orders to AstraZeneca. All orders for Co-Promoted Products shall be subject to AstraZeneca's acceptance, in its sole discretion. AstraZeneca may cancel any order for Co-Promoted Products, or any part thereof, at any time after acceptance without thereby incurring any liability to Targacept. AstraZeneca shall be solely responsible for responding to requests from physicians for individual patients who need the Co-Promoted Products but are unable to afford it. Any such request received by Targacept should originate from the patient's physician and be forwarded to AstraZeneca for processing in accordance with AstraZeneca's procedures. AstraZeneca shall have the sole right and responsibility for establishing and modifying the terms and conditions of the sale of Co-Promoted Products, including the price at which each Co-Promoted Product will be sold, whether each Co-Promoted Product will be subject to any trade or quantity discounts, whether any discount will be provided for payments on accounts receivable, whether each Co-Promoted Product will be subject to rebates, returns and allowances or retroactive price reductions, the channels of distribution of each Co-Promoted Product, and whether credit is to be granted or refused in connection with the sale of each Co-Promoted Product.

(b) Returned Product. AstraZeneca shall have the sole responsibility and right to accept any returned Co-Promoted Product. Targacept shall not solicit the return of any co-Promoted Product, but if for any reason Targacept should receive any returned Co-Promoted Product, Targacept shall promptly notify AstraZeneca. Any Co-Promoted Product returned to Targacept shall be shipped by Targacept to AstraZeneca's designated facility, and all reasonable documented shipping costs incurred by Targacept shall be promptly reimbursed by AstraZeneca. Targacept shall advise the customer that made such return that the Co-Promoted Product has

been returned to AstraZeneca. Targacept shall fully complete and deliver to AstraZeneca the returned goods form provided by AstraZeneca with respect to any returned Co-Promoted Product.

(c) Recalled Product. AstraZeneca, in its sole and absolute discretion, shall determine whether to recall any Co-Promoted Product or withdraw any Co-Promoted Product from the market, any such recall or withdrawal to be at AstraZeneca's expense, except to the extent such recall resulted from any breach by Targacept of its obligations under the Master Agreement or under the Co-Promotion Agreement or Targacept's or any of its Affiliates' negligence or willful misconduct, in which case Targacept shall bear all expenses of such recall, provided that Targacept shall not be deemed to be negligent or in breach solely for complying with the training provided by AstraZeneca under the applicable Co-Promotion Agreement, with AstraZeneca's standard operating procedures as may be provided under the applicable Co-Promotion Agreement or otherwise with direction from AstraZeneca if the activities required by such training, procedures or other direction would themselves constitute negligence or breach. At AstraZeneca's request, Targacept shall assist AstraZeneca in obtaining any Co-Promoted Product, including all samples thereof, that has been recalled or withdrawn from the market.

14. Requests for Medical Information.

(a) Response to Requests. AstraZeneca shall have the exclusive right to respond to all questions or requests for information about a Co-Promoted Product made by any medical professionals or any other Person to Targacept or its sales representatives that (i) warrant a response beyond the understanding or knowledge of such sales representative or (ii) are beyond the scope of the product labels and inserts or other Promotional Materials for such Co-Promoted Product (a "**PIR**").

(b) Communication of PIRs. Targacept shall, and shall cause its sales representatives to, promptly communicate to the AstraZeneca Information Center or Medical Resources Department all PIRs received by Targacept or such sales representatives.

(c) Communications to Prescribers. In connection with the Co-Promotion of Co-Promoted Products, Targacept shall cause its sales representatives to inform prescribers and purchasers (if any) that they may contact the AstraZeneca Information Center regarding questions or requests for information about the Co-Promoted Products by telephone or by completing a Medical Resource Form and faxing the completed form directly to AstraZeneca Medical Resources at the facsimile number provided on such form. AstraZeneca shall provide Targacept with sufficient quantities of Medical Resource Forms and Targacept shall cause the sales representatives to provide such forms to prescribers and purchasers (if any).

