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As filed with the Securities and Exchange Commission on December 15, 2004

Registration No. 333-115538

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Amendment No. 3 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. ☐ _____

If delivery of the Prospectus is expected to be made pursuant to Rule 434, please check the following box. ☐

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 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 effective. This prospectus is not an offer to sell these securities and we are not soliciting offers to buy these securities in any state where the offer is not permitted.

PROSPECTUS (Subject to Completion)
Issued December 15, 2004

Shares

COMMON STOCK

Targacept, Inc. is offering shares of its common stock. This is our initial public offering and no public market currently exists for our shares. We anticipate that the initial public offering price will be between $ and $ per share.

We have applied to have our common stock approved for listing on the NASDAQ National Market under the symbol "TRGT."

Investing in our common stock involves risks. See " Risk Factors" beginning on page 7.

PRICE $ A SHARE

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

We have granted the underwriters the right to purchase up to an additional shares of our common stock to cover over-allotments.

The Securities and Exchange Commission and state securities regulators have not approved or disapproved these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

Morgan Stanley & Co. Incorporated expects to deliver the shares to purchasers on , 2005.

MORGAN STANLEY
DEUTSCHE BANK SECURITIES
CIBC WORLD MARKETS
PACIFIC GROWTH EQUITIES, LLC

, 2005

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You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information different from the information contained in this prospectus. We are offering to sell shares of common stock, 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 when this prospectus is delivered or when any sale of our common stock occurs.

Until , 2005, 25 days after the commencement of this offering, all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

For investors outside the United States: Neither we nor any of the underwriters have done anything that would permit this offering or possession or distribution of this prospectus in any jurisdiction where action for that purpose is required, other than in the United States. You are required to inform yourselves about and to observe any restrictions relating to this offering and the distribution of this prospectus.

PROSPECTUS SUMMARY

The following summary highlights information appearing elsewhere in this prospectus. It may not contain all of the information that may be 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 nervous system by selectively targeting neuronal nicotinic acetylcholine 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 while limiting or eliminating adverse side effects. In addition to a marketed product, Inversine, we have four product candidates in clinical development and multiple ongoing preclinical programs. Our pipeline includes:

- Ispronicline (TC-1734)—in Phase II clinical development for the treatment of conditions marked by cognitive impairment that afflict elderly persons;
- TC-5231—in Phase II clinical development for the treatment of attention deficit hyperactivity disorder, commonly referred to as ADHD;
- Rivanicline (TC-2403)—in Phase II clinical development for the treatment of a form of inflammatory bowel disease known as ulcerative colitis;
- TC-2696—in Phase I clinical development for the treatment of pain; and
- preclinical research programs in schizophrenia, depression and anxiety, smoking cessation and obesity.

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 acetylcholine receptors. There is a significant amount of published clinical data relating to nicotine, including studies in which individuals with ADHD, cognitive impairment, and ulcerative colitis showed therapeutic improvement when treated with the 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 drugs to act upon. We have also developed an expertise in designing organic 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 effect while limiting or potentially eliminating 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 nervous system by selectively affecting specific NNR subtypes.

We develop product candidates using our proprietary databases and computer-based molecular design technologies, which we refer to collectively as Pentad. Together with our proprietary assays and novel screening methods, Pentad enables us to efficiently identify, prioritize, characterize and optimize novel compounds.

We have a collaboration agreement with Aventis Pharma SA relating to the development of Aventis compounds to treat Alzheimer's disease and other diseases of the central nervous system. In addition, we have a collaboration agreement with Dr. Falk Pharma GmbH relating to the development of rivanicline to treat ulcerative colitis. We also recently entered into a development agreement with The Stanley Medical Research Institute relating to the development of one of our compounds for the treatment of the cognitive impairment associated with schizophrenia.

Our Product Development Pipeline

Ispronicline (TC-1734). Ispronicline is a novel small molecule that we are developing as an oral treatment for conditions marked by cognitive impairment that afflict elderly persons, including Alzheimer's disease and age associated memory impairment, commonly referred to as AAMI. In 2004, we completed the treatment phase of a Phase II clinical trial of ispronicline in 76 elderly persons classified with AAMI. In 2004, we also completed the treatment phase of a Phase II clinical trial in 40 elderly persons classified with mild cognitive impairment, commonly referred to as MCI. Subject to the results of discussions with the United States Food and Drug Administration, or the FDA, we anticipate commencing a separate Phase II clinical trial designed to evaluate the efficacy of ispronicline in persons with AAMI in the fourth quarter of 2004. We are also evaluating ispronicline for potential additional clinical development for other indications such as cognitive impairment associated with schizophrenia, cognitive impairment following coronary artery bypass grafting, MCI, ADHD and various forms of dementia.

TC-5231. TC-5231 is a small molecule that we are developing as an oral treatment for ADHD. TC-5231 is mecamylamine hydrochloride, the active ingredient in our product Inversine, but in a lower dose than Inversine. Inversine is approved in the United States for the management of moderately severe to severe essential hypertension, a high blood pressure disorder with an unknown cause, at average daily doses of 25mg. However, our market research suggests that Inversine is prescribed predominantly for the treatment of Tourette's syndrome and other neuropsychiatric disorders at doses ranging from 2.5mg to 7.5mg. In the fourth quarter of 2004, we completed the treatment phase of a Phase II clinical trial of TC-5231 in doses between 0.2mg and 1.0mg in children and adolescents with ADHD. We are also currently evaluating TC-5231 in the same doses in a small Phase II clinical trial in young adults with ADHD.

Rivanicline (TC-2403). Rivanicline is a small molecule that we are developing for the treatment of ulcerative colitis in collaboration with Dr. Falk Pharma GmbH. In the fourth quarter of 2004, we completed the treatment phase of a Phase II clinical trial of an enema formulation of the compound designed to induce remission of acute episodes of a form of ulcerative colitis known as left-sided colitis. We are also developing a delayed release oral formulation of the compound designed to deliver the drug to the entire colon to induce and maintain remission of additional forms of ulcerative colitis. We expect to complete the oral formulation of this product candidate in the first quarter of 2005.

TC-2696. TC-2696 is a novel small molecule that we are developing as an oral treatment for acute post-operative pain. In 2004, we completed the treatment phase of a Phase I clinical trial of TC-2696. Depending on the results of future clinical trials, available resources and other considerations, we may pursue development of TC-2696 for other classes of pain as well.

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 believe that our four product candidates in clinical development may exhibit these attributes and we are aggressively pursuing their development.

- *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. We intend to continue to invest significant resources to build upon our NNR expertise and to expand our intellectual property portfolio.
- *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 drugs that selectively target specific NNR subtypes can provide a medical benefit. We prioritize our product development in an effort to sustain our product pipeline.
- *Collaborate selectively to develop and commercialize product candidates.* We intend to selectively enter into collaboration agreements with leading pharmaceutical and biotechnology companies to assist us in furthering the development of our product candidates. 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.
- *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.

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. 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 these 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.

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	shares
Common stock to be outstanding after this offering	shares
Over-allotment option	shares
Use of proceeds	To fund clinical trials, preclinical testing and other research and development activities, manufacturing expenses, 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.
Proposed NASDAQ National Market symbol	TRGT

The number of shares of our common stock that will be outstanding immediately after this offering is based on shares outstanding as of , 2004, and includes:

- 103,204,189 shares of common stock issuable upon the conversion of all currently outstanding shares of our series A, series B and series C convertible preferred stock concurrently with the completion of this offering;
- shares of common stock issuable upon the conversion of an outstanding convertible promissory note concurrently with the completion of this offering based on an assumed initial public offering price of $ per share; and
- shares of common stock issuable upon the exercise of an outstanding warrant that will expire if not exercised concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share. The cash exercise price of the warrant is $ per share.

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

- 7,419,029 shares of common stock issuable upon the exercise of options outstanding as of December 15, 2004, at a weighted average exercise price of $0.65 per share, of which options to purchase 4,099,577 shares were exercisable; and
- 302,743 shares of common stock reserved for future grant under our 2000 equity incentive plan as of December 15, 2004.

Unless otherwise indicated, all information in this prospectus assumes:

- no exercise by the underwriters of their over-allotment option to purchase up to shares of our common stock;
- the conversion of all outstanding shares of our convertible preferred stock into 103,204,189 shares of common stock concurrently with the completion of this offering;
- the issuance of shares of common stock upon the conversion of an outstanding convertible promissory note concurrently with the completion of this offering based on an assumed initial public offering price of $ per share; and
- the issuance of shares of common stock upon the exercise of an outstanding warrant that will expire if not exercised concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share.

In addition, unless otherwise noted, all information in this prospectus gives effect to the one-for- reverse stock split of our common stock that will be effective prior to 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 shares of our convertible preferred stock outstanding as of December 31, 2003 and September 30, 2004 into 73,739,905 shares of common stock concurrently with the completion of this offering, as if the conversion had occurred at the date of the original issuance. This pro forma information does not give effect to the issuance of additional shares of our convertible preferred stock on December 6, 2004, to the conversion of an outstanding convertible promissory note or to the exercise of an outstanding warrant.

	Year ended December 31,			Nine months ended September 30,	
	2001	2002	2003	2003	2004
					(unaudited)
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Net revenue	$ 1,703	$ 2,286	$ 2,458	$ 1,816	$ 1,581
Operating expenses:					
Research and development	8,152	16,244	18,179	13,376	17,782
General and administrative	2,302	4,135	3,600	2,698	3,764
Cost of product sales	—	244	743	540	28
Purchased in-process research and development	—	2,666	—		
Total operating expenses	10,454	23,289	22,522	16,614	21,574
Loss from operations	(8,751)	(21,003)	(20,064)	(14,798)	(19,993)
Interest and dividend income	1,449	88	791	546	356
Interest expense	—	(103)	(122)	(96)	(96)
Loss on disposal of fixed assets	—	(54)	—		(4)
Net loss	(7,302)	(21,072)	(19,395)	(14,348)	(19,737)
Preferred stock accretion	(3,808)	(4,173)	(8,341)	(6,199)	(6,426)
Net loss attributable to common stockholders	$ (11,110)	$ (25,245)	$ (27,736)	(20,547)	(26,163)
Basic and diluted net loss per share applicable to common stockholders	$ (26.80)	$ (45.28)	$ (33.91)	$ (27.04)	$ (16.82)
Shares used to compute basic and diluted net loss per share	414,624	557,492	817,894	759,937	1,555,090
Pro forma basic and diluted net loss per share applicable to common stockholders (unaudited)			$ (0.27)		$ (0.26)
Shares used to compute pro forma basic and diluted net loss per share (unaudited)			71,118,629		75,294,995

The pro forma balance sheet information gives effect to the issuance of additional shares of our convertible preferred stock on December 6, 2004, the issuance of a convertible promissory note on December 15, 2004 and the conversion of all outstanding shares of our convertible preferred stock into 103,204,189 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 shares of common stock in this offering at an assumed initial public offering price of $ per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us;
- our issuance of shares of common stock upon the conversion of an outstanding convertible promissory note concurrently with the completion of this offering based on an assumed initial offering price of $ per share; and
- our issuance of shares of common stock upon the exercise of an outstanding warrant that will expire if not exercised concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share. The cash exercise price of the warrant is $ per share.

	As of September 30, 2004		
	Actual	Pro Forma	Pro Forma As Adjusted
		(unaudited) (in thousands)	
Balance Sheet Data:			
Cash, cash equivalents and short-term investments	$ 24,425	$ 58,575	
Working capital	21,054	55,204	
Total assets	29,208	63,358	
Long-term debt, net of current portion	1,654	2,904	
Redeemable convertible preferred stock	136,560	—	
Accumulated deficit	(117,835)	(117,835)	
Total stockholders' equity (deficit)	(116,394)	53,066	

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 September 30, 2004, we had an accumulated deficit of $117.8 million. Our net loss was $19.7 million for the nine months ended September 30, 2004, $19.4 million for the year ended December 31, 2003 and $21.1 million for the year ended December 31, 2002. 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 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 costs to increase substantially as we expand our infrastructure. As a result, we will need to generate significant revenues to pay these costs 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 $584,000 for the nine months ended September 30, 2004 and $815,000 for the year ended December 31, 2003. Inversine is approved in the United States for the treatment of moderately severe to severe essential hypertension, a high blood pressure disorder with an unknown cause. 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 Tourette's syndrome and other neuropsychiatric disorders. 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 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 four product candidates currently in clinical development 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 2005. 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 the end of 2006. 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. Other than a modest amount of committed equipment financing, we currently have no credit facility or committed sources of capital. 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.

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.

Inversine is our only marketed product and generates limited revenues. Our most advanced product candidates are in Phase I or Phase II clinical trials. Our ability to generate product revenue in the future will depend heavily on the successful development and commercialization of these product candidates. 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 four 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 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 for each indicated use must establish the safety and efficacy of the product candidate. 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.

In addition, we currently intend to pursue marketing approval for ispronicline for conditions marked by cognitive impairment that afflict elderly persons. Cognitive impairment in the elderly ranges in severity from AAMI to MCI to dementia, including Alzheimer's disease. Neither the FDA nor, to our knowledge, any foreign regulatory authority has approved a drug indicated for use either for 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 other such regulatory authority will be willing to recognize AAMI or MCI as a defined condition or disease and grant approval of ispronicline for either of these indications.

Also, a portion of one of the inactive substances that is used to manufacture the current formulation of our product candidate rivanicline changes form over time to a different inactive substance when added to enema solution. As a result, the FDA or foreign regulatory authorities could determine that the manufacturing process of the enema formulation of rivanicline does not comply with good manufacturing practices, or cGMPs. Product formulation development is generally a long, expensive and uncertain process. If we are unable to develop, or experience significant delays in developing, a formulation for the enema form of rivanicline that is stable over time and under various storage conditions, our ability to obtain required regulatory approval and market this product candidate will be adversely affected.

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 be able to obtain regulatory approval for and commercialize 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. If we experience difficulties or failures in our 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.

Success in preclinical studies of a product candidate may not be predictive of similar results in humans during clinical trials. In addition, successful results from early clinical trials of a product candidate may not be replicated in later clinical trials. In particular, in our Phase I and Phase II clinical trials of ispronicline, our product candidate in development for the treatment of conditions marked by cognitive impairment that afflict elderly persons, we have used a battery of tests developed by CDR Ltd. to assess each subject's cognitive function. The CDR test battery is different from the test battery that is most often used to assess the efficacy of drugs for the treatment of Alzheimer's disease. We plan to consult with the FDA regarding the use of the CDR test battery in our future clinical trials of ispronicline for the treatment of AAMI. If, based on our consultation

with the FDA, we use an additional or a different test battery for our future clinical trials of ispronicline for the treatment of AAMI, there would be a greater risk that the results of our Phase I and Phase II clinical trials of ispronicline will not be predictive of similar results of those future clinical trials. We do not plan to use the CDR test battery in future clinical trials of ispronicline for the treatment of Alzheimer's disease.

We may not be able to obtain authority 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. Of the 240 patients that participated in our Phase II clinical trial of rivanicline, our product candidate for the treatment of ulcerative colitis, 10 experienced an elevation in liver enzymes in excess of three times the upper limit of normal. Five of these patients were withdrawn from the trial and their liver enzymes returned to within the normal range. Four of the other patients continued in the trial. These patients' liver enzymes returned to the normal range during the last two weeks of the six-week dosing regimen and were within the normal range at the post-regimen follow-up visit. The elevation in liver enzymes for the tenth patient was observed at the end of the six-week dosing regimen, and this patient's liver enzymes were within the normal range at the post-regimen follow-up visit. Because the trial is double blind, we do not know if these patients were administered rivanicline or a placebo. If some or all of these patients were administered rivanicline and if future clinical trials of rivanicline show similar or more prevalent elevations of liver enzymes, the FDA or other regulatory authorities may not grant us approval to market rivanicline. Also, our product candidate TC-5231, in development for ADHD, is mecamylamine hydrochloride in a low dose. Mecamylamine hydrochloride is approved in a high dose as Inversine for the treatment of moderately severe to severe essential hypertension. If clinical trials show that TC-5231 has a similar effect on blood pressure as Inversine, the FDA or other regulatory authorities may not grant us approval to market TC-5231 for the treatment of ADHD in children or at all.

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 AAMI, Alzheimer's disease, ADHD, 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 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 the enema formulation of rivanicline for the treatment of ulcerative colitis and we could experience similar delays in the future. Our failure to enroll patients in a clinical trial could delay the completion of the clinical trial beyond our current expectations. In particular, patient enrollment rates for ulcerative colitis clinical trials are generally low. In addition, the FDA could require us to conduct clinical trials with a larger number of subjects than we have projected for any of our product candidates. We 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 our clinical trials, which could impair the validity or statistical significance of the clinical trials.

Prior to commencing clinical trials in the United States, we must submit an IND to the FDA. We conducted our Phase I clinical trial for our product candidate TC-2696 outside the United States and have not submitted an IND to enable us to conduct clinical trials of that product candidate in the United States.

Our product candidate TC-5231 is a low-dose reformulation of the active ingredient in Inversine, which was approved in the 1950s. If the FDA determines that the safety and tolerability data that were used to support regulatory approval of Inversine at that time are incomplete under current standards, outdated or otherwise not in compliance with current guidelines, the FDA may not accept the data as support for a potential regulatory submission by us for approval of TC-5231. The FDA has indicated to us that we may be required to conduct lengthy non-clinical carcinogenicity studies before we could submit an NDA for the use of TC-5231 to treat ADHD in children. These carcinogenicity studies are routinely conducted prior to submission of an NDA today but were not performed on Inversine prior to its approval. If we are required to conduct these carcinogenicity studies, our development costs for TC-5231 will increase and regulatory approval and receipt of any revenues from potential sales of TC-5231 may be delayed.

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.

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 candidate or indication and fail to capitalize on 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. In addition, we may spend valuable time and managerial and financial resources on 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 our four clinical stage product candidates, all of our research and development programs 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.

Additional product candidates resulting from these research programs will require the commitment of substantial time and financial resources for further preclinical research and clinical development.

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.

Risks Related to Our Dependence on Third Parties

We 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.

We 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 royalties from our collaborators depends on our collaborators' abilities to establish the safety and efficacy of our product candidates, to obtain regulatory approvals and to achieve market acceptance.

In particular, we have granted exclusive commercialization rights to Dr. Falk Pharma GmbH with respect to rivanicline for the treatment or prevention of ulcerative colitis and other gastrointestinal and liver diseases in specified European countries, Russia, the Commonwealth of Independent States countries, Egypt and Israel. If Dr. Falk Pharma does not perform as contemplated under our agreement, our potential for revenue from rivanicline will be adversely impacted. In addition, Dr. Falk Pharma may terminate this collaboration agreement under certain conditions on short notice and at its sole discretion. Our collaboration agreement restricts Dr. Falk Pharma from developing or commercializing compounds that act upon specified NNR subtypes. If our collaboration agreement were to terminate, Dr. Falk Pharma would not be subject to those development and commercialization restrictions. Furthermore, if our collaboration agreement were to terminate, we may have to curtail the development of rivanicline, reduce or delay its development program, increase our expenditures and undertake development or commercialization activities at our own expense or seek another collaborator.

In addition to our current collaboration agreements, we also 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.

In general, strategic collaborations involving our product candidates 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 for the development of our compounds for the treatment or prevention of Alzheimer's disease will terminate on January 2, 2005. None of our compounds that were subject to this agreement were advanced into clinical development under the agreement. As a result of the termination, we will be free to pursue the development and commercialization of our product candidates, including ispronicline, for Alzheimer's disease, but without funding from Aventis.

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. For example, Sanofi-Synthelabo recently acquired a controlling interest in Aventis. We believe that Sanofi-Synthelabo has its own program to develop compounds that act on neuronal nicotinic acetylcholine receptors to treat Alzheimer's disease. This may reduce the likelihood that Aventis will pursue the development and commercialization of compounds that would entitle us to payments under another collaboration agreement that we entered into with Aventis relating to the development of Aventis compounds for the treatment of Alzheimer's disease and other diseases of the central nervous system. The research term of this agreement is scheduled to expire in December 2004, and Aventis has informed us that it does not intend to extend the research term. We are only eligible to receive future payments from Aventis for any compounds that are selected for further development within six months after the expiration of the research term.

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 face significant competition in seeking appropriate collaborators and these 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 the active ingredient of Inversine and 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 TC-5231, our product candidate in development for ADHD, and TC-2696, our product candidate in development for pain. 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 any particular compound may be limited to a particular method of use or indication such that, if a third party were to obtain approval of the 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 have composition of matter patent coverage in the United States on only two of our four clinical stage compounds, ispronicline and TC-2696. We rely on method of use patent coverage in the United States on our two other clinical stage compounds, TC-5231, for neuropsychiatric disorders including ADHD, and rivanicline, for inflammatory bowel disease including ulcerative colitis. Accordingly, we would likely be unable to prevent others from manufacturing TC-5231 or rivanicline or from marketing either of them for any use that is not protected by our patent rights. If a third party were to receive marketing approval for either compound 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.

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 sale, 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” acetylcholine 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 recently 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, ispronicline, our product candidate for conditions marked by cognitive impairment that afflict elderly persons, could be particularly affected by this law because of the product candidate’s elderly target patient population. 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 in Phase III clinical trials for smoking cessation, and Abbott Laboratories, with one compound in Phase I clinical trials for pain and another in Phase II clinical trials 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. In particular, if mecamylamine hydrochloride is effective and receives regulatory approval for the treatment of ADHD at the low doses that we are currently developing as TC-5231, physicians could prescribe partial tablets of a generic version of Inversine for the off-label treatment of ADHD. We are currently evaluating mecamylamine hydrochloride at doses ranging from 0.2mg and 1.0mg. If we determine that the higher dose is more effective or otherwise more desirable for use in treating ADHD, physicians may view the higher dose as more similar to Inversine and be even more likely to prescribe partial tablets of Inversine for the off-label treatment of ADHD. In addition, 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 AAMI. We believe that the primary competitive products for use in the other indications that we are currently targeting include:

- for Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer, 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 ADHD, stimulants such as Concerta from Johnson & Johnson, Ritalin from Novartis and Adderall from Shire Laboratories and the non-stimulant Strattera from Eli Lilly;
- for ulcerative colitis, 5-ASAs such as Asacol from Proctor & Gamble;
- for pain, non-steroidal anti-inflammatory drugs such as Celebrex from Pfizer and opioids such as OxyContin from Purdue Pharma;
- for schizophrenia, anti-psychotics such as Zyprexa from Eli Lilly, Risperdal from Johnson & Johnson and Abilify from Bristol-Myers Squibb;
- 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; 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 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 Tourette's syndrome or any other 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 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 recently 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 $(61.97) per share of our existing capital stock as of September 30, 2004. As a result, based on an assumed initial public offering price of , purchasers of our common stock in this offering will incur immediate and substantial dilution of $ 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 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 or our collaborators' inability 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 our and our collaborative partners' research and development expenditures;
- the timing of receipts of milestone payments from our collaborative partners; and
- the expiration or termination of agreements with collaborative partners 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 shares of common stock outstanding based on the number of shares outstanding as of , 2004. 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 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 Morgan Stanley & Co. Incorporated on behalf of the underwriters. However, Morgan Stanley may, in its sole discretion, release all or any portion of the common stock from the restrictions of the lock-up agreements. Morgan Stanley 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 shares of our common stock that may be issued upon the exercise of options outstanding as of , 2004, approximately 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 % of the outstanding shares of our common stock. 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.

Certain 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 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;
- 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 collaborators 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 shares of our common stock in this offering will be approximately $ million, or approximately $ million if the underwriters exercise their over-allotment option in full, assuming an initial public offering price of $ per share and after deducting estimated underwriting discounts and commissions and offering expenses payable by us.

We expect that we will use:

- approximately $ million of these net proceeds to fund clinical trials, preclinical testing and other research and development activities;
- approximately $ million of these net proceeds to fund manufacturing expenses related to the clinical development of our product candidates; and
- approximately $ million of these net proceeds to fund general and administrative expenses, working capital needs and other general corporate purposes.

We may also use a portion of the 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 will depend upon numerous factors, including the 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 collaborations, any additional strategic collaborations into which we may enter and sales of Inversine. Accordingly, our management will have significant flexibility in applying the net proceeds of this offering.

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 believe that our existing capital resources and the net proceeds from this offering will be sufficient to enable us to:

- complete the Phase II clinical trial of ispronicline for AAMI that we plan to initiate in the fourth quarter of 2004;
- initiate a Phase II clinical trial of ispronicline for Alzheimer's disease;
- initiate a Phase III clinical trial of TC-5231;
- initiate and complete a Phase I clinical trial, and potentially initiate a Phase II clinical trial, of the oral formulation of rivanicline; and
- initiate and complete an additional Phase I clinical trial and a small Phase II clinical trial of TC-2696.

However, the actual costs and timing of clinical trials are highly uncertain, subject to risk and will change depending upon the clinical indication targeted, the development strategy pursued and the results of earlier clinical trials.

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 September 30, 2004:

- on an actual basis;
- on a pro forma basis to give effect to the issuance of additional shares of our convertible preferred stock on December 6, 2004, the issuance of a convertible promissory note on December 15, 2004 and the conversion of all outstanding shares of our convertible preferred stock into 103,204,189 shares of common stock concurrently with the completion of this offering; and
- on a pro forma as adjusted basis to give further effect to:
  - Ÿ our sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us;
  - Ÿ our issuance of shares of common stock upon the conversion of an outstanding convertible promissory note concurrently with the completion of this offering based on an assumed initial public offering price of $ per share; and
  - Ÿ our issuance of shares of common stock upon the exercise of an outstanding warrant concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share.