15. Product Trademarks and Product Copyrights. Targacept shall Co-Promote Co-Promoted Products only under the Product Trademarks. AstraZeneca shall grant Targacept a non-exclusive, royalty free license to use the Product Trademarks and Product Copyrights solely for purposes of performing its obligations under the Co-Promotion Agreement, which license shall terminate upon the expiration or earlier termination of the Co-Promotion Agreement for any reason. "**Product Copyrights**" means all copyrightable subject matter included in the product labels and

inserts, the Promotional Materials, and the Co-Promoted Product training materials. "**Product Trademarks**" means the (i) any trademarks relating to a Co-Promoted Product and the registrations thereof, (ii) any pending or future trademark registration applications relating to a Co-Promoted Product, (iii) any unregistered trademark rights relating to a Co-Promoted Product as may exist through use prior to or as of the date hereof, (iv) any current or future modifications or variants of any of the foregoing trademarks, and (v) any future trademarks adopted by AstraZeneca or its Affiliates for use in connection with a Co-Promoted Product, in each case excluding the AstraZeneca corporate name and related logos.

16. Insurance. During the term of the Co-Promotion Agreement, at a minimum, and in addition to any insurance obligations under the Master Agreement, Targacept shall maintain in full force and effect the following types and amounts of insurance:

(a) commercial general liability insurance covering bodily injury, property damage and personal injury with limits of $**[********]** each occurrence and $**[********]** general aggregate;

(b) commercial automobile liability insurance with a $**[********]** combined single limit on Targacept owned and non-owned vehicles at any time during the term of the Co-Promotion Agreement;

(c) workers' compensation insurance as required by the laws of the states in which Targacept performs under the Co-Promotion Agreement, and employers liability insurance with limits of $**[********]** each accident, $**[********]** each employee and $**[********]** policy limit;

(d) umbrella or excess liability insurance with limits of $**[********]** each occurrence and $**[********]** general aggregate;

(e) employment practices liability insurance with limits of $**[********]** per event; and

(f) property insurance covering AstraZeneca's property in the care, custody and control of Targacept and its employees with limits of $**[********]** for "each and every loss".

As of the effective date of the Co-Promotion Agreement and during the term thereof, Targacept shall represent and warrant that its general liability, product liability, automobile liability and employers' liability insurance policies are scheduled as "underlying" insurance on its umbrella or excess liability insurance policy(ies).

Each of the policies in Sections 16(a) and 16(b) shall name AstraZeneca as an additional insured and shall be primary to any liability insurance carried by AstraZeneca, which insurance shall be excess and non-contributory for claims and losses arising out of the performance of this Agreement.

Certificates evidencing at least the above-required insurance coverage shall be submitted by Targacept prior to the commencement of any Co-Promotion activities by Targacept and thereafter prior to each renewal or replacement period and shall bear a certification that the

coverage specified therein will not be canceled or terminated without at least thirty (30) days' prior written notice to AstraZeneca. All such insurances shall be written with one or more companies licensed to do business in the states in which Targacept operates, which companies have a financial rating of not less than A "X" in the most current edition of Bests Key Rating Guide.

For the avoidance of doubt, Section 16 shall apply to any CSO retained by Targacept (including pursuant to Section 1(c)).

17. Indemnification.

(a) Indemnification of AstraZeneca. In addition to any other remedy available to AstraZeneca, Targacept shall defend, indemnify and hold harmless AstraZeneca, its Affiliates and its and their respective officers, directors, partners, shareholders, employees and agents from and against any and all Losses incurred by them to the extent resulting from or arising out of or in connection with (i) any breach of any obligation in this Agreement by Targacept, other than its obligations under Section 5, (ii) the inaccuracy or breach of any representation or warranty made by Targacept in the Co-Promotion Agreement or (iii) the enforcement of AstraZeneca's rights under this Section 17, except to the extent such Losses arise as a result of the negligence, fraud, willful misconduct or wrongful act of AstraZeneca, its Affiliates or its or their respective officers, directors, partners, shareholders, employees or agents.

(b) Indemnification of Targacept. In addition to any other remedy available to Targacept AstraZeneca shall defend, indemnify and hold harmless Targacept, its Affiliates and its and their respective officers, directors, partners, shareholders, employees and agents from and against any and all Losses incurred by them to the extent resulting from or arising out of or in connection with (i) any breach of any obligation in this Agreement by AstraZeneca, (ii) the inaccuracy or breach of any representation or warranty made by AstraZeneca in the Co-Promotion Agreement, (iii) the defective design of a Co-Promoted Product or inherent defects in a Co-Promoted Product that are not caused by manufacturing defects, (iv) the use of Promotional Materials without modification, in accordance with the training provided by AstraZeneca under the applicable Co-Promotion Agreement, Applicable Laws and AstraZeneca's then-current standard operating procedures as notified to Targacept, or (v) the enforcement of Targacept's rights under this Section 17, except to the extent such Losses arise as a result of the negligence, fraud, willful misconduct or wrongful act of Targacept, its Affiliates or its or their respective officers, directors, partners, shareholders, employees or agents.

18. Term and Termination.

(a) Term. Unless earlier terminated in accordance with the terms hereof or extended by mutual written agreement of the Parties, the term of the Co-Promotion Agreement (the "**Term**") shall commence on the effective date and continue until AstraZeneca is no longer fielding a Designated Sales Force for the Co-Promoted Product.

(b) Termination. In addition to any other provision of the Co-Promotion Agreement expressly providing for termination of the Agreement, the Co-Promotion Agreement may be terminated by either Party:

(i) in the event of a material breach of the Co-Promotion Agreement by the other Party (other than a breach of its obligations under Section 6), which breach remains uncured **[********]** after written notice thereof is given to the breaching Party;

(ii) upon thirty (30) days' prior written notice to the other Party in the event the FDA recommends or otherwise causes the withdrawal of the Co-Promoted Product from the market at any time after launch for a period in excess of one-hundred and twenty (120) days; or

(iii) immediately upon written notice if the other Party files for protection under bankruptcy or insolvency laws, makes an assignment for the benefit of creditors, appoints or suffers appointment of a receiver or trustee over its property that is not discharged within ninety (90) days after such filing, proposes a written agreement of composition or extension of its debts, proposes or is a party to any dissolution or liquidation, files a petition under any bankruptcy or insolvency act or has any such petition filed against it which involuntary petition is not discharged within sixty (60) days of the filing thereof.

(c) Effect of Termination or Expiration. Upon the effective date of termination or expiration of the Co-Promotion Agreement, Targacept immediately shall cease all Detailing and Co-Promotion of the Co-Promoted Products and discontinue the use of any Promotional Materials and samples.

(d) Return of All Materials. Upon the termination or expiration of the Co-Promotion Agreement, Targacept shall promptly return to AstraZeneca all Co-Promoted Product samples, all Promotional Materials, and all training materials that AstraZeneca provided to Targacept pursuant to the Co-Promotion Agreement that are in the possession of, or under the control of, Targacept or its Designated Sales Forces.

SCHEDULE 8.4

Targacept Retained INDs

Targacept shall retain ownership of **[********]** until it submits the next annual report to the FDA with respect thereto following completion or earlier termination of the Ongoing Ispronicline Trial.

SCHEDULE 10.1.1

Patent Territories

Substantive Filing

United States of America
All PCT states
Argentina
Chile
Malaysia
Malta
Pakistan
Saudi Arabia
Taiwan
Thailand
Uruguay
Venezuela

PCT Nationalization

Australia
Brazil
Canada
China
Colombia
Egypt
Europe, including all extension states available at the time of filing
Hong Kong
Iceland
India
Indonesia
Israel
Japan
Korea
Mexico
New Zealand
Norway
Philippines
Russian Federation
Singapore
South Africa
Ukraine

SCHEDULE 12.2

Part A: Owned Patent Rights

Country	Filing Date	Application #	Issue Date	Pat#
US [********]	8/21/2000	09/642,351	8/5/03	6,603,011
Australia [********]	4/16/97	2733297	1/4/01	727,976
Mexico	4/16/97	PA/A/1998/008659	8/3/04	221,928
US [********]	5/25/04	10/853,602	10/25/05	6,958,399
Europe [********]	6/3/99	99926152	8/18/04	1,086,082
Mexico	6/3/99	PA/A/2000/012858	5/31/05	228,168
US [********]	7/14/2000	09/616,743	8/13/02	6,432,954
Europe [********]	7/11/01	01984212.9	12/29/04	1,311,265
New Zealand [********]	7/11/01	523606	4/7/05	523,606

[********]

Country	Filing Date	Application #	Issue Date	Pat#
US	10/12/98	09/169,861	8/14/01	6,274,606
[********]				
Australia	2/19/98	6280698	6/20/02	749,151
[********]				
Europe	2/19/98	98905108.1	8/25/04	0,973,743
[********]				
Mexico	2/19/98	997843	4/18/05	227,337
US	8/7/98	09/130,498	4/17/01	6,218,383
[********]				
Australia	6/2/99	4328599	9/11/03	761,087
[********]				
[********]				
US	5/12/2000	09/570,226	9/24/02	6,455,554
[********]				
US	6/7/99	09/327,774	12/10/02	6,492,399

Co-owned:

Country	Filing Date	Application #	Issue Date	Pat#
[********]				

Part B: In-licensed Patent Rights

Country	Filing Date	Application #	Issue Date	Pat#
[********]				

Part C: In-License Agreements

Amended and Restated Collaborative Research and License Agreement between Aventis Pharma S.A. and Targacept, Inc. dated January 21, 2002, as amended.