If the holder of the warrant instead exercises the warrant in full for cash, we would issue shares of common stock for cash proceeds of approximately $3.1 million. The cash exercise price of the warrant is $ per share.

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 September 30, 2004		
	Actual	Pro Forma	Pro Forma As Adjusted
		(unaudited) (in thousands, except share and per share data)	
Total long-term obligations	$ 2,553	$ 3,803	$
Redeemable convertible preferred stock, $0.001 par value, 60,736,705 shares authorized, issued and outstanding actual; no shares authorized, issued or outstanding pro forma and pro forma as adjusted	136,560	—	
Stockholders' equity (deficit):			
Common stock, $0.001 par value, 85,000,000 shares authorized actual, 125,000,000 shares authorized pro forma and shares authorized pro forma as adjusted; 1,887,356 issued and outstanding actual; shares issued and outstanding pro forma; shares issued and outstanding pro forma as adjusted	2	105	
Preferred stock, $0.001 par value, no shares authorized, issued or outstanding actual and pro forma; shares authorized and no shares issued and outstanding pro forma as adjusted	—	—	
Capital in excess of par value	1,225	170,582	
Common stock warrants	214	214	
Accumulated deficit	(117,835)	(117,835)	
Accumulated other comprehensive loss	—	—	
Total stockholders' equity (deficit)	(116,394)	53,066	
Total capitalization	$ 22,719	$ 56,869	$

The table above does not include:

- 7,350,311 shares of common stock issuable upon exercise of options outstanding as of September 30, 2004, at a weighted average exercise price of $0.64 per share, of which options to purchase 4,118,303 shares were exercisable; and
- 399,525 shares of common stock reserved for future grant under our 2000 equity incentive plan as of September 30, 2004.

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 September 30, 2004 was approximately $(116,954), or approximately $(61.97) per share, based on 1,887,356 shares of common stock outstanding as of September 30, 2004. Historical net tangible book value per share represents our total tangible assets less total liabilities divided by the actual number of our common stock outstanding.

As of September 30, 2004, the pro forma net tangible book value of our common stock was approximately $ million, or approximately $ 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 a one-for- reverse stock split of our common stock that will be effective prior to the completion of this offering, the issuance of additional shares of our convertible preferred stock on December 6, 2004, the conversion of all outstanding shares of our convertible preferred stock into 103,204,189 shares of common stock concurrently with the completion of this offering, the issuance of shares of our common stock upon conversion of an outstanding convertible promissory note concurrently with the completion of this offering based on an assumed initial public offering price of $ per share and the issuance of 1,612,903 shares of common stock upon the exercise of an outstanding warrant in full for cash concurrently with the completion of this offering.

Assuming the sale of the shares of our common stock offered by this prospectus at an assumed initial public offering price of $ per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us, our pro forma net tangible book value as of September 30, 2004 would have been $, or $ per share. This represents an immediate increase in pro forma net tangible book value of $ per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of $ 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		$
Historical net tangible book value per share	$ (61.97)	
Increase attributable to the conversion of the convertible preferred stock		
Pro forma net tangible book value per share before this offering	( )	
Increase per share attributable to new investors		
Pro forma net tangible book value per share after this offering		
Dilution per share to new investors		$

The following table summarizes, on a pro forma basis as of September 30, 2004, 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 $ 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		%	$	%	$
New investors					
Total		100%	$	100%	

The share data in the table above is based on shares outstanding as of September 30, 2004, counting as outstanding:

- 103,204,189 shares of common stock underlying all outstanding convertible preferred stock, including the additional shares of convertible preferred stock issued on December 6, 2004;
- shares of common stock issuable upon conversion of an outstanding convertible promissory note concurrently with the completion of this offering based on an assumed initial public offering price of $ per share; and
- 1,612,903 shares of common stock issuable upon exercise of an outstanding warrant in full for cash concurrently with the completion of this offering.

The share data in the table above excludes:

- 7,350,311 shares of common stock issuable upon the exercise of options outstanding as of September 30, 2004, at a weighted average exercise price of $0.64 per share, of which options to purchase 4,118,303 shares were exercisable; and
- 399,525 shares of common stock reserved for future grant under our 2000 equity incentive plan as of September 30, 2004.

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 % 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 shares, or approximately % 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, 2001, 2002 and 2003 and the balance sheet data as of December 31, 2002 and 2003 from our audited financial statements included in this prospectus. We have derived the statement of operations data for the year ended December 31, 2000 and the balance sheet data as of December 31, 2000 and 2001 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. We have derived the statement of operations data for the year ended December 31, 1999 and the balance sheet data as of December 31, 1999 from our unaudited financial statements not included in this prospectus. We have derived the statement of operations data for the nine months ended September 30, 2003 and 2004 and the balance sheet data as of September 30, 2003 and 2004 from our unaudited financial statements included in this prospectus. In the opinion of our management, these unaudited financial statements reflect all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of these financial statements. Our historical results for any prior or interim period are not necessarily indicative of the results to be expected for the fiscal year ending December 31, 2004 or for any other 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 shares of our convertible preferred stock outstanding as of December 31, 2003 and September 30, 2004 into 73,739,905 shares of common stock concurrently with the completion of this offering, as if the conversion had occurred at the date of the original issuance. This pro forma information does not give effect to the issuance of additional shares of our convertible preferred stock on December 6, 2004, to the conversion of an outstanding convertible promissory note or to the exercise of an outstanding warrant.

	Year ended December 31,					Nine months ended September 30,	
	1999	2000	2001	2002	2003	2003	2004
	(unaudited)		(in thousands, except share and per share data)			(unaudited)	
Statement of Operations Data:							
Net revenue	$ 2,350	$ 2,351	$ 1,703	$ 2,286	$ 2,458	$ 1,816	$ 1,581
Operating expenses:							
Research and development	2,104	3,675	8,152	16,244	18,179	13,376	17,782
General and administrative	1,436	1,653	2,302	4,135	3,600	2,698	3,764
Cost of product sales	—	—	—	244	743	540	28
Purchased in-process research and development	—	—	—	2,666	—	—	—
Total operating expenses	3,540	5,328	10,454	23,289	22,522	16,614	21,574
Loss from operations	(1,190)	(2,977)	(8,751)	(21,003)	(20,064)	(14,798)	(19,993)
Interest and dividend income	—	536	1,449	88	791	546	356
Interest expense	—	—	—	(103)	(122)	(96)	(96)
Loss on disposal of fixed assets	—	—	—	(54)	—	—	(4)
Net loss	(1,190)	(2,441)	(7,302)	(21,072)	(19,395)	(14,348)	(19,737)
Preferred stock accretion	—	(981)	(3,808)	(4,173)	(8,341)	(6,199)	(6,426)
Net loss attributable to common stockholders	$ (1,190)	$ (3,422)	$ (11,110)	$ (25,245)	$ (27,736)	$ (20,547)	$ (26,163)
Basic and diluted net loss per share applicable to common stockholders	$ (2,380.00)	$ (30.58)	$ (26.80)	$ (45.28)	$ (33.91)	$ (27.04)	$ (16.82)
Shares used to compute basic and diluted net loss per share	500	111,915	414,624	557,492	817,894	759,937	1,555,090
Pro forma basic and diluted net loss per share applicable to common stockholders (unaudited)					$ (0.27)		$ (0.26)
Shares used to compute pro forma basic and diluted net loss per share (unaudited)					71,118,629		75,294,995

	As of December 31,					As of September 30,	
	1999	2000	2001	2002	2003	2003	2004
	(unaudited)	(in thousands, except share and per share data)				(unaudited)	
Balance Sheet Data:							
Cash, cash equivalents and short-term investments	$ —	$ 28,053	$ 21,180	$ 49,361	$ 42,977	$ 42,433	$ 24,425
Working capital	1,305	27,654	20,371	46,685	40,526	45,934	21,054
Total assets	1,804	29,338	24,396	54,379	47,390	51,966	29,208
Long-term debt, net of current portion	—	—	—	2,088	1,462	1,622	1,654
Redeemable convertible preferred stock	—	54,418	58,365	108,026	130,134	127,992	136,560
Accumulated deficit	(6,335)	(27,581)	(38,691)	(63,936)	(91,672)	(84,515)	(117,835)
Total stockholders' equity (deficit)	36	(27,314)	(38,268)	(63,335)	(90,796)	(83,665)	(116,394)

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 by selectively targeting a class of receptors known as neuronal nicotinic acetylcholine receptors, or NNRs. We are developing small molecules designed to selectively target NNRs to treat diseases and disorders of the nervous system. Our product development pipeline consists of four product candidates in clinical development and multiple ongoing preclinical programs for target indications in which we believe that NNRs can be exploited for medical benefit. In addition, we market Inversine, which we believe is the only FDA-approved product that is designed to target an NNR.

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 acetylcholine 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 September 30, 2004, we had an accumulated deficit of $117.8 million. We expect to continue to incur substantial losses for the foreseeable future. We expect our research and development expenses to increase substantially following 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 as we expand our infrastructure. 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 our entering into new collaborations. 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 product available in the market, 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, our market research suggests that it is prescribed predominantly for the treatment of Tourette's syndrome and other neuropsychiatric disorders. Sales of Inversine generated revenue of $815,000 for the year ended December 31, 2003 and $584,000 for the nine months ended September 30, 2004.

We have entered into two collaboration agreements with Aventis. One of those collaboration agreements with Aventis will terminate on January 2, 2005. The other collaboration agreement with Aventis covers the research, development and commercialization of Aventis compounds for the treatment of Alzheimer's disease and other central nervous system diseases. As of September 30, 2004, we had received a total of $8.1 million in upfront license fees and payments for research and development services under the two agreements. In addition to royalties on potential product sales, we could receive up to $8.0 million under the continuing agreement upon the achievement of pre-commercialization development and regulatory milestones related to Alzheimer's disease and up to $8.0 million for each other central nervous system disease upon the achievement of pre-commercialization development and regulatory milestones related to that disease. The achievement of these milestones is uncertain. We may not receive any of these amounts or we may receive only a portion of them. The research term of this agreement is scheduled to expire in December 2004, and Aventis has informed us that it does not intend to extend the research term. We are only eligible to receive future payments from Aventis for any compounds that are selected for further development within six months after the expiration of the research term.

In addition, we have entered into a collaboration agreement with Dr. Falk Pharma covering the development and commercialization of our product candidate rivanicline for the treatment of ulcerative colitis. Upon effectiveness of the collaboration agreement in January 2001, Dr. Falk Pharma paid us a $1.0 million upfront license fee and purchased $1.0 million of our common stock. Pursuant to the terms of the agreement, we share rivanicline development costs for territories licensed to Dr. Falk Pharma equally with Dr. Falk Pharma.

We also recently entered into a development agreement with The Stanley Medical Research Institute relating to the development of our compound TC-1827 for the treatment of the cognitive impairment associated with schizophrenia. Upon effectiveness of the agreement in December 2004, The Stanley Medical Research Institute paid us $1.25 million in return for our issuance of a convertible promissory note in an equal principal amount.

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 appearing 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 non-refundable upfront license fees, research payments for ongoing research and development, payments associated with achieving development and regulatory 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 work is performed. We defer upfront payments and amortize them over the estimated research and development period. All revenue that we have recognized to date under these collaborations, or under government grants, is non-refundable. We recognize revenue from milestones with substantive performance risk upon achievement of the milestone. We have not yet received payment of any such 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.

Accrued Expenses

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves 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.

Purchased In-process Research and Development Expense

We determine the amount of any acquired in-process research and development expense based on an analysis of the cash flows that we expect to be generated by products that may arise from in-process technologies that we have acquired. As part of this analysis, we review the project rights that we acquire to determine the stage of their development, the probability of demonstrating sufficient safety and efficacy in clinical trials to obtain regulatory approval and product specific risk factors inherent in the drug development process. The product specific risk factors that we review include the type of drug under development, the likelihood of regulatory approval, manufacturing process capability, scientific rationale, preclinical and clinical safety and efficacy data, target product profile and development plans. Different estimates and assumptions for any of these factors would, if changed, result in a different estimate of in-process research and development expense.

In August 2002, we acquired from Layton Bioscience, Inc. marketing and trademark rights to Inversine and patent rights related to its active ingredient for cash consideration of $3.5 million. In allocating the purchase price, including the amount of in-process research and development, we considered an appraisal prepared by an

independent appraiser using established valuation techniques for the pharmaceutical industry. We allocated approximately $2.7 million of the purchase price to in-process research and development, which we expensed in connection with the acquisition.

Stock-Based Compensation

We account for our employee stock-based compensation in accordance with Accounting Principles Board Opinion No. 25 and related interpretations, or APB 25. Under APB 25, we do not recognize compensation expense when we issue stock options to employees and non-employee directors, unless the exercise price is below the fair market value of the underlying common stock on the date of grant. We recognize 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 $92,600 during 2001, $129,700 during 2002 and $65,300 during 2003. We amortize 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, or SFAS, No. 123, *Accounting for Stock-Based Compensation*, 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 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 $450,000 greater and our diluted net loss per share attributable to common stockholders would have been approximately $0.55 greater in 2003. 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 commercial product generating revenue. Sales of Inversine generated revenue of $815,000 for the year ended December 31, 2003 and $584,000 for the nine months ended September 30, 2004. We have entered into an exclusive distribution agreement with a third party 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.

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 recognize these non-refundable upfront license fees over the estimated research period of each of these agreements. We received research support payments from Aventis of $1.4 million for the year ended December 31, 2002, $1.3 million for the year ended December 31, 2003 and $209,000 for the nine months ended September 30, 2004. The research term of our one continuing agreement with Aventis ends in December 2004, and we do not expect to receive any future research support payments.

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 revenues 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 78% of our total operating expenses for the year ended December 31, 2001, 81% for the year ended December 31, 2002, 81% for the year ended December 31, 2003 and 82% for the nine months ended September 30, 2004.

Research and development expenses include 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;
- purchased in-process research and development;
- consulting, license and sponsored research fees paid to third parties; and
- depreciation of capital assets used to develop our products.

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 each of our four clinical-stage product candidates:

	Year ended December 31,			Nine months ended September 30,
Product Candidate	**2001**	**2002**	**2003**	**2004**
			(in thousands)	
Ispronicline	$ —	$ 976	$3,557	$ 3,175
TC-5231	—	61	852	2,442
Rivanicline	922	2,656	1,290	1,657
TC-2696	—	—	893	1,000
Total:	$922	$3,693	$6,592	$ 8,274

We expect to continue to incur substantial research and development expenses for the foreseeable future. We anticipate that these expenses will increase substantially in 2005 and in subsequent years as we continue to advance our clinical stage product candidates through the development process, to advance additional product candidates into clinical trials and to invest in promising product opportunities in our research 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, information technology and human resource functions. Other general and administrative expenses include facility costs not otherwise included in research and development expense, patent related costs, and professional fees for consulting, legal and accounting services. We expect that general and administrative expense will increase during 2004 and subsequent years due to increased payroll, expanded infrastructure, increased consulting, legal, accounting and investor relations expenses associated with being a public company and costs incurred to secure collaborations with respect to any of our product candidates.

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.

Purchased In-process Research and Development Expense

Purchased in-process research and development expense consists of an allocated portion of the purchase price for the marketing rights to Inversine and related assets that we acquired in August 2002. We expensed the entire allocated portion as of the date of acquisition. We have not recorded purchased in-process research and development expense in any period other than 2002.

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 $57.5 million as of September 30, 2004 and $46.1 million as of December 31, 2004. 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

Nine Months ended September 30, 2004 and 2003

Revenue. We recognized revenue of $1.6 million for the nine months ended September 30, 2004 compared to $1.8 million for the corresponding period in 2003. The decrease resulted from a decrease of $756,000 in research fee revenue generated from our collaboration agreement with Aventis relating to Aventis compounds, resulting from less activity under that agreement in 2004 as we progressed in late 2003 towards completion of the research requested by Aventis. We expect research fee revenues derived from that collaboration agreement in the fourth quarter of 2004 to decrease similarly as compared to the comparable period in 2003. The research term of that collaboration agreement expires on December 31, 2004. The decrease was partially offset by $585,000 of grant revenue recognized in the first nine months of 2004, compared to $67,000 recognized during the corresponding period in 2003. These grant revenues were derived from work performed under a cooperative agreement awarded to us in 2003 by the National Institute of Standards and Technology through its Advanced Technology Program to fund the development of sophisticated molecular simulation software. Inversine sales increased to $584,000 for the first nine months of 2004 compared to $582,000 for the corresponding period in 2003. We began selling Inversine in December 2002. In the fourth quarter of 2004, we will recognize the remaining $825,000 of deferred revenue related to our collaboration agreement with Aventis that will terminate on January 2, 2005.

Research and Development Expense. Research and development expense increased by $4.4 million, or 33%, to $17.8 million for the nine months ended September 30, 2004, from $13.4 million for the corresponding

period in 2003. The increase was primarily attributable to the costs associated with our four product candidates in clinical trials in the first nine months of 2004, compared to only two product candidates in clinical trials in the corresponding period of 2003. During the nine months ended September 30, 2004, we estimate that approximately 18% of our total research and development expenses were payments made to third parties in connection with our ispronicline program for conditions marked by cognitive impairment that afflict elderly persons, 14% were payments made to third parties in connection with our TC-5231 program for ADHD, 9% were payments made to third parties in connection with our portion of the costs of our rivanicline program for ulcerative colitis and 6% were payments made to third parties in connection with our TC-2696 program for pain. We spent the remaining 53% of our total research and development expenses on salaries, benefits, and infrastructure costs for our internal research and development capabilities and on other earlier stage programs and research efforts.

General and Administrative Expense. General and administrative expense increased by $1.1 million, or 39%, to $3.8 million for the nine-month period ended September 30, 2004, from $2.7 million for the corresponding period in 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 $443,000 related to expansion of our business development staff and an increase in spending on business development pursuits, $266,000 of additional patent related expenses and increases in our legal and other professional fees.

Cost of Product Sales. Cost of product sales for the nine months ended September 30, 2004 was $28,000 compared to $540,000 for the corresponding period in 2003. All of these costs related to sales of Inversine. The decrease in cost of product sales of $512,000 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 $190,000 to $356,000 for the nine months ended September 30, 2004, from $546,000 for the corresponding period in 2003. The decrease was primarily attributable to lower levels of cash and short-term investments.

Interest Expense. Interest expense was $96,000 for the nine months ended September 30, 2004, unchanged from the corresponding period in 2003.

Years ended December 31, 2003 and 2002

Revenue. Revenue increased to $2.5 million for the year ended December 31, 2003 from $2.3 million for 2002. The increase resulted primarily from the inclusion of a full year of Inversine sales in 2003 of $815,000, compared to a partial year of Inversine sales in 2002 of $243,000. We began selling Inversine in December 2002. License fee revenues decreased to $270,000 in 2003 from $635,000 in 2003 primarily as a result of revisions to the estimated research terms used as the basis for revenue recognition of the non-refundable upfront license fees that we received in our collaborations with Aventis and Dr. Falk Pharma.

Research and Development Expense. Research and development expense increased by $2.0 million, or 12%, to $18.2 million for the year ended December 31, 2003, from $16.2 million for 2002. The increase resulted principally from increased spending of $2.9 million on our later stage clinical programs and increased personnel and infrastructure costs of $539,000 associated with the expansion of our internal clinical development and regulatory affairs capabilities. This was offset in part by a decrease of $1.8 million resulting from the conclusion in 2002 of a program to screen several of our preclinical candidates to select those to advance into clinical trials. During the year ended December 31, 2003, we estimate that approximately 20% of our total research and development expenses were payments made to third parties in connection with our ispronicline program for conditions marked by cognitive impairment that afflict elderly persons, 5% were payments made to third parties

in connection with our TC-5231 program for ADHD, 7% were payments made to third parties in connection with our portion of the costs of our rivanicline program for ulcerative colitis and 5% were payments made to third parties in connection with our TC-2696 program for pain. We spent the remaining 63% of our total research and development expense on salaries, benefits, and infrastructure costs associated with our internal research and development capabilities and on other earlier stage programs and research efforts.

General and Administrative Expense. General and administrative expense decreased by $536,000, or 13%, to $3.6 million for the year ended December 31, 2003, from $4.1 million for 2002. This decrease resulted principally from a decrease of $330,000 from the costs incurred in 2002 associated with our relocation to a new leased facility, severance costs of $257,000 and a reduction in patent related costs in 2003 compared to 2002. In 2003 we increased our spending on the development of the administrative infrastructure necessary to enable us to expand our operations, support our development efforts and facilitate the additional reporting and regulatory requirements related to becoming a public company.

Cost of Product Sales. Cost of product sales increased to $743,000 for the year ended December 31, 2003, from $244,000 for 2002. The increase in cost of product sales for 2003 resulted primarily from increased sales of Inversine.

Interest and Dividend Income. Interest and dividend income increased by $703,000 to $791,000 for the year ended December 31, 2003, from $88,000 for 2002. The increase resulted from substantially higher average cash balances during 2003 as a result of the funds we received from the sale of shares of our series C convertible preferred stock. We raised $45.5 million in this financing in November 2002 and $13.8 million in March 2003.

Interest Expense. Interest expense was $123,000 for the year ended December 31, 2003 compared to $103,000 for 2002.

Years ended December 31, 2002 and December 31, 2001

Revenue. Revenue increased to $2.3 million for the year ended December 31, 2002 from $1.7 million for 2001. The increase resulted principally from an increase of $289,000 in research fee revenue generated from our Aventis collaboration as a result of higher levels of research activity and Inversine sales of $243,000 in December 2002 when we began selling the product.

Research and Development Expense. Research and development expense increased by $8.0 million, or 98%, to $16.2 million for the year ended December 31, 2002, from $8.2 million for 2001. The increase resulted principally from $1.8 million in costs attributable to a program to screen several of our preclinical candidates to ascertain those to advance into clinical trials, increased spending of $1.7 million to fund our portion of the costs of third-party services in connection with the rivanicline program for ulcerative colitis, and $1.0 million for preclinical studies, toxicology and regulatory expenses directed towards advancing ispronicline into clinical trials. We also incurred increased salary and benefits costs as we expanded our product development capabilities with the hiring of experienced key personnel. In addition, we incurred increased infrastructure costs in connection with our relocation in March 2002 to a new leased facility which includes expanded lab and research space. This also resulted in higher depreciation charges associated with the new equipment and furnishings that we acquired.

General and Administrative Expense. General and administrative expense increased by $1.8 million, or 80%, to $4.1 million for the year ended December 31, 2002, from $2.3 million for 2001. This increase resulted from our investment in the administrative infrastructure necessary to enable us to expand our operations, to support our development efforts and to attract and hire members of executive management. In the first quarter of 2002, we relocated our operations to a new leased facility. The costs of the relocation were approximately $330,000, and the new facility increased our occupancy related costs in 2002 by $661,000 compared to 2001. Salary and benefits expenses increased by $498,000, which included the costs associated with the addition of a chief financial officer in the first quarter of 2002 and severance costs. In 2002 we also increased our spending on professional fees related to business development, legal and public relations services.

Cost of Product Sales. Cost of product sales for the year ended December 31, 2002 was $244,000. All of these sales related to Inversine, which we began selling in December 2002. We had no cost of product sales expenses for the year ended December 31, 2001.

Interest and Dividend Income. Interest and dividend income decreased by $1.4 million to $88,000 for the year ended December 31, 2002. The decrease resulted from substantially lower average cash balances during 2002 compared to 2001 and lower interest rates during the year.

Interest Expense. Interest expense was $103,000 for the year ended December 31, 2002. The interest expense related to outstanding indebtedness on a loan facility established to finance equipment and other fixed assets. We had no interest expense for the year ended December 31, 2001.

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 September 30, 2004, we had derived aggregate net proceeds of $88.4 million from these private placements. In December 2004, we completed an additional private placement of convertible preferred stock from which we derived aggregate net proceeds of $32.9 million. 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 September 30, 2004, we have received $10.0 million under our collaboration agreements. We continue to receive research support payments under only one of these collaboration agreements, and the research term of that agreement ends in December 2004. We also received loan proceeds of $1.25 million in December 2004 from The Stanley Medical Research Institute in connection with a development agreement relating to the development of our compound TC-1827 for the treatment of the cognitive impairment associated with schizophrenia. We began generating revenues from product sales of Inversine in December 2002. To date, the net contribution of Inversine sales have not been a significant source of cash and we do not expect them to be a significant source in the future.

Our cash, cash equivalents and short-term investments were $24.4 million as of September 30, 2004, $43.0 million as of December 31, 2003 and $49.4 million as of December 31, 2002. As noted above, in December 2004, we completed an additional private placement of convertible preferred stock from which we derived aggregate net proceeds of $32.9 million.

Cash Flows

Net cash used for operating activities was $18.8 million for the nine months ended September 30, 2004, reflecting a net loss of $19.7 million offset primarily by an increase of $1.0 million in accounts payable and accrued expenses resulting from increased commitments related to our clinical trials. 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 for operating activities was $17.1 million for the year ended December 31, 2002, reflecting a net loss of $21.1 million partially offset by non-cash charges for acquired in-process research and development of $2.7 million and depreciation and amortization of $1.0 million. Accounts payable and accrued expenses increased by $1.5 million as of December 31, 2002, compared to December 31, 2001 primarily as a result of an increase in outsourced development activities with contract research organizations.

Net cash used in investing activities was $556,000 for the nine months ended September 30, 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. Investing activities for the year ended December 31, 2002, exclusive of cash flows from the purchase and sale of investments, included the use of $1.3 million for the purchase of equipment and furniture, the use of $3.5 million for the purchase of the marketing rights to Inversine and related assets from Layton Bioscience, Inc. and the receipt of a $2.0 million rent incentive from the owner of our facilities in connection with our entering into a lease with a minimum five-year term.

Net cash used in financing activities was $1.0 million for the nine months ended September 30, 2004. As of September 30, 2004, we had borrowing capacity of $1.0 million available under our equipment financing loan facility. We borrowed $1.0 million under the facility in April 2004 to finance equipment that we had previously purchased. 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. Net cash provided by financing activities for the year ended December 31, 2002 was $48.2 million and consisted principally of net proceeds of $45.5 million from the issuance of shares of our series C convertible preferred stock and proceeds of $3.0 million from long-term debt, comprised of a $2.5 million equipment financing loan repayable over 48 months and a $500,000 incentive loan from the City of Winston-Salem which requires no repayments and carries no interest charges for the initial five years, partially offset by $325,000 of equipment financing principal repayments.

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. In April 2004, we borrowed $1.0 million under the amended loan facility to finance equipment. This borrowing bears a fixed interest rate of 5.9%, is payable in 48 equal monthly installments and matures in April 2008. All borrowings under the loan facility are secured by specified tangible fixed assets. As of September 30, 2004, the outstanding principal balance under the loan facility was $2.1 million.

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 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 $1.25 million convertible promissory note to The Stanley Medical Research Institute. The note bears interest at 10% per annum and matures on January 1, 2007. However, if not earlier paid, the outstanding principal and accrued interest under the note will automatically convert into shares of our common stock concurrently with the completion of this offering at a conversion price equal to the initial public offering price.

Funding Requirements

We have incurred significant losses since our inception. As of September 30, 2004, we had an accumulated deficit of $117.8 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 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.

Although we currently have not specifically identified any material commitments for capital expenditures, 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. 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, together with the net proceeds from this offering, will be sufficient to fund our operations through the end of 2006. 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.

We do not expect to generate sufficient cash from our operations to sustain our business for the foreseeable future. Unless we are able to do so, we expect our continuing operating losses to result in increases in our cash used in 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, 2003:

	Payments due by period (in thousands)				
Contractual Obligations	**Total**	**2004**	**2005-2007**	**2008-2009**	**After 2009**
Long-term debt	$ 2,038	$ 576	$ 962	$ 163	$ 337
Operating leases	5,216	1,456	2,911	849	—
Other contractual obligations	4,220	3,984	230	6	—
Total	$11,474	$6,016	$ 4,103	$ 1,018	$ 337

The amounts reflected in the above table do not include contingent payments for milestones and royalties on potential product sales that we may become obligated to make under technology license agreements to which we are a party. The amounts of long-term debt reflected in the above table include both principal and interest payments. The amounts of long-term debt reflected in the above table do not include the $1.25 million

convertible promissory note that we issued on December 15, 2004. If not earlier paid, the outstanding principal and accrued interest under the note will automatically convert into shares of our common stock concurrently with the completion of this offering.

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 September 30, 2004, we had cash, cash equivalents and short-term investments of $24.4 million consisting of cash and highly liquid investments 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 adjusted our portfolio in April 2004 to eliminate positions in investments that were subject to potentially significant interest rate risks.

We contract for the conduct of certain of our clinical trials and other research and development and manufacturing activities with contract research organizations, investigational sites and manufacturers in Europe. 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

During 2003, the Financial Accounting Standards Board, or the FASB, issued Interpretation No. 46, *Consolidation of Variable Interest Entities*, or FIN 46, which is an interpretation of Accounting Research Bulletin No. 51, *Consolidated Financial Statements*. FIN 46 requires that, if an entity has a controlling interest in a variable interest entity, the assets, liabilities and results of activities of the variable interest entity should be included in the consolidated financial statements of the entity. FIN 46 is effective immediately for all new variable interest entities created or acquired after January 31, 2003. For variable interest entities created or acquired prior to February 1, 2003, the provisions of FIN 46 must be applied in the first interim or annual period beginning after June 15, 2003. We implemented the provisions of FIN 46 for our financial statements for the year ended December 31, 2003. We have no investment in or contractual relationship or other business relationship with a variable interest entity. Therefore, the adoption of FIN 46 did not affect our financial position or results of operations.

In May 2003, the FASB issued SFAS No. 150, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity*. SFAS 150 establishes how a company classifies and measures certain financial instruments with characteristics of both liabilities and equity, including redeemable convertible preferred stock. SFAS 150 is effective for financial instruments entered into or modified after May 31, 2003 and otherwise effective at the beginning of the interim period commencing July 1, 2003, except for mandatory redeemable financial instruments of nonpublic companies. The adoption of SFAS 150 did not affect our financial position or results of operations.

In October 2004, the FASB announced that FASB Statement No. 123R, *Share-Based Payment*, which would require all companies to measure compensation cost for all share-based payments, including employee stock options, at fair value, would be effective for public companies for interim or annual periods beginning after June 15, 2005. SFAS 123R would require companies to expense the fair value of all stock options that have future vesting provisions, are modified or are newly granted beginning on the grant date of such options. We will evaluate the requirements of the final standard, which is expected to be issued in December 2004, to determine the impact on our financial position and results of operations.

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 by selectively targeting neuronal nicotinic acetylcholine receptors, or NNRs. NNRs are found on nerve cells throughout the human 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 acetylcholine 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 nervous system by selectively affecting specific NNR subtypes. We are developing drugs that target NNRs to treat diseases and disorders of the nervous system.

Our product development pipeline consists of four product candidates in clinical development and multiple ongoing preclinical programs for target indications in which we believe that NNRs can be exploited for therapeutic benefit. Our pipeline includes:

- Ispronicline—in Phase II clinical development for the treatment of conditions marked by cognitive impairment that afflict elderly persons;
- TC-5231—in Phase II clinical development for the treatment of attention deficit hyperactivity disorder, commonly referred to as ADHD;
- Rivanicline—in Phase II clinical development for the treatment of ulcerative colitis;
- TC-2696—in Phase I clinical development for the treatment of pain; and
- preclinical research programs in schizophrenia, depression and anxiety, smoking cessation and obesity.

Our product candidate for ADHD, TC-5231, is mecamylamine hydrochloride, the active ingredient in our commercial product Inversine, but in a lower dose than Inversine.

We believe that Inversine is the only FDA-approved product designed to target an NNR. Inversine is approved for the management of moderately severe to severe essential hypertension, a high blood pressure disorder with an unknown origin. Our market research suggests, however, that Inversine is prescribed predominantly for the treatment of Tourette's syndrome and other neuropsychiatric disorders at lower doses than indicated for the treatment of hypertension. Because we recognized the potential for mecamylamine hydrochloride as a treatment for ADHD, we acquired patent rights covering its use for neuropsychiatric disorders, as well as the marketing rights to Inversine, in 2002.

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 20 years. Together with our proprietary assays and novel screening methods, 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 results while limiting or potentially eliminating side effects.

We have a collaboration agreement with Aventis Pharma SA that covers the research, development and commercialization of Aventis compounds for the treatment or prevention of Alzheimer's disease and other diseases of the central nervous system. In addition, we have a collaboration agreement with Dr. Falk Pharma GmbH, a German company with a focus on treatments for gastrointestinal diseases, that covers the research, development and commercialization of our product candidate rivanicline for the treatment or prevention of ulcerative colitis. We also recently entered into a development agreement with The Stanley Medical Research Institute relating to the development of one of our compounds for the treatment of the cognitive impairment associated with schizophrenia.

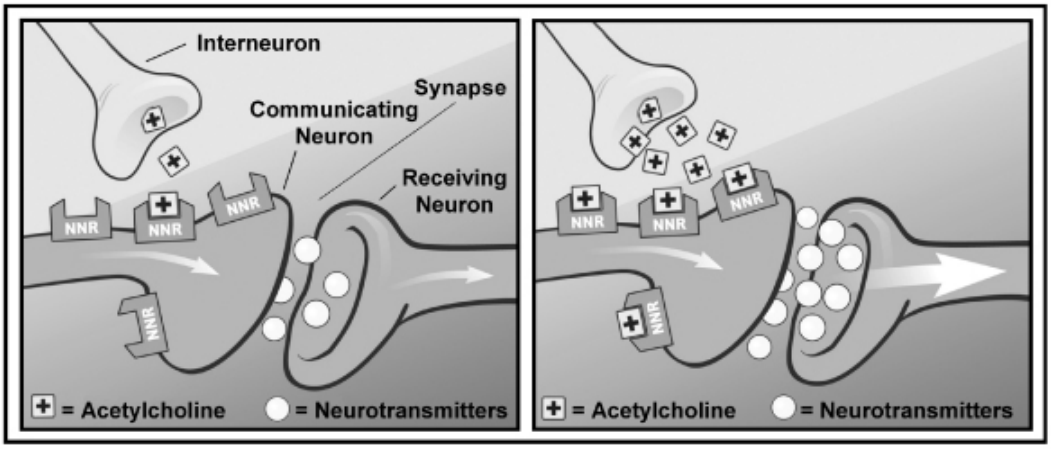
Role of NNRs in the Nervous System

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 when electrical impulses of a communicating neuron are converted into chemicals called neurotransmitters. This occurs at the gap between a communicating neuron and a receiving neuron known as a synapse. When released by a communicating neuron, neurotransmitters 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
$a7_5$	sensory gating; cognition	schizophrenia; cognitive impairment
$a4_2ß2_3$	cognition pain perception	Alzheimer's disease; AAMI; MCI; ADHD acute, chronic and neuropathic pain
$a3_2ß2_3$	gastrointestinal tone	ulcerative colitis
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 with 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 acetylcholine receptors in the muscles and 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 while limiting or potentially eliminating 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 believe that our four product candidates in clinical development may exhibit these attributes and we are aggressively pursuing their development. In addition, we use our scientific expertise and Pentad to identify additional compounds that selectively target specific NNR subtypes as potential treatments for diseases and disorders of the central nervous system and our other target indications.
- *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 85 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.
- *Collaborate selectively to develop and commercialize product candidates.* We intend to selectively enter into 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.
- *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;
- gastrointestinal diseases and disorders;
- 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. The Business Insights Healthcare Report published in association with Reuters estimated the total worldwide CNS pharmaceutical market to be $63.3 billion in 2003. Three of the top ten selling drugs in the world in 2003, Pfizer's Zoloft, Eli Lilly's Zyprexa and GlaxoSmithKline's Paxil/Seroxat, 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 disorders. We are conducting clinical development of our product candidates for use in the treatment of particular CNS disorders such as AAMI, ADHD and pain. We are also conducting clinical development of one of our product candidates for use in the treatment of the gastrointestinal disease ulcerative colitis.

Cognitive Impairment in the Elderly

Cognition refers to a collection of mental processes that enable the acquisition, storage, retrieval and use of information. Cognitive functions such as attention, learning and memory underlie fundamental day-to-day activities. Impairment of these functions can impact an individual's ability to function effectively and, in severe cases, to maintain quality of life. Cognitive impairment is particularly prominent in the growing elderly population. The most severe form of cognitive impairment is dementia, which can render a person unable to care for himself or herself. The most common form of dementia in the elderly is Alzheimer's disease. Cognitive impairment without dementia ranges in severity from age associated memory impairment, commonly known as AAMI, to mild cognitive impairment, commonly known as MCI.

Alzheimer's disease progressively impairs memory, reason, judgment, language and eventually the ability to carry out simple tasks. It may also be accompanied by other symptoms like anxiety, depression and personality changes. The Business Insights Healthcare Report estimates that Alzheimer's disease affects approximately 13.5 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 epidemiological studies 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, a provider of business information for the pharmaceutical and other industries, estimates that the worldwide market for Alzheimer's disease therapies was approximately $2.6 billion in 2003.

The term 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. The term 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." A number of published clinical trials have been conducted in AAMI or similarly characterized conditions. 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.

MCI is typically marked by memory problems that are more severe than in AAMI, but without other characteristics that would result in a diagnosis of dementia. A person who scores at least one and one-half standard deviations below the mean established for his or her age-matched peers on a standardized memory test may be classified with MCI. Datamonitor, another provider of business information for the pharmaceutical and other industries, estimates that MCI affects nearly 15 million people in the world's seven major pharmaceutical markets, including approximately 5 million people in the United States. Researchers have estimated that 10% to 15% of persons with MCI are diagnosed with Alzheimer's disease each year. Like AAMI, MCI is not currently listed in DSM-IV. However, there is ongoing discussion in the medical community as to its status as a distinct clinical classification. The FDA has acknowledged reviewing clinical trial protocols for MCI, and we are aware of clinical trials that have been conducted for MCI.

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 severe Alzheimer's disease. There are currently no products approved by the FDA for the treatment of AAMI or MCI. We believe that, when AAMI or MCI is treated at all, physicians typically prescribe acetylcholinesterase inhibitors. We believe that acetylcholinesterase inhibitors have limitations in that only about half of Alzheimer's disease patients who take them show symptomatic improvement and they do not substantially delay the progressive deterioration and death of cells in the brain that can lead to more severe impairment and debilitation.

Attention Deficit Hyperactivity Disorder

ADHD is the most commonly diagnosed childhood behavioral disorder. ADHD is characterized by varying degrees of developmentally inappropriate inattention, hyperactivity and impulsivity. Children with ADHD may have difficulty functioning at home, at school and in peer relationships. The disorder has been linked to long-term adverse effects on academic performance, success in the workplace and social and emotional development. According to a published study, two-thirds of children diagnosed with ADHD will continue to show attention deficit symptoms into adult life, although the hyperactivity typically seen in children is diminished.

Datamonitor estimates that ADHD affects approximately 8 million youths in the world's seven major pharmaceutical markets, including 4.8 million in the United States. Espicom Business Intelligence estimates that the worldwide market for ADHD drugs was approximately $1.8 billion in 2003.

We believe that the currently available treatments for ADHD have significant drawbacks or limitations. In particular, many current treatments such as Ritalin and Adderall are stimulants. Parents and physicians are often reluctant to administer stimulants to children because of concerns over addiction, abuse and side effects such as weight loss. One non-stimulant, Strattera, has been approved by the FDA to treat ADHD. However, it can cause side effects such as constipation, nausea and vomiting and may not be as effective in treating ADHD as stimulants.

Ulcerative Colitis

Ulcerative colitis is a chronic form of inflammatory bowel disease that is characterized by inflammation of the lining of the colon. The various types of ulcerative colitis are classified according to the location and extent of the inflammation, including left-sided colitis, which involves inflammation that extends up the left or descending colon, and pancolitis, which affects the entire colon. We believe that left-sided colitis represents about 40% to 60% of all cases of ulcerative colitis. The majority of ulcerative colitis patients suffer from repeated acute episodes.

Datamonitor estimates that ulcerative colitis affects approximately 920,000 people in the world's seven major pharmaceutical markets, including approximately 670,000 people in the United States.

Ulcerative colitis is typically treated with a variety of forms of the drug commonly known as 5-ASA, such as Asacol. More severe cases of ulcerative colitis are treated with steroids. We believe that there are limitations to these treatments, as the National Institute of Diabetes and Digestive and Kidney Diseases estimates that 25% to 40% of all ulcerative colitis patients ultimately require surgery to remove all or a portion of the colon.

Pain

There are two general categories of pain, nociceptive and neuropathic. 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. 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 $20 billion in 2003. That report estimates that approximately 80 million people in the world's seven major pharmaceutical markets suffer annually from acute nociceptive pain following a surgical procedure. Datamonitor estimates that 39 million people worldwide 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 such as morphine. Prolonged use of opioids, however, may result in a tolerance to the drug, ultimately making it ineffective. In addition, the use of opioids can 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

Our product development pipeline consists of four product candidates in clinical development and multiple ongoing preclinical programs for target indications in which we believe that NNRs can be exploited for therapeutic benefit. We also have one marketed product, Inversine, that is approved in the United States for the management of moderately severe to severe essential hypertension and that we believe is prescribed predominantly for the treatment of Tourette's syndrome and other neuropsychiatric disorders. Except for Inversine, neither the FDA nor any foreign regulatory authority has approved any of our product candidates for marketing.

Our product candidates in clinical development are summarized in the table below.

Product Candidate	Target Indications	Stage of Development	Status of Development	Commercial Rights
Ispronicline (TC-1734)	Conditions marked by cognitive impairment that afflict elderly persons	Phase II	Treatment phase complete for initial Phase II trials; full data expected in December 2004	Targacept worldwide
TC-5231	ADHD	Phase II	Treatment phase complete; data expected in December 2004	Targacept worldwide
Rivanicline (TC-2403)	Ulcerative colitis	Phase II	Treatment phase complete; data expected in December 2004	Dr. Falk Pharma –Europe, Russia, Egypt and Israel Targacept –United States and rest of world
TC-2696	Acute post-operative pain	Phase I	Treatment phase complete for initial Phase I trial; data expected in December 2004	Targacept worldwide

We conducted two Phase II clinical trials of ispronicline in the United Kingdom. We conducted our Phase II clinical trial of TC-5231 in children and adolescents in the United States. We conducted our Phase II clinical trial of rivanicline in the United States, Canada and Eastern Europe. We conducted our initial Phase I clinical trial of TC-2696 in France.

Ispronicline

Ispronicline (TC-1734) is a novel small molecule that we are developing as an oral treatment for conditions marked by cognitive impairment that afflict elderly persons, including Alzheimer's disease and AAMI. We have completed the treatment phase of a Phase II clinical trial of ispronicline in 76 elderly persons classified with AAMI. We have also completed the treatment phase of a Phase II clinical trial in 40 elderly persons classified 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 ispronicline 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, 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 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, ispronicline 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, ispronicline 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 ispronicline has the potential to prevent or delay neurodegeneration.

We are also evaluating ispronicline for potential additional clinical development for other indications such as cognitive impairment associated with schizophrenia, cognitive impairment following coronary artery bypass grafting, MCI, ADHD and various forms of dementia.

Clinical Development of Ispronicline

Phase I Clinical Trials. During 2003, we completed four Phase I clinical trials of ispronicline 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 48 volunteers, 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 24 volunteers, 50mg, 100mg and 200mg doses of ispronicline 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 a pharmacokinetic trial, six elderly volunteers were given a single 80mg dose to assess the compound's absorption, distribution, metabolism and excretion. 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 were administered an 80mg dose with or without having eaten and the compound was well tolerated.

Phase II Clinical Trials. In the fourth quarter of 2004, we completed the treatment phase of the last arm of a double blind, placebo-controlled Phase II clinical trial of ispronicline in 76 elderly persons classified with AAMI. We conducted the trial at multiple sites in the United Kingdom under a clinical trial exemption, the United Kingdom equivalent to an IND. The primary objective of this trial is to assess the safety and tolerability of ispronicline in elderly subjects compared to placebo. The secondary objectives of this trial are to assess the efficacy of ispronicline in improving cognitive function and changes in mood state.

In 2004, we also completed the treatment phase of a double blind, placebo-controlled clinical trial of ispronicline in 40 elderly volunteers classified with MCI. This trial has similar objectives to the AAMI trial and was also conducted in the United Kingdom.

In the AAMI trial, the subjects were divided into three dose groups – 20 subjects in the 50mg group, 20 subjects in the 100mg group, 20 subjects in the 125mg dose group and 16 subjects in the 150mg group. In the MCI trial, the subjects were divided into 50mg and 100mg dose groups of 20 subjects each. In both trials, each subject was initially dosed either with the applicable dose of ispronicline 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 ispronicline, as the case may be, daily for another three-week period. Each subject took ispronicline 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 and mood state before and after dosing on the first day of the three-week dosing period and then again on the last day of the 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 trials, we tested subjects for changes in cognitive function using a computer-based test battery developed by CDR Ltd. This 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. CDR has indicated that its battery has been used to assess cognitive performance in over 500 clinical trials worldwide. We also used the CDR test battery in our Phase I clinical trials of ispronicline. We selected it because of its comprehensive measures and CDR's extensive database of test results in unimpaired persons that enable assessment of clinical relevance.

In the 50mg and 100mg arms of the AAMI trial, ispronicline was well tolerated, with no serious adverse events reported. In addition, subjects in the 50mg dose group that received ispronicline showed improvements in measures of attention, speed of cognitive processes and memory as compared to subjects receiving placebo. These results were 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. The improvements observed in the 50mg dose group ranged from a p-value of 0.008 to a p-value of 0.043. These effects were consistent with the effects seen in our Phase I trials. The positive effects that we observed in the 50mg dose group were less pronounced in the 100mg dose group, which is consistent with the dose-related effects on cognition that we observed in our preclinical animal studies. In the 150mg dose group, three out of eight subjects treated with ispronicline experienced side effects such as headache, lightheadedness, dizziness and vomiting and dropped out of the trial. In light of these effects, we ceased dosing new subjects at 150mg. The results of the AAMI trial suggest that ispronicline is well tolerated at a dose range of up to 100mg, that 150mg is the maximum tolerated dose of ispronicline for this trial design and that the compound had positive effects on cognition at a dose within the tolerated range.

To generate additional data related to the tolerability of ispronicline, we are also testing eight elderly persons classified with AAMI at a dose of 150mg, after having eaten, using the same trial design. This will enable us to assess the impact of food on the tolerability of ispronicline by comparing it in volunteers dosed at 150mg who have eaten and in volunteers dosed at 150mg who have not eaten.

Plans for Future Development. We plan to meet with the FDA regarding whether AAMI is an indication for which the FDA would approve a drug and, if so, the additional trials that we would need to perform to support an application for approval of ispronicline for the treatment of AAMI. Following these discussions with the FDA, we expect to evaluate the specific target indication or indications for continued clinical development of ispronicline. Subject to the results of our discussions with the FDA, we anticipate commencing a separate Phase II clinical trial designed to evaluate the efficacy of ispronicline in the fourth quarter of 2004.

TC-5231

TC-5231 is a small molecule that we are developing as an oral treatment for ADHD. TC-5231 is a low-dose reformulation of mecamylamine hydrochloride, the active ingredient in our FDA-approved product, Inversine. Inversine is approved in the United States for the management of moderately severe to severe essential hypertension at average daily doses of 25mg. Our market research suggests, however, that Inversine is prescribed predominantly for the treatment of Tourette's syndrome and other neuropsychiatric disorders at doses ranging from 2.5mg to 7.5mg. We have reformulated mecamylamine hydrochloride as TC-5231 in a liquid gel cap. We

are evaluating this product candidate in doses between 0.2mg and 1.0mg in two Phase II clinical trials, one in ADHD in children and adolescents and one in ADHD in young adults.

In published studies conducted by third parties, mecamylamine hydrochloride at low doses:

- improved attention and reduced mood instability and rage outbursts in a double-blind, placebo-controlled study of 61 children and adolescent patients with Tourette's syndrome in the United States; and
- improved memory in animals.

Although the means by which mecamylamine hydrochloride acts to cause these effects is not known, scientists have suggested that it may prevent interference with the activity of the a4ß2 NNR, which regulates neurotransmitters involved in attentional processes such as dopamine, norepinephrine and serotonin, or it may block a4ß2 from releasing the neurotransmitter GABA, which inhibits attentional processes.

The results of human and animal studies in which nicotine was shown to improve cognition also suggest the potential for drugs that target NNRs to treat ADHD. For example, in a placebo-controlled study with 34 adult non-smokers conducted by researchers at Duke University, nicotine was as effective in improving symptoms of ADHD as the active ingredient in Ritalin, a stimulant that is commonly prescribed for the treatment of ADHD. At low doses, mecamylamine hydrochloride shows pharmacological effects that are similar to those of nicotine.

Based on these study results, we believe that TC-5231 may have a positive effect in the treatment of ADHD. Moreover, decades of adult use of Inversine at substantially higher doses than TC-5231 suggest that the compound may not exhibit the side effects characteristic of existing treatments for ADHD.

Clinical Development of TC-5231

Phase II Trial in Children and Adolescents. We have completed the treatment phase of a flexible dose, double blind, placebo-controlled, Phase II clinical trial of TC-5231 in children and adolescents with ADHD. We enrolled 176 patients between the ages of 6 and 17 into the treatment phase of the trial at 14 sites in the United States. The primary objective of this trial is to determine whether TC-5231 is effective in the treatment of symptoms of ADHD in subjects within this age group. The trial will also assess the safety, tolerability and pharmacokinetics of TC-5231. In addition, because mecamylamine hydrochloride at the Inversine dose is used to treat forms of hypertension, an independent safety board monitored the effects of TC-5231 on subjects' blood pressure.

In the trial, each patient was randomly selected to receive either drug or a placebo each day for six weeks. Each patient selected to receive the drug was administered a 0.2mg dose of TC-5231 for the first two weeks of the trial. Based on the investigating physician's assessment of tolerability of the 0.2mg dose, the physician could elect to increase the dose to 0.5mg for the next two weeks, or could elect to maintain the dose for the next two weeks at 0.2mg. Following that second two-week period, the investigating physician could again elect to increase the dose either to 0.7mg or 1.0mg, or maintain the existing dose for a third two-week period. The maximum dosage for subjects under the age of 13 was 0.7mg and the maximum dosage for subjects aged 13 to 17 was 1.0mg. The primary efficacy endpoint in this trial is the change after six weeks of therapy in a subject's score on a standard rating system for ADHD patients known as the ADHD rating scale. This is an 18-item rating scale in which the investigating physician measures attention, hyperactivity and impulsivity of the subject. Secondary endpoints include changes in ratings on other standard rating scales. We expect the results of this trial to be available in December 2004.