Development Agreement between The Stanley Medical Research Institute and Targacept, Inc. dated December 15, 2004.

License Agreement between the University of Kentucky Research Foundation and Targacept, Inc. dated May 26, 1999, as amended.

Sabbatical Leave Agreement between the University of Kentucky and Targacept, Inc. dated August 15, 1996.

License Agreement between the Medical College of Georgia Research Institute, Inc. and Targacept, Inc. dated June 9, 2002.

Part D: Targacept Patent Rights relating to Ispronicline

Country	Filing Date	Application #	Issue Date	Pat#
US [********]	8/21/2000	09/642,351	8/5/03	6,603,011
Australia [********]	4/16/97	2733297	1/4/01	727,976
Mexico	4/16/97	PA/A/1998/008659	8/3/04	221,928
US [********]	5/25/04	10/853,602	10/25/05	6,958,399
Europe [********]	6/3/99	99926152	8/18/04	1,086,082
Mexico	6/3/99	PA/A/2000/012858	5/31/05	228,168
US [********]	7/14/2000	09/616,743	8/13/02	6,432,954
Europe [********]	7/11/01	01984212.9	12/29/04	1,311,265
New Zealand [********]	7/11/01	523606	4/7/05	523,606

Country	Filing Date	Application #	Issue Date	Pat#
US [********]	10/12/98	09/169,861	8/14/01	6,274,606
Australia [********]	2/19/98	6280698	6/20/02	749,151
Europe [********]	2/19/98	98905108.1	8/25/04	0,973,743
Mexico	2/19/98	997843	4/18/05	227,337
US [********]	8/7/98	09/130,498	4/17/01	6,218,383
Australia [********]	6/2/99	4328599	9/11/03	761,087
[********]				
US [********]	5/12/2000	09/570,226	9/24/02	6,455,554
US	6/7/99	09/327,774	12/10/02	6,492,399
US	2/21/97	08/804,224	9/22/98	5,811,442
US	8/7/97	08/908,440	6/22/99	5,914,337
US [********]	2/25/99	09/257,368	9/12/2000	6,117,891
Europe	8/7/99	98940814	10/19/05	1,011,672

Country	Filing Date	Application #	Issue Date	Pat#
US [********]	10/5/2000	09/622,675	6/19/01	6,248,744
Europe [********]	2/24/99	99936030.8	4/27/05	1,056,458
US	4/20/99	09/295,181	12/26/2000	6,166,048
US [********]	9/6/2000	09/656,284	12/3/2002	6,489,349
Europe [********]	4/20/2000	00926142.1	9/14/05	1,171,127

SCHEDULE 16.17

Ancillary Agreements

PO	Vendor	Description	Bal Due
[********]	[********]	[********]	[********]
		[********]	
[********]	[********]	[********]	[********]
[********]	[********]	[********]	[********]
[********]	[********]	[********]	[********]
[********]	[********]	[********]	[********]
[********]	[********]	[********]	[********]
[********]	[********]	[********]	[********]
[********]	[********]	[********]	[********]
[********]	[********]	[********]	[********]
		Total Balance Due	$[********]

SCHEDULE 16.18.1

Manufacturing Specifications

API Specifications

[********]	[********]	[********]
[********]	[********]	[********]
[********]	[********]	[********]
[********]	[********]	[********]
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[********]	[********]	[********]
[********]	[********]	[********]

Capsule Specifications ([********])

[********]	[********]	[********]
[********]	[********]	[********]
[********]	[********]	[********]
[********]	[********]	[********]
[********]	[********]	[********]
[********]	[********]	[********]

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the reference to our firm under the caption “Experts” and to the use of our report dated February 10, 2006, in Amendment No. 5 to the Registration Statement (Form S-1 No. 333-131050) and related Prospectus of Targacept, Inc. dated April 6, 2006.

/s/ Ernst & Young LLP

Greensboro, North Carolina
April 6, 2006