Phase II Trial in Young Adults. We have contracted with a physician-investigator to conduct a placebo-controlled, Phase II clinical trial of TC-5231 on our behalf. This trial is being conducted in the United States with 12 ADHD patients between the ages of 17 and 24. In the trial, the investigator doses patients once per week over a five-week period. Each week patients receive one of a 0.2mg, 0.5mg or 1.0mg dose of TC-5231, nicotine administered via patch or a placebo. The primary objective of the trial is to measure effects of TC-5231 on

sustained attention. In particular, the trial measures the time needed for a patient to cancel a planned movement, referred to as "stop signal reaction time," as well as other aspects of attention. In addition, the investigator is measuring performance on a word recognition test. The investigator has advised us that the trial will be completed and the results available in the first quarter of 2005.

Plans for Future Development. If the results of our Phase II clinical trials are favorable, we plan to conduct Phase III clinical trials of TC-5231 for the treatment of ADHD in children and possibly adults.

Rivanicline

Rivanicline (TC-2403) is a small molecule that we are developing for the treatment of ulcerative colitis in collaboration with Dr. Falk Pharma GmbH. We are currently conducting a Phase II clinical trial of an enema formulation of the compound designed to induce remission of acute episodes of left-sided colitis. In addition, we are developing a delayed release oral formulation of the compound designed to deliver the drug to the entire colon to induce and maintain remission of additional forms of ulcerative colitis. We expect to complete the oral formulation of this product candidate in the first quarter of 2005.

Ulcerative colitis is characterized by inflammation of the lining of the colon. Our preclinical studies of rivanicline suggest that the compound interacts with the a3b2 NNR that is present in nerve endings in the gastrointestinal tract. We believe that a3b2 may play an important role in preventing inflammation and maintaining the lining of the colon. In other preclinical in vitro studies that we conducted, rivanicline inhibited the release of proteins called cytokines that cause inflammation in humans and did not interact significantly with nicotinic acetylcholine receptors in the peripheral tissues associated with side effects like nausea and cardiovascular effects.

Rivanicline is related structurally to nicotine, and studies have shown that nicotine has positive effects for limited periods in treating the symptoms of ulcerative colitis. Specifically, in published third-party studies involving humans and animals, nicotine modulated the release of acetylcholine from nerves, increased secretion of mucus in the colon, inhibited the production of cytokines and reduced chemicals called prostaglandins that are involved in the process of inflammation. Collectively, these effects would help to maintain the normal structure of the colon. Also, in published studies conducted at the Mayo Clinic, nicotine was administered to non-smoking ulcerative colitis patients either via a nicotine patch or an enema. In these studies, remission of ulterative colitis symptoms and tissue healing was observed in approximately 40% of patients treated with the patch, as compared to 9% of patients treated with placebo, and approximately 70% of patients treated with an enema. Unlike the patch study, the enema study was not placebo controlled. However, serious side effects like nausea were observed in patients treated with nicotine, particularly when administered via patch. Because rivanicline is designed to selectively target the a3b2 NNR, we believe that it may have positive effects on ulcerative colitis similar to those of nicotine, but without the side effects.

Clinical Development of Rivanicline

Phase I Clinical Trials. We conducted two Phase I, placebo-controlled clinical trials of the enema formulation of rivanicline, including:

- a single rising dose trial in which 32 healthy volunteers received rivanicline enemas in dosages ranging from 5mg to 800mg; and
- a multiple rising dose trial in which 12 volunteers received rivanicline enemas in dosages of 50mg, 200mg and 400mg over a period of 14 days.

In each trial, rivanicline was well tolerated and we observed no clinically significant adverse events.

Phase II Clinical Trial. We have completed the treatment phase of a double blind, placebo-controlled, dose range finding Phase II clinical trial designed to determine whether rivanicline in the enema formulation is effective in treating mild to moderate left-sided colitis. In the trial, 240 patients were enrolled at 35 sites in the

United States, 10 sites in Canada and 26 sites in three Eastern European countries. Two contract research organizations monitored and managed the trial for us.

In the trial, patients were administered an enema with 100mg, 200mg or 400mg of rivanicline or a placebo each day over six weeks. Endoscopic examinations of the colon were made at the beginning and end of the six-week period and routine safety assessments were made throughout the trial. The primary efficacy endpoint of the trial is the change in patients' U.S. Disease Activity Index for ulcerative colitis from baseline, as compared to placebo. This index measures stool frequency, rectal bleeding, appearance of the lining of the colon and a physician's global rating of disease severity. A secondary endpoint is the change in patients' European Union's Clinical Activity Index for ulcerative colitis, which measures items such as number of stools, blood in stools, abdominal pain and cramps, general well-being, presence or absence of fever and clinical manifestations such as arthritis outside of the intestines, as compared to placebo. We expect the results of this trial to be available in December 2004.

Of the 240 patients who had participated in the trial, 10 experienced an elevation in liver enzymes in excess of three times the upper limit of normal. Five of these patients were withdrawn from the trial and their liver enzymes returned to within the normal range. Four of the other patients continued in the trial. These patients' liver enzymes returned to the normal range during the last two weeks of the six-week dosing regimen and were within the normal range at the post-regimen follow-up visit. The elevation in liver enzymes for the tenth patient was observed at the end of the six-week dosing regimen, and this patient's liver enzymes were within normal limits at the post-regimen follow-up visit. Because the trial is double blind, we do not know if these patients were administered rivanicline or a placebo.

Plans for Future Development. We plan to file an IND or a foreign equivalent to conduct a Phase I clinical trial of the oral formulation of rivanicline in the first half of 2005. If the results of the Phase II trial of the enema formulation and the planned Phase I trial of the oral formulation are favorable, we expect that we and Dr. Falk Pharma will further assess the development plans for both the oral and enema formulations.

TC-2696

TC-2696 is a novel small molecule that we are developing as an oral treatment for acute post-operative pain. We have completed the treatment phase of a Phase I clinical trial of TC-2696. Depending on clinical trial results, available resources and other considerations, we may pursue development of TC-2696 for other classes of pain as well.

In our preclinical in vitro studies of TC-2696, we found the compound to be a potent activator of the a4b2 NNR and to avoid interaction with nicotinic acetylcholine receptors in the muscles and ganglia that are associated with side effects. Published studies conducted by third parties have shown that compounds that activate a4b2 have pain-relieving effects in animals. These effects may be 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 our preclinical animal studies, TC-2696:

- demonstrated pain-relieving effects in models of acute, chronic and inflammatory nociceptive pain and of neuropathic pain with comparable or higher potency than morphine or indomethacin, the generally accepted standards of comparison;
- did not result in tolerance following repeated administration; and
- was rapidly absorbed and demonstrated an acceptable toxicology profile.

Clinical Development of TC-2696

Phase I Clinical Trial. In 2004, we completed the treatment phase of 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. We expect the results to be available in December 2004.

Plans for Future Development. To further assess the safety and tolerability profile of TC-2696, we expect to commence a Phase I multiple rising dose clinical trial in the second quarter of 2005. If the results of our Phase I trials are favorable, we expect to advance TC-2696 into Phase II clinical development for the treatment of acute post-operative pain.

Inversine

Inversine is currently our only marketed product. Inversine is approved in the United States for the management of moderately severe to severe essential hypertension. Our market research suggests, however, that Inversine is prescribed predominantly for the treatment of Tourette's syndrome and other neuropsychiatric disorders. 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.

We have reformulated mecamylamine hydrochloride and are developing it in a lower dose as TC-5231 for the treatment of ADHD. We are also exploring the potential use of mecamylamine hydrochloride in the same dose as Inversine for additional indications. For example, we have recently initiated a clinical trial of Inversine in patients with major depressive disorder.

Our Preclinical Research Programs

We focus our preclinical research efforts on indications for which we believe that selective NNR-targeted drugs have the potential for use in the treatment of disease and 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 ongoing preclinical research programs for schizophrenia, depression and anxiety, smoking cessation and obesity. Each of these indications represents a substantial market opportunity. Our current research objective is to file at least one IND or foreign equivalent each year beginning in 2005.

Schizophrenia

Schizophrenia is a chronic, severe and disabling form of psychosis. Although the precise cause of schizophrenia is unknown, the disease is thought to be associated with an imbalance of neurotransmitter levels in the brain, particularly dopamine levels. Because NNRs act to regulate levels of neurotransmitters in the brain, we believe that NNRs may be useful targets for schizophrenia therapies. A number of published studies have indicated an association between the a7 NNR and schizophrenia. In a survey of experts in connection with a National Institute of Mental Health schizophrenia initiative, a7 was selected more often than any other target as

the target of most interest in the development of treatments for psychosis. Because schizophrenic patients are frequently cognitively impaired, we believe that the a4ß2 NNR, which plays a role in cognition, also may be associated with schizophrenia. In addition, published studies have linked nicotine to improvements in the ability to filter or disregard unremarkable stimuli, a common symptom of schizophrenia, and cognitive impairment in schizophrenic patients. These studies further suggest the potential relevance of NNRs as targets for the treatment of schizophrenia.

We are evaluating a number of compounds for the treatment of schizophrenia in preclinical studies. Some of these compounds are designed to interact selectively with a7 and others are designed to interact selectively with both a7 and a4ß2. In addition, we plan to pursue the development of our proprietary compound TC-1827, which interacts selectively with a4ß2, for the treatment of the cognitive impairment associated with schizophrenia. In December 2004, we entered into an agreement with The Stanley Medical Research Institute, a non-profit organization that supports research and development of treatments for schizophrenia, under which it paid us $1.25 million in return for our issuance of a convertible promissory note in an equal principal amount and agreed to pay us up to an additional $4.25 million upon the achievement of specified Phase I and Phase II clinical development milestones for TC-1827 in the treatment of the cognitive impairment associated with schizophrenia.

Depression and Anxiety

Depression is thought to be associated with the disruption and imbalance in the brain of the neurotransmitters dopamine, norepinephrine and serotonin. As noted above, because NNRs act to regulate levels of these key neurotransmitters in the brain, we believe that they may be useful targets for depression therapies. Because patients are often diagnosed with both depression and anxiety, we believe that NNRs may also be useful targets for anxiety therapies. A number of reported studies in humans and animals have linked nicotine to improvements in symptoms of depression. In particular, depressed patients who were administered nicotine via patch had short-term improvements in symptoms after only the second day of treatment based on a reduction in scores on the Hamilton Rating Scale, an accepted rating scale for depression. Because many current anti-depressant therapies do not take effect for an extended period, the rapid onset of action of nicotine in these studies suggests a potentially significant advantage for NNR-targeted therapeutics. In addition, in animal studies conducted by third parties, nicotine and other compounds that act on NNRs have shown greater potency than, and similar anti-depressant effects as, common anti-depressant therapies such as selective serotonin reuptake inhibitors and tricyclics.

We are currently evaluating two compounds for the treatment of depression and anxiety. In preclinical evaluation, each of these compounds showed activity in various rodent models of depression and general anxiety disorder and panic disorder. In depression models, the compounds showed greater potency than, and comparable anti-depressant effects as, selective serotonin reuptake inhibitors and tricyclics. We are currently undertaking the additional preclinical toxicology studies necessary to support an IND filing to initiate human clinical trials of these compounds. If we advance both of these compounds, we expect that we would develop one of them initially for the treatment of anxiety disorders and the other initially for the treatment of depression.

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 ß2 NNR may be involved. These studies have shown that selectively blocking ß2 reduced the rewarding effects of nicotine in mice. Other studies have shown that mice deficient in ß2 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 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 currently plan to conduct additional preclinical evaluation of the most promising compounds for obesity in 2005.

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 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. 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 low binding affinity for 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 as part of our schizophrenia program.

Strategic Collaborations

We have a collaboration agreement with Aventis Pharma SA that relates to the development and potential commercialization of Aventis compounds. Another collaboration agreement that we entered into with Aventis Pharma for the development of our compounds will terminate on January 2, 2005. We also have a collaboration agreement with Dr. Falk Pharma GmbH and we recently entered into a development agreement with The Stanley Medical Research Institute.

Aventis Pharma SA

In January 2002, we entered into a collaborative research, development and commercialization agreement with Aventis. Under the agreement, we granted Aventis a worldwide, sublicensable license under our patent rights and know-how, excluding Pentad, to develop and commercialize designated Aventis compounds for Alzheimer's disease and other CNS disorders. Aventis retains worldwide commercialization rights for all compounds that it develops under the agreement.

We could receive up to $8 million upon the achievement of specified pre-commercialization development and regulatory milestones related to Alzheimer's disease and up to $8 million for each other CNS indication upon the achievement of specified pre-commercialization development and regulatory milestones. None of these milestones has been achieved, and the achievement of any of these milestones is uncertain. We are also entitled

to receive royalties based on net sales by Aventis, its affiliates and sublicensees of each product under the agreement. Our right to receive royalties would continue on a country-by-country and product-by-product basis until the later of ten years from the first commercial sale of a product in that country or the expiration of the patent rights covering the product in that country.

An executive committee comprised of an equal number of representatives from us and Aventis is responsible for initially recommending further development of any compound under the agreement. Aventis also has the independent right to recommend further development of any compound. A scientific review board from Aventis determines whether to advance a compound into clinical development. Under the agreement, Aventis is responsible for conducting all preclinical and clinical development activities and obtaining all required regulatory approvals for compounds selected for advancement. Any compound that Aventis initially selects for advancement but ultimately rejects is terminated from the collaboration and becomes available to us for in-licensing. We would be permitted to in-license the terminated compound 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.

If not terminated earlier, this agreement terminates upon expiration of all royalty and other payment obligations. In addition, either party may terminate the agreement in the event of an uncured material breach by the other party. However, if Aventis is developing or commercializing more than one compound or product, or if we are developing or commercializing more than one compound or product that has been terminated from the collaboration and in-licensed by us, and the breach relates to a particular compound or product, then the non-breaching party can terminate the agreement only as applied to that compound or product.

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 ispronicline, for the treatment or prevention of Alzheimer's disease. This agreement will terminate on January 2, 2005. As a result, we will be free to pursue the development and commercialization of our product candidates for Alzheimer's disease. While the agreement was in effect, both we and Aventis were restricted from pursuing the development or commercialization of 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. None of our compounds that were subject to this agreement were advanced into clinical development under the agreement.

Dr. Falk Pharma GmbH

In January 2001, we entered into a collaborative research, development and license agreement with Dr. Falk Pharma. The agreement provides for the research, development, and commercialization of our compound rivanicline and, if selected by Dr. Falk Pharma and us, at least one additional compound for the treatment or prevention of ulcerative colitis and other gastrointestinal or liver diseases. We recently completed the treatment phase of a Phase II clinical trial of rivanicline.

Under the agreement, we granted Dr. Falk Pharma a license under our patent rights and know-how relating to rivanicline and additional compounds that may become part of the agreement, excluding Pentad, in a territory in Europe consisting of all of the major European pharmaceutical markets, Russia and the Commonwealth of Independent States countries, Egypt and Israel. The license is exclusive in the licensed territory with respect to the sale of compounds for the treatment or prevention of ulcerative colitis and other gastrointestinal or liver diseases and joint, or co-exclusive, with us with respect to all other purposes. We retained all commercialization rights in the rest of the world. Dr. Falk Pharma granted us a license under its patent rights and know-how relating to rivanicline and additional compounds that may become part of the agreement to develop and commercialize pharmaceutical products for the treatment or prevention of ulcerative colitis and other gastrointestinal or liver diseases in the rest of the world.

Upon effectiveness of this agreement, Dr. Falk Pharma paid us a non-refundable upfront license fee of $1.0 million and purchased $1.0 million of our common stock. We are also entitled to receive a percentage of net

profits from the sale of licensed products by Dr. Falk, its affiliates and its sublicensees in its licensed territory. Dr. Falk Pharma is entitled to receive royalties from us based on net sales by us, our affiliates and sublicensees of products developed under the agreement in the United States and Japan. Our right to receive a percentage of Dr. Falk Pharma's net profits and Dr. Falk Pharma's right to receive royalties would continue on a country-by-country and product-by-product basis until the earlier of 12 years from the first commercial sale of a product in that country or the expiration of the patent rights covering the product in that country.

We are jointly responsible with Dr. Falk Pharma for all clinical development in the territories licensed to Dr. Falk Pharma, and we share all related development expenses evenly. To the extent that particular clinical development is required as a condition to commercialization in the rest of the world, we would be responsible for that clinical development and related expenses. Dr. Falk Pharma may terminate a compound's development under the agreement in its sole discretion after completion of Phase II clinical evaluation. If the development of a compound is terminated and the compound is not designated as a back-up compound for possible future development, then the compound is removed from the agreement. Dr. Falk Pharma is required to use commercially reasonable efforts to commercialize products under the agreement in each country in its licensed territory, and we are required to use commercially reasonable efforts to commercialize products under the agreement in the United States and Japan. If we fail to use commercially reasonable efforts to commercialize licensed products in the United States or Japan, the percentage of net profits that Dr. Falk Pharma would otherwise pay to us for sales in its licensed territory would be equitably adjusted to reflect Dr. Falk Pharma's loss of anticipated royalty revenue from sales by us in the rest of the world.

We may terminate Dr. Falk Pharma's commercialization rights for a compound in a country in its licensed territory if Dr. Falk Pharma does not use commercially reasonable efforts to commercialize the product in that country without sound business or commercial reasons. If we terminate these rights for a product in all of France, Germany and the United Kingdom, the agreement would no longer apply to that product and we could commercialize that product ourselves without obligation to Dr. Falk Pharma. We may also terminate the agreement with thirty days notice to Dr. Falk Pharma if required regulatory approvals have not been obtained for at least one compound in at least one of France, Germany or the United Kingdom by a specified date. Also, either party may terminate the agreement in the event of an uncured material breach by the other party, including a failure to use commercially reasonable efforts to commercialize products. However, in the case of a breach by Dr. Falk Pharma with respect to a particular compound, product or market, our right to terminate would be limited to the applicable compound, product or market. Upon termination of the agreement, the licenses that we granted to Dr. Falk Pharma terminate.

The Stanley Medical Research Institute

On December 15, 2004, we entered into a development agreement for our compound TC-1827 with The Stanley Medical Research Institute, or SMRI, a nonprofit organization that supports research and development of treatments for schizophrenia. The development term of this agreement is five years and may be extended for additional consecutive one-year periods by mutual agreement. During the development term, we are required to use commercially reasonable efforts to conduct a Phase I clinical development program and a Phase II clinical trial of TC-1827 for the treatment of the cognitive impairment associated with schizophrenia in accordance with a development plan that we will prepare.

Upon effectiveness of this agreement, SMRI paid us $1.25 million in return for our issuance of a convertible promissory note in an equal principal amount. The note bears interest at 10% and matures on January 1, 2007. However, if not earlier paid, the outstanding principal and accrued interest under the note will automatically convert into shares of our common stock concurrently with the completion of this offering at a conversion price equal to the initial public offering price. We could receive up to an additional $4.25 million from SMRI upon the achievement of specified Phase I and Phase II clinical development milestones for TC-1827. If TC-1827 is successfully developed and commercialized, we will be required to pay to SMRI royalties based on net sales of TC-1827 by us, our affiliates and our licensees. In addition, if intellectual property is generated in the course of the development of TC-1827 that is funded by SMRI and we subsequently sublicense that intellectual property to a third party, we will be required to pay to SMRI a portion of any other amounts that we receive from the

sublicensee. Our obligation to continue to make payments to SMRI under the agreement will terminate on various specified future dates if our total payments to SMRI as of any of those dates equal or exceed specified amounts.

We can terminate the agreement if we enter into a development agreement for TC-1827 with a third party that does not relate solely to the manufacturing, sale or promotion of TC-1827. SMRI can terminate the agreement if we abandon the development program or if we propose a change to the development plan for TC-1827 that is rejected by a majority of the members of a development committee. The development committee is comprised of two members that we appoint, one member that SMRI appoints and two other members with experience in the development of schizophrenia therapies that we and SMRI mutually agree upon. In addition, either party may terminate the agreement in the event of an uncured material breach by the other party.

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 constructs 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 November 30, 2004, our patent estate includes 61 patents issued in the United States, five patent applications allowed in the United States and not yet issued, 19 patent applications pending in the United States, and numerous issued patents and patent applications pending in countries outside 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. 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. 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.

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

Product Candidate	Patent Scope	Patent Expiration
Ispronicline (TC-1734)	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
	Composition of matter claims to TC-1734	June 2018—allowed but not yet issued
TC-5231	Methods of use of TC-5231 for treatment of ADHD, Tourette's syndrome and nicotine-responsive neuropsychiatric disorders	September 2017
Rivanicline (TC-2403)	Methods of use of TC-2403 and analogs for inflammatory bowel disease, including ulcerative colitis	January 2015
TC-2696	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

In addition, 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 five 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, which we refer to as TC-5231, and other specified compounds. The licensed patents and patent applications include an issued patent covering methods of use for the treatment of ADHD, Tourette's syndrome and nicotine-responsive neuropsychiatric disorders and pending patent applications covering the pharmaceutical composition of the 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.

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 ispronicline, TC-2696, TC-1827 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 with respect to products covered by these patents. In addition, under the license agreement, RJR paid UKRF an upfront license fee of $20,000.

Medical College of Georgia Research Institute

Pursuant to a license agreement with Medical College of Georgia Research Institute, or MCGRI, we hold an exclusive worldwide license to a patent covering a method of use of a substance that stimulates the activity of nicotinic acetylcholine receptors by inhibiting the activity of another class of receptors, a method of use of increasing the presence of a therapeutic substance to treat neurodegeneration and a screening method. Under the agreement, we paid MCGRI an upfront license fee of $25,000 and are obligated to pay to MCGRI:

- royalties on net sales of products subject to the license, with an annual minimum of $12,000 beginning in the first year of product sales;
- aggregate payments of up to $425,000 based on the achievement of specified development and regulatory milestones; and
- a percentage of other amounts that we receive from a sublicensee.

If not earlier terminated, the agreement will terminate upon the earlier of expiration of the licensed patent rights or July 2027.

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 a third party pursuant to an exclusive distribution agreement.

Manufacturing

All of our drug candidates are organic 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. Beginning in February 2006, 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 in Phase III 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, Sanofi-Synthélabo, 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 for AAMI. We believe that the primary competitive products for use in the other indications that we are currently targeting include:

- for Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer, 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 ADHD, stimulants such as Concerta from Johnson & Johnson, Ritalin from Novartis and Adderall from Shire Laboratories and the non-stimulant Strattera from Eli Lilly;
- for ulcerative colitis, 5-ASAs such as Asacol from Proctor & Gamble;
- for pain, non-steroidal anti-inflammatory drugs such as Celebrex from Pfizer and opioids such as OxyContin from Purdue Pharma;
- for schizophrenia, anti-psychotics such as Zyprexa from Eli Lilly, Risperdal from Johnson & Johnson and Abilify from Bristol-Myers Squibb;
- 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; 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, 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. 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 and the efficacy criteria to be evaluated. 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, typically involving the following three phases:

- Phase I clinical trials are 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 conducted with groups of patients afflicted with the therapeutic condition for which the investigational drug is being tested with a specific disease in order to determine potential efficacy preliminarily, and an expanded safety profile that identifies possible adverse effects; and

- Phase III clinical trials are large-scale, geographically diverse, adequate and well-controlled, conducted with patients afflicted with a target disease in order to collect data to establish the safety and efficacy profile and assure compliance with the requirements of the Federal Food, Drug and Cosmetic Act.

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 required to generate and compile the requisite data and the significant user fees required for NDA submission.

The FDA has 45 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 50% 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 180 or 365 days to respond, 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 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, and has been demonstrated to be bioequivalent to the listed drug. 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 generally 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 imposes a number of complex regulations on entities that advertise and promote marketed pharmaceuticals. These regulations include requirements for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. The FDA enforces the regulations under the Federal Food Drug and Cosmetic Act. Failure to abide by these 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. They may also include a requirement that future advertising and promotional materials be pre-cleared by the FDA, as well as civil and criminal investigations and prosecutions.

Holders of an NDA are also subject to laws and regulations regarding non-clinical laboratory practices that support human safety and product distribution, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances. In each of these areas, the FDA has broad 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.

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 November 30, 2004, we had 73 full-time employees, 30 of whom are Ph.D.s, M.D.s or both. 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 generally exercisable until August 2005 to lease additional space in this facility as and when it becomes available. The term of our lease expires August 1, 2007, and we have renewal options for an additional five-year term. The current monthly payment under our lease is approximately $120,000. We believe that these facilities 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 November 30, 2004 are as follows:

Name	Age	Position
Mark Skaletsky (1) (2)	56	Chairman of the Board of Directors
J. Donald deBethizy, Ph.D.	54	Chief Executive Officer, President and Director
Merouane Bencherif, M.D., Ph.D.	49	Vice President, Preclinical Research
Jeffrey P. Brennan	46	Vice President, Business and Commercial Development
William S. Caldwell, Ph.D.	50	Vice President, Drug Discovery and Development
Geoffrey C. Dunbar, M.D.	57	Vice President, Clinical Development and Regulatory Affairs
Alan A. Musso	42	Vice President, Chief Financial Officer, Treasurer and Secretary
M. James Barrett, Ph.D. (1)	62	Director
Charles A. Blixt (2) (3)	53	Director
G. Steven Burrill (3)	60	Director
Errol B. De Souza, Ph.D. (2)	51	Director
Elaine V. Jones, Ph.D. (1) (2)	49	Director
John P. Richard (3)	47	Director
Alan G. Walton, Ph.D.	68	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 Paradigm Genetics, Inc., Isis Pharmaceuticals, 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.

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. and Pharmion Corporation.

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 been executive vice president, general counsel and assistant secretary of R.J. Reynolds Tobacco Holdings, Inc., the parent company of R.J. Reynolds Tobacco Company.

G. Steven Burrill has been a member of our board of directors since August 2000. Since January 1994, he has been chief executive officer of Burrill & Company LLC, a merchant bank that he founded. Prior to founding Burrill & Company LLC, Mr. Burrill spent 27 years with Ernst & Young LLP, including the last 17 as a partner of the firm. He is chairman of the board of Paradigm Genetics, Inc. and a member of the boards of directors of DepoMed, Inc. and Third Wave Technologies, Inc., each of which is a publicly traded company.

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.

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. Since April 1999, he has been an independent biotechnology consultant. He also has been a 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.

Alan G. Walton, Ph.D. has been a member of our board of directors since March 2003. He joined Oxford Partners, a venture capital firm, as a general partner in March 1987. In July 1992, Dr. Walton founded Oxford Bioscience Partners, a life science venture capital firm where he is a general partner. He is chairman of the board of directors of the management company Oxford Bioscience IV Corporation and serves as a member of the board of directors of Alexandria Real Estate Equities, Inc. and ACADIA Pharmaceuticals Inc., both of which are publicly traded companies. Dr. Walton is also a founder of Human Genome Sciences, Inc. and Gene Logic Inc., both of which are publicly traded companies.

Board Composition

Our board of directors consists of nine 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 nine members divided into three classes:

- Class I, for a term expiring at the 2005 annual meeting of stockholders;
- Class II, for a term expiring at the 2006 annual meeting of stockholders; and
- Class III, for a term expiring at the 2007 annual meeting of stockholders.

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, John P. Richard and Alan G. Walton. Our Class II directors will be M. James Barrett, Charles A. Blixt and J. Donald deBethizy. Our Class III directors will be G. Steven Burrill, Errol B. De Souza and Mark Skaletsky.

Board Committees

Audit Committee. The members of our audit committee are Messrs. Burrill, Blixt and Richard. Mr. Burrill 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, Dr. Barrett and Dr. 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 our 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 serves 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 has received a nonqualified stock option to purchase 25,000 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 has been granted a nonqualified stock option to purchase 7,500 shares of common stock. However, our chairman received a nonqualified stock option to purchase 35,000 shares upon his or her initial election and a nonqualified stock option to purchase 12,500 shares upon his or her annual reelection. Each of these options:

- has a ten-year term;
- has an exercise price of $0.01 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 $0.01 per share. Each non-employee director that is not a designee of 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 $10,000 per year as an annual

retainer. 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.

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 an option for 25,000 shares upon initial election as a director and an option for 7,500 shares upon annual reelection. The chairman of the board will receive an option for 10,000 shares upon initial election as chairman, in addition to the option for 25,000 shares upon initial election as a director, and an option for 12,500 shares upon annual reelection. For more information, please see "Executive Compensation—Stock-Based Plans—2004 Stock Incentive Plan."

Executive Compensation

The following table sets forth other information regarding compensation awarded to, earned by or paid to our chief executive officer and our five other most highly compensated executive officers during the year ended December 31, 2003 whose annual salary and bonus exceeded $100,000 during the year ended December 31, 2003. We refer to these officers in this prospectus as our named executive officers.

Summary Compensation Table

	Annual Compensation		Long-Term Compensation	
Name and Principal Position	Salary	Bonus	Shares Underlying Options (#) (1)	All Other Compensation (2)
J. Donald deBethizy, Ph.D. President and Chief Executive Officer	$ 275,000	$66,000	1,969,332	$ 12,000
Merouane Bencherif, M.D., Ph.D. Vice President, Preclinical Research	161,000	38,640	585,623	11,485
Jeffrey P. Brennan (3) Vice President, Business and Commercial Development	75,000	13,500	169,000	4,500
William S. Caldwell, Ph.D. Vice President, Drug Discovery and Development	161,750	29,115	534,385	11,314
Geoffrey C. Dunbar, Ph.D. Vice President, Clinical Development and Regulatory Affairs	246,750	44,415	668,396	12,000
Alan A. Musso Vice President, Chief Financial Officer, Treasurer and Secretary	181,731(4)	32,400	533,671	12,000

(1) 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. For information regarding these options, please see "—Stock Options," below.
(2) Consists of our contributions under the Targacept Retirement Savings Plan, our 401(k) plan.
(3) Mr. Brennan joined our company in September 2003. His current annual base salary is $225,000.
(4) 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, 2003.

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 (5)	
					5%	10%
J. Donald deBethizy, Ph.D.	110,000 (1)	1.9%	$ 0.68	1/14/2013	$	$
	250,000 (2)	4.3	0.68	1/31/2013		
	1,565,332 (3)	26.7	0.68	10/31/2013		
	44,000 (4)	15.8	0.75	1/26/2014		
Merouane Bencherif, M.D., Ph.D.	48,406 (1)	0.8	0.68	1/14/2013		
	120,000 (2)	2.0	0.68	1/31/2013		
	417,217 (3)	7.1	0.68	10/31/2013		
Jeffrey P. Brennan	160,000 (2)	2.7	0.68	9/1/2013		
	9,000 (4)	3.2	0.75	1/26/2014		
William S. Caldwell, Ph.D.	48,631 (1)	0.8	0.68	1/14/2013		
	120,000 (2)	2.0	0.68	1/31/2013		
	346,344 (3)	5.9	0.68	10/31/2013		
	19,410 (4)	7.0	0.75	1/26/2014		
Geoffrey C. Dunbar, Ph.D.	74,210 (1)	1.3	0.68	1/14/2013		
	120,000 (2)	2.0	0.68	1/31/2013		
	444,576 (3)	7.6	0.68	10/31/2013		
	29,610 (4)	10.7	0.75	1/26/2014		
Alan A. Musso	38,250 (1)	0.7	0.68	1/14/2013		
	125,000 (2)	2.1	0.68	1/31/2013		
	348,821 (3)	5.9	0.68	10/31/2013		
	21,600 (4)	7.8	0.75	1/26/2014		

(1) These options reflect grants made on January 14, 2003 under our 2000 equity incentive plan in lieu of a cash bonus for fiscal year 2002.

(2) These options reflect grants made under our 2000 equity incentive plan. They have a term of 10 years, an exercise price equal to the fair market value of the common stock on the date of grant and vest 25% on the grant date and then quarterly over four years.

(3) These options reflect grants made under our 2000 equity incentive plan. They have a term of 10 years, an exercise price equal to the fair market value of the common stock on the date of grant and vest 20% on the grant date and then quarterly over four years.

(4) These options reflect grants made on January 26, 2004 under our 2000 equity incentive plan in lieu of a cash bonus for fiscal year 2003.

(5) 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 estimated initial public offering price of $ 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, 2003 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, 2003. There was no public trading market for our common stock as of December 31, 2003. 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, 2003 equal to an assumed initial offering price of $ per share, the mid-point of the estimated price range shown on the cover page of this prospectus.

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, 2003		Value of Unexercised In-the-Money Options at December 31, 2003	
			Exercisable	Unexercisable	Exercisable	Unexercisable
J. Donald deBethizy, Ph.D.	101,530	$ 21,321	898,338 (1)	1,390,772	$	$
Merouane Bencherif, M.D., Ph.D.	—	—	376,270	413,048		
Jeffrey P. Brennan	—	—	52,334 (1)	116,666		
William S. Caldwell, Ph.D.	—	—	378,306 (1)	359,893		
Geoffrey C. Dunbar, Ph.D.	—	—	399,503 (1)	458,120		
Alan A. Musso	6,000	70	267,929 (1)	424,742		

(1) 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.

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 2004, the base salary of Dr. deBethizy is

$283,250; the base salary of Dr. Dunbar is $254,150; the base salary of Mr. Brennan is $225,000; the base salary of Mr. Musso is $190,000; the base salary of Dr. Bencherif is $170,000; and the base salary of Dr. Caldwell is $170,000.

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. 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 December 15, 2004, an aggregate of 9,216,657 shares of common stock had been authorized for issuance under our 2000 plan, of which options to purchase an aggregate of 7,419,029 shares of common stock were outstanding at a weighted average exercise price of $0.65 per share, 97,500 shares of common stock were issued and outstanding in the form of restricted stock and 302,743 shares of common stock were available for future grant. Upon completion of this offering, 751,468 shares of common stock subject to unvested options outstanding as of December 15, 2004 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 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 and options intended to qualify as performance-based compensation under Section 422 of the Internal Revenue Code to optionees holding more than 10% of the voting power of all shares of our capital stock at an exercise price less than 110% of the fair market value of our common stock on the date of grant. 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 would 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. Our 2004 stock incentive plan, which we refer to as our 2004 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 in order for grants of incentive stock options to meet the requirements of Section 422 of the Internal Revenue Code, or if stockholder approval is required in order to exempt compensation under our 2000 plan from the deduction limit under Section 162(m) of the Internal Revenue Code.

2004 Stock Incentive Plan

Introduction. Our 2004 plan is intended to serve as the successor equity incentive program to our 2000 plan. Our 2004 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 be transferred to our 2004 plan and no further options will be granted under our 2000 plan.

Subject to adjustments as provided in our 2004 plan, the maximum number of shares that we may issue pursuant to awards granted under our 2004 plan may not exceed the sum of (i) shares and (ii) up to shares of common stock (a) remaining available for issuance as of the effective date under our 2000 plan or any other employee stock incentive plan that we maintain prior to the effective date and/or (b) subject to an award granted under our 2000 plan or any other prior plan, which award 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 2004 plan pursuant to the grant of (i) incentive stock options is and (ii) restricted awards is . In any calendar year, (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 shares of common stock; (ii) we may not grant to any participant awards for more than shares of common stock; and (iii) participants may not receive awards paid in cash having an aggregate dollar value in excess of $, subject to adjustments as provided in our 2004 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 2004 plan that is forfeited, cancelled, terminated, expires or lapses for any reason without the issuance of shares underlying the award; 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 2004 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 2004 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 2004 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 2004 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 2004 plan. In this discussion, we refer to our board of directors and the compensation committee collectively as the administrator. Under the terms of our 2004 plan, the administrator has full and final authority to take any action with respect to our 2004 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 2004 plan; (iii) establish, amend and rescind rules and regulations for the administration of our 2004 plan; and (iv) construe and interpret our 2004 plan, awards and award agreements made under the plan, interpret rules and regulations for administering the plan and make all other determinations deemed necessary or advisable for administering the 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 2004 plan with respect to such awards.

Our board of directors may amend, alter or terminate our 2004 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 2004 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.

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 2004 plan or necessary or appropriate to comply with applicable laws, rules or regulations. The administrator may cause any award or any portion of an award granted under our 2004 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.

Options. Our 2004 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 the 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 and who possesses 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.

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 at least six months or for such other time period that the administrator determines and which is 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, in the case of incentive stock options, the option term 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. 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 2005 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. The term of a director option may not exceed 10 years from the date of grant. 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 2004 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. We may pay consideration upon exercise of an SAR currently or on a deferred basis.

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 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 2004 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 whole shares of common stock, or partly in cash and partly in whole shares of common stock, in accordance with the terms of our 2004 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 hiring 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.

The administrator has authority to determine whether and to what degree restricted awards have vested and been earned and are payable. 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 2004 plan and the individual award, the participant will forfeit the award unless the administrator determines otherwise.

Performance Awards. Subject to the limitations of our 2004 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.

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. 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 2004 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 2004 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 based on the fair market value of a share of common stock.

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. 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 2004 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 2004 plan and the individual award, the participant will forfeit the award unless the administrator determines otherwise.

Dividend and Dividend Equivalents. The administrator may, in its sole discretion, provide that awards granted under our 2004 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 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 2004 plan, and unless an award agreement provides otherwise, our 2004 plan provides that: (i) all options and SARs outstanding as of the date of the change in control will become fully exercisable, whether or not then otherwise exercisable; and (ii) any restrictions applicable to any restricted award, performance award and/or phantom stock award will be deemed to have been met, and such awards will become fully vested, earned and payable to the fullest extent of the original grant of the applicable award. However, our 2004 plan authorizes the administrator, in the event of a merger, share exchange, reorganization, sale of all or substantially all of our assets or other similar transaction or event affecting us or one of our affiliates or stockholders, to determine that any or all awards will not vest or become exercisable on an accelerated basis, if we or the surviving or acquiring corporation takes action, including but not limited to the assumption of awards or the grant of substitute awards, that, in the opinion of the administrator, is equitable or appropriate to protect the rights and interest of participants under our 2004 plan.

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 Section 422 of the Internal Revenue Code and related regulations. 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 that have not vested and been earned are not 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 2004 plan are taxable under Section 83 of the Internal Revenue Code upon their 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 taxable 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.

Performance-Based Compensation—Section 162(m) Requirements. Our 2004 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 2004 plan to covered employees. Section 162(m) of the Internal Revenue Code generally denies an employer a deduction for compensation paid to covered employees, which 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 2004 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, we must advise stockholders, and stockholders must 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 2004 plan limits the maximum amount of awards that we may grant to any employee. In particular, in any calendar year, (i) we may not grant to any participant options and SARs that are not related to an option for more than shares of common stock; (ii) we may not grant to any participant awards for more than shares of common stock; and (iii) no participant may receive awards paid in cash having an aggregate dollar value in excess of $. 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 2004 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 and 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 August 22, 2000, 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

Issuance of Common Stock

On August 22, 2000, at the time that we became an independent company, we issued and sold an aggregate of 309,424 shares of our common stock for an aggregate purchase price of approximately $309. The following table sets forth the number of shares of common stock sold to our founders.

Name	Number of Shares of Common Stock	Aggregate Purchase Price
J. Donald deBethizy, Ph.D.	135,373	$ 135
Merouane Bencherif, M.D., Ph.D.	58,017	58
William S. Caldwell, Ph.D.	58,017	58
Patrick M. Lippiello, Ph.D.	58,017	58

On August 8, 2002, we issued 47,500 shares of restricted stock to Mr. Skaletsky for an aggregate purchase price of $475. On June 11, 2003, we issued 12,500 shares of restricted stock to Mr. Skaletsky for an aggregate purchase price of $125. On October 15, 2004, we issued 12,500 shares of restricted stock to Mr. Skaletsky for an aggregate purchase price of $125.

On April 18, 2003, we issued 25,000 shares of restricted stock to Mr. Richard for an aggregate purchase price of $250.

Issuance of Series A Convertible Preferred Stock

On August 22, 2000, we recapitalized our 500 outstanding shares of common stock held by R.J. Reynolds Tobacco Company, our then parent corporation, into 5,000,000 shares of series A convertible preferred stock and a warrant to purchase 1,612,903 shares of common stock at an exercise price of $4.65 per share. As a result of price protection provisions contained in the warrant, the exercise price was reduced to $1.95 upon our issuance of series C convertible preferred stock in November 2002 and March 2003. All of the shares of series A convertible preferred stock and the warrant were subsequently assigned to R.J. Reynolds Tobacco Holdings, Inc. Each share of series A convertible preferred stock will convert into one share of common stock concurrently with the completion of this offering. The warrant will be cancelled if it is not exercised prior to the completion of this offering. If R.J. Reynolds exercises the warrant in full for cash, we would issue 1,612,903 shares of common stock and receive cash proceeds of approximately $3.1 million. If R.J. Reynolds exercises the warrant on a cashless basis, we would issue shares of common stock, based on an assumed initial public offering price of $ per share.

Mr. Blixt, one of our directors, is the executive vice president and general counsel of R.J. Reynolds Tobacco Company and is executive vice president, general counsel and assistant secretary of its parent company, R.J. Reynolds Tobacco Holdings, Inc.

Issuance of Series B Convertible Preferred Stock

On August 22, November 30, December 5 and December 19, 2000, we issued and sold an aggregate of 6,537,634 shares of our series B convertible preferred stock at a purchase price per share of $4.65 for an aggregate purchase price of approximately $30.4 million. On January 26, 2001, we issued an additional 29,933 shares of our series B convertible preferred stock in partial satisfaction of an outstanding payment obligation.

The following table sets forth the aggregate number of shares of series B convertible preferred stock sold to our 5% stockholders and their affiliates on August 22, November 30, December 5 and December 19, 2000.

Name	Number of Shares of Series B Preferred Stock	Aggregate Purchase Price
Entities affiliated with EuclidSR Partners, L.P.	2,021,505	$ 9,399,998
Entities affiliated with Burrill & Company LLC	1,075,269	5,000,001
Entities affiliated with Advent Private Equity Fund II	1,075,269	5,000,001

These shares of our series B convertible preferred stock will convert into an aggregate of 9,948,718 shares of our common stock concurrently with the completion of this offering.

Dr. Jones, one of our directors, is a general partner of EuclidSR Associates, L.P., the general partner of EuclidSR Partners, L.P. Mr. Burrill, one of our directors, is the chief executive officer of Burrill & Company LLC.

Issuances of Series C Convertible Preferred Stock

On November 26, 2002 and March 14, 2003, we issued and sold an aggregate of 49,169,138 shares of our series C convertible preferred stock at a purchase price per share of $1.21 for an aggregate purchase price of approximately $59.5 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 November 26, 2002 and March 14, 2003.

Name	Number of Shares of Series C Preferred Stock	Aggregate Purchase Price
Entities affiliated with New Enterprise Associates	12,396,694	$ 15,000,000
Nomura International plc	8,264,462	9,999,999
Entities affiliated with Oxford Bioscience Partners	6,198,347	7,500,000
Entities affiliated with EuclidSR Partners, L.P.	5,123,966	6,199,999
Entities affiliated with Burrill & Company LLC	1,540,440	1,863,932
Entities affiliated with Advent Private Equity Fund II	1,540,440	1,863,932

These shares of our series C convertible preferred stock will convert into an aggregate of 37,882,020 shares of our common stock concurrently with the completion of this offering.

On December 6, 2004, we issued and sold an aggregate of 27,272,728 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 $33.0 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 December 6, 2004.

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 LP	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 23,839,285 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. Dr. Walton, one of our directors, is a general partner of OBP Management IV L.P., the general partner of Oxford Bioscience Partners IV L.P., which is an affiliate of Oxford Bioscience Partners.

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. 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 R.J. Reynolds determined to be sufficient at the time of disbursement. In April 2004, we borrowed $1.0 million under the amended loan facility to finance equipment. The borrowing bears a fixed interest rate of 5.9%, is payable in 48 equal monthly installments and matures in April 2008. 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 September 30, 2004, the outstanding principal balance under the loan facility was $2.1 million.

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 the nine months ended September 30, 2004, we continued to use only the copy and printing services and have paid $39,000 for these services.

Director Compensation

For information regarding stock options granted to our non-employee directors, see "Management—Director Compensation."

Executive Compensation and Employment Agreements

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

PRINCIPAL STOCKHOLDERS

The following table sets forth information regarding the beneficial ownership of our common stock as of December 15, 2004 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 December 15, 2004 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	21,907,500	20.8%	
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	14,146,226	13.5%	
Entities affiliated with Nomura Phase4 Ventures Limited (4) Nomura House 1 St. Martins le Grand London EC1A 4NP England	16,026,785	15.2%	
Entities affiliated with Oxford Bioscience Partners (5) 222 Berkeley Street, Suite 1650 Boston, Massachusetts 02116	6,728,928	6.4%	
R.J. Reynolds Tobacco Holdings, Inc. (6) 401 North Main Street Winston-Salem, North Carolina 27102	8,455,342	7.9%	
Entities affiliated with Burrill & Company LLC (7) One Embarcadero Center, Suite 2700 San Francisco, California 94111	5,875,471	5.6%	
Entities affiliated with Advent Private Equity Fund II (8) 25 Buckingham Gate London SW1E 6LD England	5,344,399	5.1%	

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)	1,732,767	1.6%	
Merouane Bencherif, M.D., Ph.D. (10)	617,865	*	
Jeffrey P. Brennan (11)	85,667	*	
William S. Caldwell, Ph.D. (12)	605,726	*	
Geoffrey C. Dunbar, M.D. (13)	613,106	*	
Alan A. Musso (14)	506,819	*	
Mark Skaletsky	72,500	*	
M. James Barrett, Ph.D. (15)	21,907,500	20.8%	
Charles A. Blixt (16)	8,455,342	7.9%	
G. Steven Burrill (17)	5,875,471	5.6%	
Errol B. De Souza, Ph.D. (18)	25,000	*	
Elaine V. Jones, Ph.D. (19)	14,146,226	13.5%	
John P. Richard (20)	32,500	*	
Alan G. Walton, Ph.D. (21)	6,728,928	6.4%	
All executive officers and directors as a group (14 persons) (22)	61,405,417	55.8%	

* Indicates less than one percent.

(1) Our calculation of the percentage of shares of common stock beneficially owned before this offering is based on 105,119,609 shares of our common stock and common stock equivalents outstanding as of December 15, 2004, 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 shares of common stock to be outstanding after this offering, including the shares that we are selling in this offering, our issuance of shares of common stock upon conversion of an outstanding convertible promissory note concurrently with completion of this offering based on an assumed initial offering price of $ per share and our issuance of shares of common stock upon the exercise of an outstanding warrant that will be cancelled if not exercised concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share.

(2) Includes 21,851,340 shares owned of record by New Enterprise Associates 10, Limited Partnership, for which voting and investment power is shared by M. James Barrett, Stewart Alsop, 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; 23,660 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 32,500 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004 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 as a result of 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 disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his pecuniary interest therein.

(3) Includes 11,320,512 shares owned of record by, and 40,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004 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, A. Bliss McCrum, 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 2,785,714 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, A. Bliss McCrum, 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 8,928,571 shares owned of record by Nomura International plc and 7,098,214 shares owned of record by Nomura Phase4 Ventures LP. The board of directors of Nomura International plc has delegated voting and investment power to Mr. Yasushi Ii, the Head of Merchant Banking Europe, Nomura International plc. Mr. Ii acts in consultation with Dr. Denise Pollard-Knight, the Head of Nomura Phase4 Ventures. Dr. Knight has voting and investment power of the shares owned of record by Nomura Phase4 Ventures LP. Each member of the board of directors of Nomura International plc, Mr. Ii and Dr. Pollard-Knight disclaims beneficial ownership of these shares.

(5) Includes 6,629,907 shares owned of record by Oxford Bioscience Partners IV L.P. and 66,521 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.; and 32,500 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004 held by Oxford Bioscience IV Corporation, for which voting and investment power is shared by Alan G. Walton and Jonathan J. Fleming, each of whom are directors of Oxford Bioscience IV Corporation. 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. Dr. Walton, one of our directors, and each of the other 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 31,725 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004 and 1,612,903 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 Andrew J. Schindler, the chief executive officer of R.J. Reynolds Tobacco Holdings, Inc. Mr. Blixt, one of our directors, is executive vice president, general counsel and assistant secretary of R.J. Reynolds Tobacco Holdings, Inc. and disclaims beneficial ownership of these shares.

(7) Includes 5,835,471 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, Michael K. Ullman and Ann F. Hanham, members of Burrill & Company (Biotechnology GP), LLC, the general partner of Burrill Biotechnology Capital Fund, L.P.; and 40,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004 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. Mr. Burrill, 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 1,955,138 shares owned of record by Advent Private Equity Fund II ‘A’ Limited Partnership; 1,192,418 shares owned of record by Advent Private Equity Fund II ‘B’ Limited Partnership; 1,775,200 shares owned of record by Advent Private Equity Fund II ‘C’ Limited Partnership; and 421,643 shares owned of record by Advent Private Equity Fund II ‘D’ Limited Partnership. Patrick Lee is a director of Advent Limited and a general partner of Advent Venture Partners LLP, which owns 100% of Advent Limited. Advent Limited owns 100% of Advent Management II Limited, which is the general partner of Advent Management II Limited Partnership, the general partner of each of the partnerships constituting Advent Private Equity Fund II. Voting and investment power over the shares held by each of the partnerships constituting Advent Private Equity Fund II is exercised by Advent Limited in its role as manager. The board of directors of Advent Limited consists of Sir David James Scott Cooksey (chairman), Peter Anthony Baines, Jerry Christopher Benjamin, David Cheesman, Leslie Ian Gabb, Patrick Pak-tin Lee, Martin Alexander McNair, James Anthony McNaught-Davis and Nicholas James Teasdale. Each director disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein.

(9) Includes 1,029,003 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004.

(10) Includes 559,848 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004.

(11) Consists of 85,667 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004.

(12) Includes 547,709 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004.

(13) Includes 443,584 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004.

(14) Includes 489,819 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004.

(15) Includes 21,851,340 shares owned of record by New Enterprise Associates 10, Limited Partnership, for which voting and investment power is shared by M. James Barrett, Stewart Alsop, 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; 23,660 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 32,500 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004 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 disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his pecuniary interest therein.

(16) Includes 31,725 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004 and 1,612,903 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 Andrew J. Schindler, the chief executive officer of R.J. Reynolds Tobacco Holdings, Inc. Mr. Blixt is executive vice president, general counsel and assistant secretary of R.J. Reynolds Tobacco Holdings, Inc. and disclaims beneficial ownership of these shares.

(17) Includes 5,835,471 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, Michael K. Ullman and Ann F. Hanham, members of Burrill & Company (Biotechnology GP), LLC, the general partner of Burrill Biotechnology Capital Fund, L.P.; and 40,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004 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. Mr. Burrill, 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.

(18) Issuable upon exercise of stock options exercisable within sixty days of December 15, 2004.

(19) Includes 11,320,512 shares owned of record by, and 40,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004 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, A. Bliss McCrum, 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 2,785,714 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, A. Bliss McCrum, 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 7,500 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004.

(21) Includes 6,629,907 shares owned of record by Oxford Bioscience Partners IV L.P. and 66,521 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.; and 32,500 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004 held by Oxford Bioscience IV Corporation, for which voting and investment power is shared by Alan G. Walton and Jonathan J. Fleming, each of whom are directors of Oxford Bioscience IV Corporation. Dr. Walton and each of the other 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.

(22) Includes 3,188,130 shares of common stock issuable upon exercise of stock options exercisable within 60 days of December 15, 2004 and 1,612,903 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 shares of common stock, par value $0.001 per share, and shares of undesignated preferred stock, par value $0.001 per share.

As of December 15, 2004, we had outstanding:

- 1,915,420 shares of common stock held by 55 stockholders of record;
- 5,000,000 shares of series A convertible preferred stock;
- 6,567,567 shares of series B convertible preferred stock; and
- 76,441,866 shares of series C convertible preferred stock.

As of December 15, 2004, we also had outstanding a convertible promissory note in the original principal amount of $1.25 million that will convert into shares of common stock based on the price per share in this offering and a warrant to purchase 1,612,903 shares of common stock at an exercise price of $1.95 per share.

All of our outstanding shares of preferred stock will convert into 103,204,189 shares of common stock concurrently with the completion of this offering. In addition, the convertible promissory note will convert into shares of common stock concurrently with completion of this offering based on an assumed initial public offering price of $ per share. Also, the warrant will be cancelled if it is not exercised prior to the completion of this offering. If R.J. Reynolds exercises the warrant in full for cash, we would issue 1,612,903 shares of common stock and receive cash proceeds of approximately $3.1 million. If R.J. Reynolds exercises the warrant on a cashless basis, we would issue shares of common stock, based on an assumed initial public offering price of $ per share.

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 shares of preferred stock in one or more series and to fix the rights, preferences, 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 December 15, 2004, options to purchase 7,419,029 shares of common stock at a weighted average exercise price of $0.65 per share were outstanding.

Registration Rights

After this offering, holders of approximately 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 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 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

We have applied to have our common stock listed 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 shares of common stock, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into 103,204,189 shares of common stock concurrently with the completion of this offering, our issuance of shares of common stock upon conversion of an outstanding convertible promissory note concurrently with the completion of this offering based on an assumed initial public offering price of $ per share and our issuance of shares of common stock upon the exercise of an outstanding warrant that will be cancelled if not exercised concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share. If the warrant is exercised in full for cash, we would issue 1,612,903 shares of our common stock.

All of the 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 shares of common stock to be outstanding after this offering are "restricted securities" under Rule 144. All of these restricted securities will be subject to the 180-day lock-up period described below. Immediately after the 180-day period, shares will be freely tradable under Rule 144(k) or Rule 701(c)(3) under the Securities Act and shares will be eligible for resale under Rule 144, 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 shares immediately after this offering; and
- 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, the 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 stock plan or other written agreement 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 Morgan Stanley & Co. Incorporated 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 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. Morgan Stanley 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 2004 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 December 15, 2004, options to purchase 7,419,029 shares of common stock were outstanding under our 2000 plan with a weighted average exercise price of $0.65, of which approximately 4,099,577 were vested and exercisable with a weighted average exercise price of $0.62 and an additional 302,743 shares were reserved for issuance under our 2000 plan. Upon completion of this offering, those shares reserved under our 2000 plan plus an additional shares of common stock will become reserved for issuance under our 2004 plan.

Registration Rights

Upon completion of this offering, the holders of 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 whom Morgan Stanley & Co. Incorporated, Deutsche Bank Securities Inc., CIBC World Markets Corp. and Pacific Growth Equities, 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:

Name	Number of Shares
Morgan Stanley & Co. Incorporated	
Deutsche Bank Securities Inc.	
CIBC World Markets Corp.	
Pacific Growth Equities, LLC	
Total	

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 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 outstanding stock have agreed that, without the prior written consent of Morgan Stanley & Co. Incorporated 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 equity incentive plan or our 2004 stock incentive 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.

We have applied for quotation of our common stock 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 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. Recipients of reserved shares will be required to agree with the underwriters not to sell, transfer, assign, pledge or hypothecate these shares for a period of 180 days after purchasing the shares.

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, 2003 and 2002 and for each of the three years in the period ended December 31, 2003, 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 450 Fifth Street, N.W., 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 450 Fifth Street, N.W., 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. Upon approval of our common stock for listing on the NASDAQ National Market, 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, 2002 and 2003, 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, 2003. 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. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as 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, 2002 and 2003, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2003, in conformity with U.S. generally accepted accounting principles.

ERNST & YOUNG LLP

January 22, 2004, except for Note 18,
as to which the date is , 2004
Greensboro, North Carolina

The foregoing report is in the form that will be signed upon the completion of the restatement of capital accounts described in Note 18 to the financial statements.

/S/ ERNST & YOUNG LLP

December 15, 2004
Greensboro, North Carolina

Targacept, Inc.

Balance Sheets

	December 31,		September 30,	Pro forma Stockholders' equity as of September 30, 2004
	2002	2003	2004	
			(unaudited)	
Assets				
Current assets:				
Cash and cash equivalents	$ 44,353,320	$ 11,609,157	$ 24,425,286	
Short-term investments	5,008,139	31,367,500	—	
Research fees and accounts receivable	1,335,648	818,618	205,328	
Inventories	169,536	118,520	106,275	
Prepaid expenses	423,016	514,552	1,521,330	
Total current assets	51,289,659	44,428,347	26,258,219	
Property and equipment, net	2,462,944	2,373,035	2,389,452	
Intangible assets, net of accumulated amortization of $15,735, $53,499 and $81,822 at December 31, 2002, 2003 and September 30, 2004, respectively	626,265	588,501	560,178	
Total assets	$ 54,378,868	$ 47,389,883	$ 29,207,849	
Liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)				
Current liabilities:				
Accounts payable	$ 1,503,170	$ 1,246,975	$ 1,873,536	
Accrued expenses	1,477,034	1,406,778	1,759,279	
Current portion of long-term debt	586,816	576,072	898,907	
Current portion of deferred rent incentive	402,647	402,647	402,647	
Current portion of deferred license fee revenue	634,881	269,537	269,537	
Total current liabilities	4,604,548	3,902,009	5,203,906	
Long-term debt, net of current portion	2,088,293	1,461,554	1,654,113	
Deferred rent incentive, net of current portion	1,442,818	1,040,171	738,185	
Deferred license fee revenue, net of current portion	1,551,875	1,647,687	1,445,534	
Total liabilities	9,687,534	8,051,421	9,041,738	
Commitments				
Redeemable convertible preferred stock:				
Series A, $0.001 par value, 5,000,000 shares authorized, issued and outstanding, aggregate liquidation preference of $26,826,253, $28,496,497 and $29,749,180 at December 31, 2002, 2003, and September 30, 2004, respectively, or $4.65 per share plus accreted redemption value	26,826,253	28,496,497	29,749,180	
Series B, $0.001 par value, 6,567,567 shares authorized, issued and outstanding, aggregate liquidation preference of $35,346,675, $37,484,419 and $39,087,725 at December 31, 2002, 2003, and September 30, 2004, respectively, or $4.65 per share, plus accreted redemption value	35,346,675	37,484,419	39,087,725	
Series C, $0.001 par value, 37,764,180, 49,169,138 and 49,169,138 shares authorized, issued and outstanding at December 31, 2002, 2003, and September 30, 2004, respectively, aggregate liquidation preference of $45,853,329, $64,153,421 and $67,723,100 at December 31, 2002, 2003, and September 30, 2004, or $1.21 per share, plus accreted redemption value	45,853,329	64,153,421	67,723,100	
Total redeemable convertible preferred stock	108,026,257	130,134,337	136,560,005	
Stockholders' equity (deficit):				
Common stock, $0.001 par value, 75,000,000, 85,000,000 and 85,000,000 shares authorized at December 31, 2002, 2003, and September 30, 2004, respectively, 624,584, 1,082,771 and 1,887,356 shares issued and outstanding at December 31, 2002, 2003, and September 30, 2004, respectively.	625	1,083	1,888	$
Capital in excess of par value	386,854	690,675	1,225,177	
Common stock warrants	213,710	213,710	213,710	
Accumulated deficit	(63,936,112)	(91,672,061)	(117,834,669)	
Accumulated other comprehensive loss	—	(29,282)	—	
Total stockholders' equity (deficit)	(63,334,923)	(90,795,875)	(116,393,894)	
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 54,378,868	$ 47,389,883	$ 29,207,849	$

See accompanying notes.

Targacept, Inc.

Statements of Operations

	Year ended December 31,			Nine months ended September 30,	
	2001	2002	2003	2003	2004
				(unaudited)	
Revenue:					
Research fee revenue	$ 1,100,000	$ 1,388,824	$ 1,302,500	$ 965,000	$ 208,806
License fee revenue	602,807	634,881	269,532	202,149	202,153
Product sales	—	242,861	814,724	582,365	584,167
Other	687	19,792	71,529	66,639	585,422
Net revenue	1,703,494	2,286,358	2,458,285	1,816,153	1,580,548
Operating expenses:					
Research and development	8,151,785	16,243,888	18,179,542	13,376,468	17,782,199
General and administrative	2,302,161	4,135,262	3,599,673	2,698,385	3,763,700
Cost of product sales	—	243,718	742,941	539,736	27,629
Purchased in-process research and development	—	2,666,000	—	—	—
Total operating expenses	10,453,946	23,288,868	22,522,156	16,614,589	21,573,528
Loss from operations	(8,750,452)	(21,002,510)	(20,063,871)	(14,798,436)	(19,992,980)
Other income (expense):					
Interest and dividend income	1,448,182	87,691	791,339	546,263	355,638
Interest expense	—	(102,891)	(122,789)	(95,753)	(95,755)
Loss on disposal of fixed assets	—	(53,996)	—	—	(3,843)
Total other income (expense)	1,448,182	(69,196)	668,550	450,510	256,040
Net loss	(7,302,270)	(21,071,706)	(19,395,321)	(14,347,926)	(19,736,940)
Preferred stock accretion	(3,807,988)	(4,173,545)	(8,340,628)	(6,198,736)	(6,425,668)
Net loss attributable to common stockholders	$ (11,110,258)	$ (25,245,251)	$ (27,735,949)	$ (20,546,662)	$ (26,162,608)
Basic and diluted net loss attributable to common stockholders per share	$ (26.80)	$ (45.28)	$ (33.91)	$ (27.04)	$ (16.82)
Weighted average common shares outstanding—basic and diluted	414,624	557,492	817,894	759,937	1,555,090
Pro forma basic and diluted net loss per share attributable to common stockholders assuming conversion of preferred stock (unaudited)			$ (0.27)		$ (0.26)
Pro forma weighted average shares outstanding—basic and diluted (unaudited)			71,118,629		75,294,995

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	Deferred Compensation	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Deficit
	Series A	Series B	Series C	Shares	Amount						
Balances at December 31, 2000	$23,485,765	$30,932,000	$ —	309,424	$ 309	$145,120	$ 213,710	$ (92,638)	$ (27,580,603)	$ —	$ (27,314,102)
Stock issuance costs	—	—	—	—	—	(42,496)	—	—	—	—	(42,496)
Issuance of 29,933 shares of Series B redeemable convertible preferred stock at $4.65 per share	—	139,188	—	—	—	—	—	—	—	—	—
Issuance of 111,111 shares of common stock valued at $0.68 per share, related to collaborative research and development agreement	—	—	—	111,111	111	75,445	—	—	—	—	75,556
Issuance of 65,565 shares of common stock at $0.001 per share par value, related to exercise of stock options	—	—	—	65,565	66	30,749	—	—	—	—	30,815
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 and Series B redeemable convertible preferred stock	1,627,500	2,137,744	—	—	—	—	—	—	(3,765,244)	—	(3,765,244)
Amortization of deferred compensation	—	—	—	—	—	—	—	92,638	—	—	92,638
Net loss	—	—	—	—	—	—	—	—	(7,302,270)	—	(7,302,270)
Balances at December 31, 2001	25,156,009	33,208,932	—	486,100	486	208,818	213,710	—	(38,690,861)	—	(38,267,847)
Stock issuance costs	—	—	(206,887)	—	—	—	—	—	—	—	—
Issuance of 37,764,180 shares of Series C redeemable convertible preferred stock at $1.21 per share	—	—	45,694,658	—	—	—	—	—	—	—	—
Issuance of 138,484 shares of common stock at $0.001 per share par value, related to exercise of stock options	—	—	—	138,484	139	178,036	—	—	—	—	178,175
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	2,137,743	365,558	—	—	—	—	—	(4,130,801)	—	(4,130,801)
Net loss	—	—	—	—	—	—	—	—	(21,071,706)	—	(21,071,706)
Balances at December 31, 2002	$26,826,253	$35,346,675	$45,853,329	624,584	$ 625	$386,854	$ 213,710	$ —	$ (63,936,112)	$ —	$ (63,334,923)

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	Deferred Compensation	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Deficit
	Series A	Series B	Series C	Shares	Amount						
Balances at December 31, 2002 (carried forward)	$26,826,253	$35,346,675	$45,853,329	624,584	$ 625	$ 386,854	$ 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 458,187 shares of common stock at $0.001 per share par value, related to exercise of stock options	—	—	—	458,187	458	303,821	—	—	—	—	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	1,082,771	1,083	690,675	213,710	—	(91,672,061)	(29,282)	(90,795,875)
Issuance of 804,585 shares of common stock at $0.001 per share par value, related to exercise of stock options (unaudited)	—	—	—	804,585	805	534,502	—	—	—	—	535,307
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock (unaudited)	32,058	—	—	—	—	—	—	—	(32,058)	—	(32,058)
Accreted redemption value for Series A Series B and Series C redeemable convertible preferred stock (unaudited)	1,220,625	1,603,306	3,569,679	—	—	—	—	—	(6,393,610)	—	(6,393,610)
Net change in unrealized holding loss on available-for-sale securities (unaudited)	—	—	—	—	—	—	—	—	—	29,282	29,282
Net loss (unaudited)	—	—	—	—	—	—	—	—	(19,736,940)		(19,736,940)
Comprehensive loss (unaudited)											(19,707,658)
Balances at September 30, 2004 (unaudited)	$29,749,180	$39,087,725	$67,723,100	1,887,356	$ 1,888	$1,225,177	$ 213,710	$ —	$(117,834,669)	$ —	$(116,393,894)

See accompanying notes.

Targacept, Inc.

Statements of Cash Flows

	Year ended December 31,			Nine months ended September 30,	
	2001	2002	2003	2003	2004
				(unaudited)	
Operating activities					
Net loss	$ (7,302,270)	$ (21,071,706)	$ (19,395,321)	$ (14,347,926)	$ (19,736,940)
Adjustments to reconcile net loss to net cash used in operating activities:					
Depreciation and amortization	308,594	958,105	672,927	502,780	564,010
Loss on disposal of equipment	—	53,996	—	—	3,843
Write-off of in-process research and development	—	2,666,000	—	—	—
Non-cash compensation expense	92,638	129,710	65,325	43,131	32,700
Recognition of deferred rent incentive	—	(167,769)	(402,647)	(301,986)	(301,986)
Realized loss on sale of investments	—	—	20,978	—	99,023
Amortization of discount on held-to-maturity investments	(460,701)	(48,446)	—	—	—
Changes in operating assets and liabilities, excluding the effects from acquired assets and liabilities:					
Research fees and accounts receivable	(210,448)	(713,109)	517,030	187,621	613,290
Inventories	—	22,464	51,016	12,464	12,245
Prepaid expenses and accrued interest receivable	(555,929)	158,605	(205,054)	70,961	(885,121)
Accounts payable and accrued expenses	742,837	1,503,132	(326,451)	(1,107,816)	979,062
Deferred license fee revenue	1,321,637	(634,881)	(269,532)	(202,144)	(202,153)
Net cash used in operating activities	(6,063,642)	(17,143,899)	(19,271,729)	(15,142,915)	(18,822,027)
Investment activities					
Purchase of investments	(29,284,891)	(11,500,000)	(84,796,103)	(48,500,000)	(6,191,930)
Proceeds from sale of investments	32,700,000	26,400,000	58,500,000	48,503,548	37,368,032
Purchase of property and equipment	(1,522,064)	(1,281,840)	(545,254)	(284,707)	(591,539)
Proceeds from sale of property and equipment	—	—	—	—	35,592
Proceeds from rent incentive	—	2,013,234	—	—	—
Purchase of Inversine product	—	(3,500,000)	—	—	—
Net cash provided by (used in) investing activities	1,893,045	12,131,394	(26,841,357)	(281,159)	30,620,155
Financing activities					
Proceeds from borrowing of long-term debt	—	3,000,000	—	—	1,027,000
Principal payments on long-term debt	—	(324,891)	(637,483)	(436,471)	(511,606)
Proceeds from issuance of redeemable convertible preferred stock, net of transaction costs	96,692	45,487,771	13,767,452	13,767,452	—
Proceeds from issuance of common stock	106,371	48,465	238,954	173,147	502,607
Net cash provided by (used in) financing activities	203,063	48,211,345	13,368,923	13,504,128	1,018,001
Net (decrease) increase in cash and cash equivalents	(3,967,534)	43,198,840	(32,744,163)	(1,919,946)	12,816,129
Cash and cash equivalents at beginning of period	5,122,014	1,154,480	44,353,320	44,353,320	11,609,157
Cash and cash equivalents at end of period	$ 1,154,480	$ 44,353,320	$ 11,609,157	$ 42,433,374	$ 24,425,286

See accompanying notes.

Targacept, Inc.

Notes to Financial Statements
December 31, 2003

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 acetylcholine 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 forseeable 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.

The accompanying balance sheet as of September 30, 2004, the statements of operations and statements of cash flows for the nine months ended September 30, 2003 and 2004 and the statement of redeemable convertible preferred stock and stockholders' equity (deficit) for the nine months ended September 30, 2004 are unaudited. The unaudited interim financial statements have been prepared on the same basis as the annual financial statements and, in the opinion of the Company's management, reflect all adjustments, which include only normal recurring adjustments necessary to present fairly the Company's financial position and results of operations and cash flows for the nine months ended September 30, 2003 and 2004. The financial data and other information disclosed in these notes to financial statements related to the nine-month periods are unaudited. The results for the nine months ended September 30, 2004 are not necessarily indicative of the results to be expected for the year ending December 31, 2004 or for any other interim period or for any other future year.

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 a mutual fund that invests in Government National Mortgage Association and other mortgage-backed 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 have been classified as available-for-sale and are stated at market value with the unrealized holding gains and losses reported as a component of stockholders' equity in comprehensive loss. Interest and dividend income on investments, as well as realized gains and losses, are included in "Interest and dividend income." 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 15, and trade sales of Inversine. All of the Company's trade

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

accounts receivable are due from customers located within the United States. The Company makes judgments with respect to the collectibility of trade accounts receivable based on historical experience and current economic trends. Actual losses could differ from those estimates.

During 2001, 2002, 2003 and the nine months ended September 30, 2004, the Company recognized revenues of $1,703,000, $2,024,000, $1,572,000 and $411,000, respectively, or 99%, 89%, 64% and 26%, respectively, of net revenues, from two collaborative research and license agreements discussed in Note 15.

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 7-10 years, and leasehold improvements are amortized over the life of the applicable lease.

Intangible assets consist of patents acquired (See Note 16). 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 loss 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 loss, if recognized, would be based on the excess of the carrying value of the impaired asset over its respective fair value. Through September 30, 2004, there has been no such impairment.

Patents

The Company capitalizes the costs of patents purchased from external sources. The Company expenses all other patent-related costs.

Research and Development Costs

Research and development costs are expensed as incurred and include related salaries of 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 2001, 2002 and 2003 and the nine months ended September 30, 2004, research and development expenses were reduced by $412,000, $514,000, $131,000 and $95,000, respectively, for costs reimbursed primarily by Dr. Falk Pharma, GmbH and under the terms of the collaboration described in Note 15.

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

Clinical Trials Accounting

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.

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 $168,000, $403,000 and $302,000 of the incentive during 2002, 2003 and the nine months ended September 30, 2004, respectively.

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, short-term investments, 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 is $2,590,000, $1,961,000 and $2,495,000 at December 31, 2002, 2003 and September 30, 2004, respectively. The Company estimates the fair value of long-term debt using discounted cash flows based on its incremental borrowing rates for similar debt.

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.

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, *Revision of Topic 13*. Revenues are recorded under collaboration agreements at the time of performance of services. Research fee revenues are earned and recognized in accordance with contract provisions. License fees for access to the Company's

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

intellectual properties 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 statements of operations into revenue over the estimated life of the research and development period. Revenues from milestones are only recognized upon achievement of the milestone criteria. Product sales revenues are recorded when goods are shipped, at which point title has passed.

Shipping and Handling Costs

During 2002, 2003 and the nine months ended September 30, 2004, $22,000, $173,000 and $129,000 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 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.

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 under the terms presently

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

anticipated, all of the redeemable convertible preferred stock outstanding at the time of the IPO will automatically convert into 73,739,905 shares of common stock. Unaudited pro forma stockholders' equity, as adjusted for the assumed conversion of the preferred stock, is set forth on the accompanying balance sheets. 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, 2003, or the date of issuance, if later.

The following table sets forth the computation of basic and diluted, and unaudited pro forma basic and diluted, net loss per share attributable to common stockholders:

	Year ended December 31,			Nine months ended September 30,	
	2001	2002	2003	2003	2004
				(unaudited)	
Historical					
Numerator:					
Net loss attributable to common stockholders	$ (11,110,258)	$ (25,245,251)	$ (27,735,949)	$ (20,546,662)	$ (26,162,608)
Denominator:					
Weighted-average common shares outstanding	414,624	557,492	817,894	759,937	1,555,090
Basic and diluted net loss per share attributable to common stockholders	$ (26.80)	$ (45.28)	$ (33.91)	$ (27.04)	$ (16.82)
Pro forma					
Numerator:					
Net loss attributable to common stockholders			$ (19,395,321)		$ (19,736,940)
Denominator:					
Shares used above			817,894		1,555,090
Pro forma adjustments to reflect assumed conversion of preferred stock, on a weighted average basis (unaudited)			70,300,735		73,739,905
Shares used to compute pro forma basic and diluted net loss per share attributable to common stockholders (unaudited)			71,118,629		75,294,995
Pro forma basic and diluted net loss per share attributable to common stockholders (unaudited)			$ (0.27)		$ (0.26)

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

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,			Nine Months ended September 30,	
	2001	2002	2003	2003	2004
Outstanding common stock options	1,496,707	2,150,650	4,601,270	3,918,198	7,637,869
Redeemable convertible preferred stock	11,567,567	15,980,048	70,300,735	69,141,747	73,739,905
Outstanding warrants	1,612,903	1,612,903	1,612,903	1,612,903	1,612,903
Total	14,677,177	19,743,601	76,514,908	74,672,848	82,990,677

Stock-Based Compensation

In December 2002, the Financial Accounting Standards Board ("FASB") issued SFAS No. 148, *Accounting for Stock-Based Compensation—Transition and Disclosure.* SFAS No. 148 amends SFAS No. 123 to provide alternative methods of transition for a voluntary change to the fair value based method of accounting for stock-based employee compensation. In addition, SFAS No. 148 amends the disclosure provisions of SFAS No. 123 and Accounting Principles Board ("APB") Opinion No. 28, *Interim Financial Reporting*, to require more prominent disclosure in the summary of significant accounting policies about the method of accounting for the effects of an entity's accounting policy with respect to stock-based employee stock compensation and the effect of the method used on reported net loss results.

The Company has elected to continue to account for stock options granted to employees using the intrinsic-value method as prescribed by APB Opinion No. 25, *Accounting for Stock Issued to Employees*, and, thus recognizes no compensation expense for options granted with exercise prices equal to the fair market value of the Company's common stock on the date of grant. The information regarding net loss as required by SFAS No. 123 has been determined as if the Company had accounted for its employee stock options under the fair value method of that Statement.

The following table illustrates the weighted-average assumptions for the Black-Scholes model used in determining the fair value of options granted to employees:

	Year ended December 31,			Nine months ended September 30,	
	2001	2002	2003	2003	2004
Dividend yield	—	—	—	—	—
Risk-free interest rate	4.0%	3.5%	2.8%	2.5%	2.7%
Volatility	0.8	0.8	0.8	0.8	0.8
Expected life	4 years	4 years	4 years	4 years	4 years

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

For purposes of disclosures pursuant to SFAS No. 123, as amended by SFAS No. 148, the estimated fair value of the options is amortized to expense over the options' vesting period. The following table illustrates the effect on net loss if the Company had applied the fair value recognition provisions of SFAS No. 123:

	Year Ended December 31,			Nine months ended September 30,	
	2001	2002	2003	2003	2004
Net loss attributable to common stockholders, as reported	$ (11,110,258)	$ (25,245,251)	$ (27,735,949)	$ (20,546,662)	$ (26,162,608)
Add: Stock-based employee compensation expense included in reported net income, net of related tax effects	92,638	129,710	65,325	43,131	32,700
Deduct: Stock-based employee compensation expense determined under fair value based method for all awards, net of related tax effects	(205,710)	(312,830)	(515,405)	(320,882)	(681,777)
Pro forma net loss	$ (11,223,330)	$ (25,428,371)	$ (28,186,029)	$ (20,824,413)	$ (26,811,685)
Net loss per share:					
Basic and diluted, as reported	$ (26.80)	$ (45.28)	$ (33.91)	$ (27.04)	$ (16.82)
Basic and diluted, pro forma	$ (27.06)	$ (45.61)	$ (34.46)	$ (27.40)	$ (17.24)

Stock compensation arrangements to non-employees are accounted for in accordance with SFAS No. 123, as amended by SFAS No. 148, and EITF No. 96-18, *Accounting for Equity Instruments That Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services*, using a fair value approach.

Recent Accounting Pronouncements

In 2003, FASB Statement No. 150, *Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity* ("SFAS 150"), was issued. This statement establishes how a company classifies and measures certain financial instruments with characteristics of both liabilities and equity, including redeemable convertible preferred stock. This statement is effective for financial instruments entered into or modified after May 31, 2003, and otherwise effective at the beginning of the interim period commencing July 1, 2003, except for mandatory redeemable financial instruments of nonpublic companies. The FASB has indefinitely deferred implementation of certain provisions of SFAS 150. The adoption of SFAS 150 did not affect the financial position or results of operations of the Company.

In 2003, the FASB issued Interpretation No. 46, *Consolidation of Variable Interest Entities* ("FIN 46"), which is an interpretation of Accounting Research Bulletin No. 51, *Consolidated Financial Statements*. FIN 46 requires that if an entity has a controlling interest in a variable interest entity, the assets, liabilities, and results of activities of the variable interest entity should be included in the consolidated financial statements of the entity. FIN 46 is effective immediately for all new variable interest entities created or acquired after January 31, 2003. The Company implemented the provisions of FIN 46 for its financial statements for the year ending December 31, 2003 for any variable interest entities created before February 1, 2003. The adoption of FIN 46 did not affect the financial position or results of operations of the Company.

In October 2004, the FASB announced that FASB Statement No. 123R, *Share-Based Payment*, which would require all companies to measure compensation cost for all share-based payments, including employee stock

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

options, at fair value, would be effective for public companies for interim or annual periods beginning after June 15, 2005. SFAS 123R would require companies to expense the fair value of all stock options that have future vesting provisions, are modified or are newly granted beginning on the grant date of such options. The Company will evaluate the requirements of the final standard, which is expected to be issued in December 2004, to determine the impact on its financial position and results of operations.

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 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 or previously recorded amounts.

3. Short-term investments

The following is a summary of available-for-sale securities as of December 31, 2002 and 2003. During 2004, all short-term investments present at December 31, 2003 were converted to cash.

December 31, 2002	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Certificates of deposit	$5,000,000	$ —	$ —	$5,000,000
Interest receivable	8,139	—	—	8,139
Total	$5,008,139	$ —	$ —	$5,008,139

December 31, 2003	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Adjustable rate mortgage fund	$20,177,033	$ —	$(29,282)	$20,147,751
Certificates of deposit	11,098,092	—	—	11,098,092
Interest receivable	121,657	—	—	121,657
Total	$31,396,782	$ —	$(29,282)	$31,367,500

The adjustable rate mortgage fund investment has remained in an unrealized loss position for less than 6 months. Accordingly the Company believes this is a temporary decline. The Company recognized $1,448,000, $88,000, $591,000 and $159,000 of interest income during 2001, 2002, 2003 and the nine months ended September 30, 2004, respectively. The Company recognized $200,000 and $193,000 of dividend income during 2003 and the nine months ended September 30, 2004, respectively.

4. Inventories

Inventories consisted of the following:

	December 31,		September 30,
	2002	2003	2004
Raw materials	$137,706	$ 46,988	$ 46,988
Work-in-process	9,042	6,892	6,400
Finished goods	22,788	64,640	52,887
	$169,536	$118,520	$ 106,275

Targacept, Inc.

Notes to Financial Statements—(continued)

5. Property and equipment

Property and equipment consists of the following:

	December 31,		September 30,
	2002	2003	2004
Lab equipment	$ 4,674,369	$ 5,057,345	$ 4,746,687
Office furniture and fixtures	1,030,406	1,192,685	1,426,680
Leasehold improvements	87,875	87,875	132,941
	5,792,650	6,337,905	6,306,308
Less: accumulated depreciation	3,329,706	3,964,870	3,916,856
Property and equipment, net	$ 2,462,944	$ 2,373,035	$ 2,389,452

The Company recorded $309,000, $577,000, $635,000 and $536,000 of depreciation expense during 2001, 2002, 2003 and the nine months ended September 30, 2004, respectively.

6. Intangible Assets

Intangible assets consist of the following:

	December 31,		September 30,
	2002	2003	2004
Patents (See Note 16)	$642,000	$642,000	$ 642,000
Less: accumulated amortization	(15,735)	(53,499)	(81,822)
Total	$626,265	$588,501	$ 560,178

The Company recognized amortization expense of $0, $16,000, $38,000 and $28,000 in 2001, 2002, 2003 and the nine months ended September 30, 2004, respectively. The Company expects to recognize $38,000 of amortization expense in each of the next five years.

7. Accrued Expenses

Accrued expenses consists of the following:

	December 31,		September 30,
	2002	2003	2004
Clinical trials costs	$ 361,119	$ 623,158	$ 935,058
Employee compensation	860,368	676,900	759,301
Other	255,547	106,720	64,920
	$ 1,477,034	$ 1,406,778	$ 1,759,279

8. 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

Targacept, Inc.

Notes to Financial Statements—(continued)

8. Long-term debt (continued)

Winston-Salem note until the 5-year anniversary of the loan. The note payable to RJRT accrues interest at 6.6%, is repayable in monthly payments of $59,403 through the maturity date of May 1, 2006, and is secured by equipment owned by the Company with a book value of approximately $2,373,000, net of accumulated depreciation, at December 31, 2003. 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 on 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 paid $91,000, $135,000 and $84,000 for interest under the RJRT note during 2002, 2003 and the nine months ended September 30, 2004, respectively.

Maturities of long-term debt are as follows:

	Maturities as of	
	December 31, 2003	September 30, 2004
2004	$ 576,072	$ 219,372
2005	669,379	913,378
2006	292,175	550,889
2007	69,438	343,753
2008	93,830	188,896
Thereafter	336,732	336,732
	$ 2,037,626	$ 2,553,020

See Note 18—Subsequent Events.

9. 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.

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 $13,767,452, net of offering costs.

See Note 18—Subsequent Events.

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, 2003 and September 30, 2004, conversion of the Series A, Series B and Series C would result in the issuance of 5,000,000, 15,619,675, and 53,120,230 shares of common stock, respectively. Future sales of equity at prices below the respective

Targacept, Inc.

Notes to Financial Statements—(continued)

9. Redeemable Preferred Stock (continued)

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 $3.60 (subject to certain adjustments) and (ii) the gross proceeds to the Company are not less than $50,000,000. 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 liquidation or redemption. At December 31, 2003 and September 30, 2004, cumulative accrued dividends on the Series C stock totaled $4,898,000 and $8,468,000, respectively.

Dividends on the Series A, Series B and Series C are payable when and if declared by the 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

Targacept, Inc.

Notes to Financial Statements—(continued)

9. Redeemable Preferred Stock (continued)

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 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.

10. Stockholders' Equity (Deficit)

Prior to August 22, 2000, the Company was a wholly owned subsidiary of RJRT. On August 22, 2000, the Company reclassified its 500 shares of common stock as 5,000,000 shares of Series A and a warrant to purchase 1,612,903 shares of the Company's common stock at $4.65 per share. The fair value of the Series A redeemable convertible preferred stock was determined to be $4.65 per share based on the sales price of Series B of $4.65 per share redeemable convertible preferred stock with rights containing identical terms as Series A. As cash was not received in connection with this reclassification of the 500 shares of common stock into shares of Series A redeemable convertible preferred stock, the fair value of $23,250,000 was recorded as redeemable convertible preferred stock. On the same date, the Company sold 5,892,473 shares of the Company's Series B to an investor group. The Company then issued 309,424 shares of the common stock to management, at par value, for proceeds of $309, which was less than fair value. As a result, the Company recorded compensation expense of $145,120. An aggregate of 645,161 shares of Series B redeemable convertible preferred stock were subsequently sold in a second offering to certain of the Company's investors.

On January 2, 2001, the Company amended its Certificate of Incorporation to increase the number of authorized shares of preferred stock to 11,567,567 shares and issued 29,933 shares of Series B to consultants in exchange for the partial satisfaction of a cash liability on January 26, 2001.

On November 26, 2002, the Company amended its Certificate of Incorporation to increase the number of authorized shares of common stock to 75,000,000 and preferred stock to 49,331,747 and issued 37,764,180 shares of Series C.

On March 14, 2003, the Company amended its Certificate of Incorporation to increase the number of authorized shares of common stock to 85,000,000 and preferred stock to 60,736,705 and issued 11,404,958 shares of Series C.

In conjunction with the issuance of Series A, the Company issued a warrant to purchase 1,612,903 shares of the Company's common stock at an original exercise price of $4.65 per share (subject to certain adjustments). In

Targacept, Inc.

Notes to Financial Statements—(continued)

10. Stockholders' Equity (Deficit) (continued)

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 $1.95. 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 August 2005 through an increase in redemption value to Series A and an increase to retained deficit. The fair value of the warrant to purchase 1,612,903 shares of the Company's common stock was estimated at the grant date to be $213,710 or $0.53 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.

At December 31, 2003 and September 30, 2004, the Company had reserved shares of common stock for future issuance as follows:

	December 31, 2003	September 30, 2004
Convertible preferred stock	73,739,905	73,739,905
Warrant	1,612,903	1,612,903
Options	8,554,421	7,749,836
	83,907,229	83,102,644

11. 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,			Nine months ended September 30,
	2001	2002	2003	2004
Expected federal income tax benefit at statutory rate	(34)%	(34)%	(34)%	(34)%
Increase (decrease) resulting from:				
Research and development credits	—	(1)	(6)	(3)
Purchased in-process research and development	—	4	—	—
State income tax expense, net of federal benefit	(5)	(4)	(5)	(5)
Net operating loss and credit limitations	—	14	3	—
Change in valuation allowance	38	21	41	42
Other	1	—	1	—
	—%	—%	—%	—%

At December 31, 2002 and 2003 and September 30, 2004, the Company had net operating loss carryforwards for federal income tax purposes of approximately $17,637,000, $38,409,000 and $57,489,000, respectively, $25,317,000, $46,090,000 and $65,170,000, respectively, for state income tax purposes, and research and development tax credits of approximately $299,000, $1,456,000 and $1,202,000, 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 will begin to expire in 2021.

Targacept, Inc.

Notes to Financial Statements—(continued)

11. Income Taxes (continued)

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 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, 2002, 2003 and the nine months ended September 30, 2004, the valuation allowance increased approximately $7,380,000, $8,617,000 and $4,736,000, respectively.

Significant components of the Company's deferred tax assets (liabilities) are as follows:

	December 31,		September 30,
	2002	2003	2004
Deferred tax assets:			
Net operating loss carryforward	$ 7,149,405	$ 15,158,059	$ 22,514,223
Research and development tax credit	48,153	638,153	1,202,482
Equipment and other	226,338	—	—
Patents	682,413	641,008	557,356
Unearned revenue	843,084	739,167	661,229
Total gross deferred tax assets	8,949,393	17,176,387	24,935,290
Valuation allowance	(8,949,393)	(16,999,275)	(24,782,695)
Net deferred tax asset	—	177,112	152,595
Deferred tax liabilities:			
Equipment and other	—	(177,112)	(152,595)
Net deferred tax asset	$ —	$ —	$ —

12. Equity Incentive Plan

On August 22, 2000, the Company established an Equity Incentive Plan (the "Plan") and authorized the issuance of up to 2,011,259 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 2,611,259. In conjunction with the Series C financing, the Company authorized the issuance of an additional 3,000,000 shares, increasing the number of authorized shares to 5,611,259. Upon the issuance of the additional Series C shares in March 2003, the number of authorized shares was increased to 9,216,657. Awards may be made to participants under the Plan in the form of incentive and nonqualified stock options, restricted stock, stock appreciation rights,

Targacept, Inc.

Notes to Financial Statements—(continued)

12. Equity Incentive Plan (continued)

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. 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. The following summarizes stock option activity and balances:

	Options Granted	Price	Weighted Average Exercise Price Per Share
Outstanding at January 1, 2001	1,234,999	0.47	$ 0.47
Granted	440,000	0.47-4.65	0.90
Forfeited	(31,717)	0.47	0.47
Exercised	(65,565)	0.47	0.47
Outstanding at December 31, 2001	1,577,717	0.47-4.65	0.59
Granted	838,550	0.01-0.68	0.58
Forfeited	(18,672)	0.56	0.56
Exercised	(90,984)	0.47-0.68	0.53
Outstanding at December 31, 2002	2,306,611	0.47-4.65	0.59
Granted	5,996,095	0.01-0.75	0.67
Forfeited	(35,980)	0.01-0.68	0.26
Exercised	(458,187)	0.01-0.68	0.52
Outstanding at December 31, 2003	7,808,539	0.01-0.75	0.65
Granted	381,900	0.01-0.75	0.70
Forfeited	(35,543)	0.68-4.65	3.47
Exercised	(804,585)	0.47-0.75	0.62
Outstanding at September 30, 2004	7,350,311	$0.01-0.75	$ 0.64

The weighted average fair value of options granted during 2001, 2002, 2003 and the nine months ended September 30, 2004 was $0.38, $0.46, $0.41 and $0.47, respectively. At December 31, 2001, 2002, 2003 and September 30, 2004, 83,305, 958,059, 3,538,218 and 4,118,303 options, respectively, were exercisable at a weighted-average price of $0.47, $0.64, $0.63 and $0.62, respectively.

A summary of options outstanding as of December 31, 2003 is as follows:

	Options Outstanding			Options Exercisable	
Exercise Price	Number Outstanding	Weighted Average Remaining Contractual Exercise Life	Weighted Average Exercise Price	Number Exercisable	Weighted Average Price
0.01	184,225	9.0	$ 0.01	184,225	$ 0.01
0.47	919,437	6.7	0.47	692,331	0.47
0.68	6,629,877	9.4	0.68	2,636,662	0.68
0.75	50,000	9.9	0.75	—	—
4.65	25,000	7.1	4.65	25,000	4.65
	7,808,539	9.1	$ 0.65	3,538,218	$ 0.63

Targacept, Inc.

Notes to Financial Statements—(continued)

12. Equity Incentive Plan (continued)

A summary of options outstanding as of September 30, 2004 (unaudited) is as follows:

	Options Outstanding			Options Exercisable	
Exercise Price	Number Outstanding	Weighted Average Remaining Contractual Exercise Life	Weighted Average Exercise Price	Number Exercisable	Weighted Average Price
0.01	209,225	8.4	$ 0.01	184,225	$ 0.01
0.47	702,078	6.0	0.47	698,423	0.47
0.68	6,050,382	8.7	0.68	2,957,955	0.68
0.75	388,626	9.3	0.75	277,700	0.75
	7,350,311	8.5	$ 0.64	4,118,303	$ 0.62

During 2001, the Company granted 25,000 options above fair value at a weighted-average exercise price of $4.65. The options had a weighted-average fair value of $0. During 2002 and 2003, respectively, the Company granted 130,000 and 97,500 options below fair value at an exercise price of $0.01 and fair value of $0.67 per share. The fair value of these shares was recorded as compensation expense in the amounts $129,710 and $65,325, during 2002 and 2003, respectively. During the nine months ended September 30, 2004, the Company granted 25,000 options below fair value at an exercise price of $0.01 and a fair value of $0.74 per share. The fair value of these shares was recorded as compensation expense in the amount of approximately $33,000.

See Note 18—Subsequent Events.

13. Leases

Prior to March 1, 2002, the Company leased its office space and certain equipment under a non-cancelable, one-year operating lease agreement with RJRT. Rent expense incurred by the Company under the RJRT lease was approximately $609,000 and $106,000 for the years ended December 31, 2001 and 2002, respectively. The Company has no future minimum lease payments to RJRT as of December 31, 2003.

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. Rent expense incurred by the Company under this lease was approximately $904,000, $1,456,000 and $1,092,000 for the years ended December 31, 2002, 2003 and the nine months ended September 30, 2004, respectively. Rent expense is offset by the monthly recognition of the deferred rent incentive discussed in Note 2. At December 31, 2003, the Company has the following future minimum lease payments in relation to this lease:

2004	$ 1,455,552
2005	1,455,552
2006	1,455,552
2007	849,072
2008 and thereafter	—
	$ 5,215,728

Targacept, Inc.

Notes to Financial Statements—(continued)

14. 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 $171,000, $290,000, $298,000 and $290,000 to the plan for the years ended December 31, 2001, 2002, 2003 and the nine months ended September 30, 2004, respectively.

15. Collaborative Research and License Agreements

Aventis Pharma

In December 1998, the Company entered into a collaborative research and license agreement with Aventis Pharma ("Aventis") 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 provides 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, 2001, 2002, and 2003 and the nine months ended September 30, 2004, these fees were $1,100,000, $1,389,000, $1,303,000 and $209,000, respectively. The Company is entitled to receive milestone payments under the contract at specified dates during the development period. The Company did not receive milestone payments under the agreement during 2001, 2002, 2003 or the nine months ended September 30, 2004. In addition, Aventis agreed to make royalty payments based on net sales of products developed and sold. In general, either party may 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 may 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. The product candidate subject to the agreement has not completed the research and clinical development process. Accordingly, the Company has deferred recognition of the license fee and is amortizing it over the expected term of the research and development period. The Company recognized $250,000, $250,000, $100,000 and $75,000 of the license fee payment during 2001, 2002, 2003 and the nine months ended September 30, 2004, respectively.

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 terms of the agreement will extend for two years.

See Note 18—Subsequent Events.

Dr. Falk Pharma

On January 26, 2001, the Company entered into a collaborative research development and license agreement with Dr. Falk Pharma GmbH ("Dr. Falk Pharma"), 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 license fee and purchased 111,111 shares of the Company's common stock for $1,000,000. The Company is continuing to advance the compound subject to the agreement through the research and clinical development process. Therefore, the Company has deferred recognition of the license fee payment and is amortizing it over the expected term of the research and development period. To account for the

Targacept, Inc.

Notes to Financial Statements—(continued)

15. Collaborative Research and License Agreements (continued)

$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 $75,556, with the remaining proceeds of $924,494 allocated to deferred revenue. This deferred revenue is also being amortized over the expected term of the research and development period. The Company recognized $353,000, $385,000, $170,000 and $127,000 of deferred revenue under this agreement during 2001, 2002, 2003 and the nine months ended September 30, 2004, respectively. As of September 30, 2004, deferred revenue under this agreement was approximately $890,000 and was included in deferred license fee revenue in the accompanying balance sheet.

Dr. Falk Pharma agreed to make royalty payments based on net profits from products containing compounds developed under the agreement. For the years ended December 31, 2001, 2002, 2003 and the nine months ended September 30, 2004, the Company did not pay or receive any royalties related to this agreement.

16. Acquisition of Inversine Product

On August 5, 2002, the Company purchased from Layton Bioscience the Inversine product line, inventory and related patent rights for cash consideration of $3,500,000. The purchase was made in order to further the Company's science and portfolio of compounds, and to further the Company's development in certain neuropsychiatric indications.

This transaction was accounted for as an acquisition of assets. The aggregate purchase price was allocated to the assets acquired based on their fair values as follows:

	Amount
Inventories	$ 192,000
Intangible assets acquired:	
Core technology	296,000
Developed product technology	346,000
In-process research and development	2,666,000
Aggregate purchase price	$ 3,500,000

In determining the total consideration as well as the allocation of the purchase price including the amount of in-process research and development, the Company considered as part of its analysis an appraisal prepared by an independent appraiser that used established valuation techniques appropriate for the pharmaceutical industry. The amount allocated to in-process research and development was expensed upon acquisition. A one-time charge of $2,666,000 for purchased in-process research and development arising from the acquisition has been reflected in the Statement of Operations for the year ended December 31, 2002.

17. Related Party Transactions

RJRT is the holder of 5,000,000 shares of Series A redeemable preferred stock convertible to 5,000,000 shares of common stock, a warrant to purchase 1,612,903 shares of common stock, and options to purchase 31,725 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, and is secured by equipment owned by us with a book value of approximately $2,373,000, net of accumulated

Targacept, Inc.

Notes to Financial Statements—(continued)

17. Related Party Transactions (continued)

depreciation, at December 31, 2003. 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. Under this related party note payable, the Company paid RJRT $416,000, $772,000 and $596,000 during 2002, 2003 and the nine months ended September 30, 2004, respectively.

Prior to March 1, 2002, the Company leased office space and certain equipment under a non-cancelable operating lease agreement with RJRT. Rent expense incurred by the Company under the RJRT lease was approximately $609,000 and $106,000 for the years ended December 31, 2001 and 2002, respectively. The Company has no future minimum lease payments to RJRT as of December 31, 2003.

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, 2001, 2002 and 2003 and the nine months ended September 30, 2004 in connection with the director's services are 0, 32,500, 7,500 and 0, respectively. In addition, a stock option for an additional 32,500 shares was granted to RJRT during the year ended December 31, 2002 in connection with the services of a former director. A portion of that option, representing 15,775 shares, was forfeited when that director ceased to serve as a director. In connection with the issuance of the stock options, the Company recognized compensation expense of $0, $43,550, $2,512 and $2,512 during 2001, 2002, 2003 and the nine months ended September 30, 2004, 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 $810,000, $525,000 and $201,000 for these services during 2001, 2002, and 2003, respectively.

18. Subsequent Events

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 between the companies entered into in December 1998 and restated in January 2002 (see Note 15). The termination of the agreement is effective January 2, 2005 and is within the provisions of termination clauses of the agreement. As a result of the termination of the agreement, the Company will recognize the remaining deferred revenue of $825,000 related to the agreement during the fourth quarter of 2004.

On December 6, 2004, the Company completed a private placement of 27,272,728 shares of Series C and received cash of approximately $32,900,000, net of offering costs. The terms of the issuance are consistent with those of the previous Series C issuances as discussed in Note 9. 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 will record a non-cash preferred stock charge at the date of issuance by offsetting charges and credits to additional paid-in-capital of $, which is the difference in the conversion price of the Series C shares issued on December 6, 2004 and the underlying value of the conversion shares.

On December 6, 2004, the Company amended its certificate of incorporation to, among other things, increase the authorized shares of common stock to 125,000,000 and to reduce the public offering price per share that would trigger automatic conversion of the redeemable convertible preferred stock from $3.60 to $2.15.

Targacept, Inc.

Notes to Financial Statements—(continued)

18. Subsequent Events (continued)

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 bears interest at 10% per annum and matures on January 1, 2007. However, if not earlier paid, the outstanding principal and accrued interest under the note will automatically convert into shares of the Company's common stock concurrently with the completion of the Company's initial public offering at a conversion price equal to the initial public offering price. The Company is entitled to receive milestone payments under the agreement upon the achievement of specified milestones during the development period. The Company is required to make royalty payments based on net sales of products developed and sold.

On , 2005 the Company's Board of Directors adopted, and on , 2005 the stockholders approved, a to reverse stock split of the Company's common stock effective as of . 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 common stock split.

Targacept, Inc.

Notes to Financial Statements—(continued)

19. Selected Quarterly Financial Data (Unaudited)

	2002 Quarter			
	First	Second	Third	Fourth
Net revenue	$ 489,891	$ 412,339	$ 471,219	$ 912,909
Gross profit (loss) on product sales	—	—	—	(857)
Operating loss	(4,335,806)	(3,537,219)	(8,250,014)	(4,879,471)
Net loss	(4,421,557)	(3,510,492)	(8,250,530)	(4,889,127)
Net loss attributable to common stockholders	(5,373,554)	(4,462,489)	(9,202,527)	(6,206,681)
Basic and diluted net loss per share attributable to common stockholders(1)	$ (10.83)	$ (8.38)	$ (15.81)	$ (10.05)
Weighted average common shares outstanding—basic and diluted	496,382	532,673	581,894	617,423

	2003 Quarter			
	First	Second	Third	Fourth
Net revenue	$ 690,796	$ 526,517	$ 598,840	$ 642,132
Gross profit (loss) on product sales	111,509	(67,923)	(957)	29,154
Operating loss	(4,275,065)	(5,997,799)	(4,525,572)	(5,265,435)
Net loss	(4,185,042)	(5,775,002)	(4,387,882)	(5,047,395)
Net loss attributable to common stockholders	(6,100,000)	(7,916,891)	(6,529,771)	(7,189,287)
Basic and diluted net loss per share attributable to common stockholders(1)	$ (9.48)	$ (10.99)	$ (7.15)	$ (7.26)
Weighted average common shares outstanding—basic and diluted	643,571	720,093	913,185	989,874

	2004 Quarter		
	First	Second	Third
Net revenue	496,939	528,026	555,583
Gross profit (loss) on product sales	6,061	494,780	55,697
Operating loss	(6,843,593)	(6,437,455)	(6,711,932)
Net loss	(6,637,935)	(6,433,767)	(6,665,238)
Net loss attributable to common shareholders	(8,779,826)	(8,575,657)	(8,807,125)
Basic and diluted net loss per share attributable to common stockholders(1)	(7.89)	(5.14)	(4.68)
Weighted average common shares outstanding—basic and diluted	1,112,591	1,668,778	1,880,325

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.


TARGACEPT

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	$ 10,928
NASDAQ National Market listing fee	100,000
NASD filing fee	9,125
Blue sky fees and expenses	*
Accounting fees and expenses	*
Legal fees and expenses	*
Transfer agent and registrar fees and expenses	*
Printing and engraving expenses	*
Miscellaneous	*
Total	$ *

* To be filed by amendment.

Item 14. Indemnification of Directors and Officers.

Our Second Amended and Restated Certificate of Incorporation, as amended and in effect as of the date of this registration statement, and our Third 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 August 22, 2000. 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 August 22, 2000, at the time that we became an independent company, we issued an aggregate of 309,424 shares of our common stock at a purchase price per share of $0.001 to each of Dr. deBethizy, Dr. Bencherif, Dr. Caldwell and Dr. Patrick M. Lippiello for an aggregate purchase price of approximately $309.

2. On August 22, 2000, we recapitalized our 500 outstanding shares of common stock held by R.J. Reynolds Tobacco Company, our then parent corporation, into 5,000,000 shares of series A convertible preferred stock and a warrant to purchase 1,612,903 shares of common stock at an exercise price of $1.95 per share. All of the shares of series A convertible preferred stock and the warrant were issued to R.J. Reynolds Tobacco Company, which subsequently assigned them to R.J. Reynolds Tobacco Holdings, Inc. Each share of series A convertible preferred stock will convert into one share of common stock concurrently with the completion of this offering.

3. On August 22, 2000, we issued and sold an aggregate of 5,892,473 shares of our series B convertible preferred stock at a purchase price per share of $4.65 to investors affiliated with EuclidSR Partners, L.P., Burrill & Company LLC, Societe Generale Asset Management Finance (which subsequently assigned its shares to FCPR SGAM Biotechnology Fund), Genavent Venture Fund, Auriga Ventures, Advent Private Equity Fund II, FCPR CDC-Innovation 2000 and Longleaf Venture Fund, LLC (now known as Academy Venture Fund, LLC) for an aggregate purchase price of approximately $27.4 million. These shares will convert into common stock at the rate of approximately 2.38 shares of common stock for each share of series B convertible preferred stock concurrently with the completion of this offering.

4. On November 30, December 5 and December 19, 2000, we issued and sold an aggregate of 645,161 shares of our series B convertible preferred stock at a purchase price per share of $4.65 to investors affiliated with EuclidSR Partners, L.P. and Longleaf Venture Fund, LLC (now known as Academy Venture Fund, LLC) for an aggregate purchase price of approximately $3.0 million. These shares will convert into common stock at the rate of approximately 2.38 shares of common stock for each share of series B convertible preferred stock concurrently with the completion of this offering.

5. On January 26, 2001, we issued and sold an aggregate of 29,933 shares of our series B convertible preferred stock, valued at $4.65 per share, to Andre L. Lamotte, Joseph F. Lovett and Jeffrey D. Wager in partial satisfaction of amounts payable by us for consulting services rendered. The aggregate amount of consideration was approximately $139,000. These shares will convert into common stock at the rate of one share of common stock for each share of series B convertible preferred stock concurrently with the completion of this offering.

6. On January 30, 2001, we issued and sold an aggregate of 111,111 shares of our common stock at a purchase price of $9.00 per share to Dr. Falk Pharma GmbH, our collaborative partner, for an aggregate purchase price of approximately $1.0 million.

7. On August 8, 2002, June 11, 2003 and October 15, 2004, we issued and sold an aggregate of 72,500 shares of restricted stock to Mr. Skaletsky for an aggregate purchase price of $725.

8. On November 26, 2002, we issued and sold an aggregate of 37,764,180 shares of our series C convertible preferred stock at a purchase price per share of $1.21 to investors affiliated with Nomura International plc, New Enterprise Associates 10, Limited Partnership, CDIB Bioscience Ventures I, Inc., Easton Hunt Capital Partners, L.P., EuclidSR Partners, L.P., Burrill & Company LLC, Genavent Fund, FCPR SGAM AI Biotechnology Fund, Auriga Ventures, FCPR CDC-Innovation 2000, Advent Private Equity Fund II and Academy Venture Fund, LLC for an aggregate purchase price of approximately $45.7 million. These shares will convert into common stock at the rate of approximately 1.08 shares of common stock for each share of series C convertible preferred stock concurrently with the completion of this offering.

9. 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 1.08 shares of common stock for each share of series C convertible preferred stock concurrently with the completion of this offering.

10. On April 18, 2003, we issued and sold an aggregate of 25,000 shares of restricted stock to Mr. Richard for an aggregate purchase price of $250.

11. 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 1.08 shares of common stock for each share of series C convertible preferred stock concurrently with the completion of this offering.

12. On December 15, 2004, we issued a $1.25 million convertible promissory note to The Stanley Medical Research Institute. The note bears interest at 10% per annum and matures on January 1, 2007. However, if not earlier paid, the outstanding principal and accrued interest under the note will automatically convert into shares of our common stock concurrently with the completion of this offering at a conversion price equal to the initial public offering price.

13. Since inception to December 15, 2004, we have granted:

- options to purchase an aggregate of 8,693,819 shares of common stock at exercise prices ranging from $0.01 to $4.65 per share under our 2000 Equity Incentive Plan, as amended, with a weighted average exercise price of $0.66 per share, to employees, directors and individual consultants;
- restricted stock awards for an aggregate of 97,500 shares of common stock at a purchase price of $0.01 per share under our 2000 Equity Incentive Plan, as amended; and
- options to purchase an aggregate of 255,000 shares of common stock at an exercise price of $0.01 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 inception and outstanding on December 15, 2004 is $0.65 per share. As of December 15, 2004, there were 55 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)—(12) 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 paragraph (a)(1)—(12) 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 issuance of stock options and the common stock issuable upon the exercise of such options as described in paragraph (a)(13) of this Item 15 were issued pursuant to written compensatory 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(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.
4.3**	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.
4.4	Convertible Promissory Note of the Company in favor of The Stanley Medical Research Institute dated December 15, 2004.
5.1*	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
5.2*	Opinion of Womble Carlyle Sandridge & Rice, PLLC.

Exhibit No.	Description
10.1*	Form of Indemnification Agreement between the Company and each of its directors and officers.
10.2**	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**	2000 Equity Incentive Plan, as amended.
10.6*	2004 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+	Collaborative Research, Development and License Agreement, dated as of January 26, 2001, by and between the Company and Dr. Falk Pharma GmbH.
10.15**	Asset Purchase Agreement, dated as of June 28, 2002, by and between the Company and Layton Bioscience, Inc.
10.16+**	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.
10.17+	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.
10.18(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.
10.18(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.

Exhibit No.	Description
10.19+	License Agreement, dated as of July 9, 2002, by and between the Company and the Medical College of Georgia Research Institute, Inc.
10.20+	License Agreement, dated May 26, 1999, by and between the Company and the University of Kentucky Research Foundation.
10.21+	License Agreement, dated as of August 12, 2002, between the Company and Wake Forest University Health Sciences.
10.22+	Development and Production Agreement for Active Pharmaceutical Ingredients, dated as of February 1, 2004, by and between the Company and Siegfried Ltd.
10.23++	Development Agreement, dated as of December 15, 2004, by and between the Company and The Stanley Medical Research Institute.
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).
23.3*	Consent of Womble Carlyle Sandridge & Rice, PLLC (included in Exhibit 5.2).
24.1**	Power of Attorney (included on signature page).

* To be filed by amendment.
** Previously filed.
*** Replaces Exhibit 3.1(a) filed with the Company's Registration Statement on Form S-1 dated May 14, 2004.
\+ 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 a confidential treatment pursuant to the Securities Act of 1933, as amended.

(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. 3 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 December 15, 2004.

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. 3 to the registration statement has been signed by the following persons in the capacities indicated on December 15, 2004.

/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:** **G. Steven Burrill** **Title:** **Director**
*	*
Name: **Errol B. De Souza** **Title:** **Director**	**Name:** **Elaine V. Jones** **Title:** **Director**
*	*
Name: **John P. Richard** **Title:** **Director**	**Name:** **Alan G. Walton** **Title:** **Director**

*By: /s/ ALAN A. MUSSO

Alan A. Musso
Attorney-in-fact

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EXHIBIT INDEX

Exhibit No.	Description
1.1*	Form of Underwriting Agreement.
3.1(a)***	Third Amended and Restated Certificate of Incorporation of the Company.
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.
4.3**	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.
4.4	Convertible Promissory Note of the Company in favor of The Stanley Medical Research Institute dated December 15, 2004.
5.1*	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
5.2*	Opinion of Womble Carlyle Sandridge & Rice, PLLC.
10.1*	Form of Indemnification Agreement between the Company and each of its directors and officers.
10.2**	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**	2000 Equity Incentive Plan, as amended.
10.6*	2004 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.

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Exhibit No.	Description
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+	Collaborative Research, Development and License Agreement, dated as of January 26, 2001, by and between the Company and Dr. Falk Pharma GmbH.
10.15**	Asset Purchase Agreement, dated as of June 28, 2002, by and between the Company and Layton Bioscience, Inc.
10.16+**	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.
10.17+	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.
10.18(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.
10.18(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.
10.19+	License Agreement, dated as of July 9, 2002, by and between the Company and the Medical College of Georgia Research Institute, Inc.
10.20+	License Agreement, dated May 26, 1999, by and between the Company and the University of Kentucky Research Foundation.
10.21+	License Agreement, dated as of August 12, 2002, between the Company and Wake Forest University Health Sciences.
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** Previously filed.
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\+ 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 a confidential treatment pursuant to the Securities Act of 1933, as amended.

Exhibit 3.1(a)

THIRD AMENDED AND RESTATED CERTIFICATE OF INCORPORATION
OF
TARGACEPT, INC.

Pursuant to Section 242 and Section 245 of the General Corporation Law of Delaware (the "**DGCL**"), the undersigned corporation hereby submits the following for the purpose of amending and restating its Certificate of Incorporation, as amended, and does hereby certify as follows.

1. The name of the corporation is Targacept, Inc. The corporation's original Certificate of Incorporation was filed on March 7, 1997, an Amended and Restated Certificate of Incorporation was filed on August 22, 2000, a Certificate of Amendment was filed on January 2, 2001, a Second Amended and Restated Certificate of Incorporation was filed on November 26, 2002 and a Certificate of Amendment was filed on March 14, 2003.

2. The corporation's Certificate of Incorporation is hereby amended and restated in its entirety, as set forth in the text of the Third Amended and Restated Certificate of Incorporation attached hereto as Exhibit A.

3. This Third Amended and Restated Certificate of Incorporation was duly adopted in accordance with Section 245(c) of the DGCL and will be effective upon filing.

IN WITNESS WHEREOF, said Targacept, Inc. has caused this Third Amended and Restated Certificate of Incorporation to be signed by its President and Chief Executive Officer and attested by its Secretary, this 6th day of December, 2004.

TARGACEPT, INC.

By: /s/ J. Donald deBethizy
J. Donald deBethizy
President and Chief Executive Officer

ATTEST:

By: /s/ Alan A. Musso
Alan A. Musso, Secretary

Exhibit A

THIRD AMENDED AND RESTATED CERTIFICATE OF INCORPORATION
OF
TARGACEPT, INC.

FIRST: The name of the corporation (hereinafter called the "**corporation**") is Targacept, Inc.

SECOND: The address, including street, number, city and county of the registered office of the corporation in the State of Delaware, is 1013 Centre Road, City of Wilmington 19805, County of New Castle; and the name of the registered agent of the corporation in the State of Delaware at such address is Corporation Service Company.

THIRD: The purpose of the corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation law of the State of Delaware.

FOURTH:

The corporation is authorized to issue shares of stock as follows:

A. The number of shares that the corporation is authorized to issue is Two Hundred Eighteen Million, Three Hundred Nine Thousand, Five Hundred Thirty-Two (218,309,532), of which: (1) One Hundred Twenty-Five Million (125,000,000) 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**."

The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares then outstanding) by the affirmative vote or written consent or approval of the holders of a majority of the then outstanding shares of the corporation's capital stock entitled to vote, voting together as a single class on an as-converted to Common Stock basis, irrespective of the provisions of Section 242(b)(2) of the Delaware General Corporation Law.

B. The preferences, limitations and relative rights relating to the Common Stock and Preferred Stock are as set forth below. Series C Preferred shall rank senior to each other Preferred Series and to the Common Stock with respect to the payment and distribution of

dividends (to the extent of the Series C Dividend (as defined in Section 1(a))), in liquidation and, to the extent provided herein, with respect to redemption. Except as expressly provided above, each of the Preferred Series shall rank *pari passu* with the other Preferred Series with respect to the payment of dividends, in liquidation and with respect to redemption. Unless otherwise indicated, all references to sections or subsections set forth in this Section B of Article FOURTH are deemed to refer to sections or subsections within this Section B of Article FOURTH.

1. Dividends.

(a) The holders of record of the then outstanding shares of Series C Preferred shall be entitled to receive, when, as and if declared by the corporation's Board of Directors (the "**Board**") out of any funds legally available therefor, cumulative dividends (the "**Series C Dividend**") at the annual rate (and no more) of 8% of the Series C Original Price (as defined in Section 4(a)(iii)) per share, computed on the basis of a 360-day year and rounded to the nearest whole cent (subject to equitable adjustment for stock splits, stock dividends, reverse stock splits and other similar corporate reorganizations or reclassifications that result in any change in the number of outstanding shares of Series C Preferred). The accrued but unpaid Series C Dividend, if any, may be declared and paid at any time. The Series C Dividend shall be fully cumulative and, with respect to each share of Series C Preferred, shall accrue (whether or not declared), without interest, daily from the previous anniversary of the date on which such share was issued, except that the first annual dividend shall accrue with respect to each share of Series C Preferred from the date on which such share was issued. No dividends shall be declared or paid with respect to any other class or series of the Corporation's capital stock unless prior to or contemporaneously therewith, the Board declares and pays the Series C Dividend in full. Notwithstanding anything herein to the contrary, upon any conversion of Series C Preferred pursuant to Section 4, the accrued but unpaid Series C Dividend, if any, shall be forfeited if not yet declared and shall cease to accrue or be payable thereafter.

(b) The holders of record of then outstanding shares of Series A Preferred and Series B Preferred shall not be entitled to receive any fixed, stated or regular dividend, but shall receive such dividends when, as and if declared by the Board out of any funds legally available therefor; provided, that no dividend shall be declared or paid on either the Series A Preferred or the Series B Preferred unless, simultaneously with such declaration or payment, (i) the same dividend per share is declared or paid on both the Series A Preferred and the Series B Preferred and (ii) the same dividend per share is declared or paid on the Series C Preferred and (iii) any accrued but unpaid Series C Dividend is declared and paid in full.

(c) Each holder of then outstanding shares of a Preferred Series shall be entitled to share ratably with the holders of Common Stock in all dividends or other distributions declared and paid on the Common Stock, other than those payable solely in shares of Common Stock (which shall have the effects described in Section 4(e)), on the basis that such holder held, on the record date for such dividend or distribution, the number of shares of Common Stock into which such holder's shares of Series A Preferred, Series B Preferred or Series C Preferred, as the case may be, would have been convertible on such date upon exercise of the Conversion Rights described in Section 4.

(d) Notwithstanding anything herein to the contrary, so long as any shares of: (i) Series A Preferred or Series B Preferred are outstanding, no dividends or other distributions shall be declared or paid on the Common Stock without the approval of the holders of 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 (ii) Series C Preferred are outstanding, no dividends or other distributions shall be declared or paid on the Common Stock without the approval of the holders of at least sixty-five percent (65%) of the then outstanding shares of Series C Preferred.

2. Liquidation.

(a) Series C Liquidation Preference.

(i) In the event of any liquidation, dissolution or winding up of the affairs of the corporation, whether voluntary or involuntary (a "**General Liquidation Event**"), after payment or provision for payment of the debts and other liabilities and obligations of the corporation as required by law, the holder of each share of Series C Preferred then outstanding shall be entitled to be paid out of the net assets of the corporation available for distribution to its stockholders, before any payment or declaration and setting apart for payment of any amount shall be made in respect of Series B Preferred, Series A Preferred or Common Stock, an amount equal to the greater of (A) the Series C Original Price (as defined in Section 4(a)(iii)) per share of Series C Preferred, plus the accrued but unpaid Series C Dividend plus any other previously declared but unpaid dividends thereon to and including the date full payment is tendered to the holders of the Series C Preferred with respect to such General Liquidation Event, or (B) the amount per share of Series C Preferred that would be received by such holder in respect of such General Liquidation Event if all of the corporation's outstanding shares of Preferred Stock were converted to Common Stock immediately prior to such General Liquidation Event (such greater amount, the "**Series C Liquidation Preference**"). If the corporation shall at any time or from time to time effect a subdivision of the outstanding Series C Preferred (or declare and pay a dividend thereon payable in additional shares of Series C Preferred), the calculation of Section 2(a)(i)(A) then in effect immediately before that subdivision (or dividend) shall be proportionately decreased; conversely, if the corporation shall at any time or from time to time reduce the outstanding shares of Series C Preferred by combination or reverse stock split, the calculation of Section 2(a)(i)(A) then in effect immediately before the combination shall be proportionately increased. Any such adjustment pursuant to the preceding sentence shall become effective at the close of business on the date the subdivision or combination becomes effective or the dividend is paid.

(ii) Unless the holders of at least sixty-five percent (65%) of then outstanding shares of Series C Preferred otherwise elect, a Fundamental Transaction (as defined in Section 2(a)(iii)) shall be treated as a General Liquidation Event with respect to the Series C Preferred. If a Fundamental Transaction is treated as a General Liquidation Event with respect to the Series C Preferred, the respective holders of Series C Preferred shall have the right to receive, in connection with the closing of the

Fundamental Transaction and upon surrender of such holder's Series C Preferred certificate(s), duly endorsed, at the office of the corporation or of any transfer agent therefor, payment of the Series C Liquidation Preference and, if the Series C Liquidation Preference is the amount calculated pursuant to Section 2(a)(i)(A), the other amounts specified in Section 2(d) (such payment to be in the form of the securities or other consideration issued or paid in the Fundamental Transaction) in lieu of receiving the consideration and other securities and property that it would otherwise receive in the Fundamental Transaction. Upon payment of the Series C Liquidation Preference and the other amounts specified in Section 2(d) (or such amount thereof as may be payable as provided in Section 2(d)(iii)), each share of such Series C Preferred shall thereafter be deemed retired and no longer outstanding.

(iii) "**Fundamental Transaction**" shall mean the consummation by the corporation of (A) a share exchange, consolidation, merger, reorganization or other similar transaction in which the corporation is a constituent party in which outstanding shares of capital stock of the corporation are exchanged for, or converted into, securities or other consideration issued, or caused to be issued, by another entity (other than a mere reincorporation transaction) or (B) a sale, lease or other disposition of all or substantially all of the assets of the corporation.

(b) Series B Liquidation Preference.

(i) In the event of a General Liquidation Event, after (A) payment or provision for payment of the debts and other liabilities and obligations of the corporation as required by law and (B) payment of the Series C Liquidation Preference in full, the holder of each share of Series B Preferred then outstanding shall be entitled to be paid out of the net assets of the corporation available for distribution to its stockholders, before any payment or declaration and setting apart for payment of any amount shall be made in respect of Common Stock and on a *pari passu* basis with the holders of each share of Series A Preferred then outstanding as provided in Section 2(c), an amount equal to $4.65 per share of Series B Preferred, plus any previously declared but unpaid dividends thereon to and including the date full payment is tendered to the holders of the Series B Preferred with respect to such General Liquidation Event (the "**Series B Liquidation Preference**"). If the corporation shall at any time or from time to time effect a subdivision of the outstanding Series B Preferred (or declare and pay a dividend thereon payable in additional shares of Series B Preferred), the Series B Liquidation Preference then in effect immediately before that subdivision (or dividend) shall be proportionately decreased; conversely, if the corporation shall at any time or from time to time reduce the outstanding shares of Series B Preferred by combination or reverse stock split, the Series B Liquidation Preference then in effect immediately before the combination shall be proportionately increased. Any such adjustment pursuant to the preceding sentence shall become effective at the close of business on the date the subdivision or combination becomes effective or the dividend is paid.

(ii) Unless the holders of a majority of then outstanding shares of Series B Preferred otherwise elect, a Fundamental Transaction (as defined in

Section 2(a)(iii)) shall be treated as a General Liquidation Event with respect to the Series B Preferred. If a Fundamental Transaction is treated as a General Liquidation Event with respect to the Series B Preferred, the respective holders of Series B Preferred shall have the right to receive, in connection with the closing of the Fundamental Transaction and upon surrender of such holder's Series B Preferred certificate(s), duly endorsed, at the office of the corporation or of any transfer agent therefor, payment of the Series B Liquidation Preference and the other amounts specified in Section 2(d) (such payment to be in the form of the securities or other consideration issued or paid in the Fundamental Transaction) in lieu of receiving the consideration and other securities and property that it would otherwise receive in the Fundamental Transaction; provided, that if the Fundamental Transaction is treated as a General Liquidation Event with respect to the holders of (A) Series A Preferred, payment of the Series B Liquidation Preference shall be on a *pari passu* basis with the payment of the Series A Liquidation Preference and (B) Series C Preferred, payment of the Series B Liquidation Preference shall be expressly subject to, and conditional on, the prior payment of the Series C Liquidation Preference in full. Upon payment of the Series B Liquidation Preference and the other amounts specified in Section 2(d) (or such amount thereof as may be payable as provided in Section 2(d)(iii)), each share of such Series B Preferred shall thereafter be deemed retired and no longer outstanding.

(c) Series A Liquidation Preference.

(i) In the event of a General Liquidation Event, after (A) payment or provision for payment of the debts and other liabilities and obligations of the corporation as required by law and (B) payment of the Series C Liquidation Preference in full, the holder of each share of Series A Preferred then outstanding shall be entitled to be paid out of the net assets of the corporation available for distribution to its stockholders, before any payment or declaration and setting apart for payment of any amount shall be made in respect of Common Stock and on a *pari passu* basis with the holders of each share of Series B Preferred then outstanding as provided in Section 2(b), an amount equal to $4.65 per share of Series A Preferred, plus any previously declared but unpaid dividends thereon to and including the date full payment is tendered to the holders of the Series A Preferred with respect to such General Liquidation Event (the "**Series A Liquidation Preference**"). If the corporation shall at any time or from time to time effect a subdivision of the outstanding Series A Preferred (or declare and pay a dividend thereon payable in additional shares of Series A Preferred), the Series A Liquidation Preference then in effect immediately before that subdivision (or dividend) shall be proportionately decreased; conversely, if the corporation shall at any time or from time to time reduce the outstanding shares of Series A Preferred by combination or reverse stock split, the Series A Liquidation Preference then in effect immediately before the combination shall be proportionately increased. Any such adjustment pursuant to the preceding sentence shall become effective at the close of business on the date the subdivision or combination becomes effective or the dividend is paid.

(ii) Unless the holders of a majority of then outstanding shares of Series A Preferred otherwise elect, a Fundamental Transaction (as defined in

Section 2(a)(iii)) shall be treated as a General Liquidation Event with respect to the Series A Preferred. If a Fundamental Transaction is treated as a General Liquidation Event with respect to the Series A Preferred, the respective holders of Series A Preferred shall have the right to receive, in connection with the closing of the Fundamental Transaction and upon surrender of such holder's Series A Preferred certificate(s), duly endorsed, at the office of the corporation or of any transfer agent therefor, payment of the Series A Liquidation Preference and the other amounts specified in Section 2(d) (such payment to be in the form of the securities or other consideration issued or paid in the Fundamental Transaction) in lieu of receiving the consideration and other securities and property that it would otherwise receive in the Fundamental Transaction; provided, that if the Fundamental Transaction is treated as a General Liquidation Event with respect to the holders of (A) Series B Preferred, payment of the Series A Liquidation Preference shall be on a *pari passu* basis with the payment of the Series B Liquidation Preference and (B) Series C Preferred, payment of the Series A Liquidation Preference shall be expressly subject to, and conditional on, payment of the Series C Liquidation Preference in full. Upon payment of the Series A Liquidation Preference and the other amounts specified in Section 2(d) (or such amount thereof as may be payable as provided in Section 2(d)(iii)), each share of such Series A Preferred shall thereafter be deemed retired and no longer outstanding.

(d) Distribution of Remaining Liquidation Proceeds; Participation of Preferred Series.

(i) After payment in full of the Series C Liquidation Preference, the Series B Liquidation Preference and the Series A Liquidation Preference, the remaining net assets of the corporation shall next be distributed ratably per share to the holders of Common Stock and, if the Series C Liquidation Preference is paid pursuant to Section 2(a)(i), the Series B Liquidation Preference is paid pursuant to Section 2(b)(i) and/or the Series A Liquidation Preference is paid pursuant to Section 2(c)(i), each such Preferred Series, as if the holders of each such Preferred Series had converted their shares into Common Stock as provided in Section 4 immediately prior to the event resulting in the distributions under this Section 2.

(ii) For purposes of this Section 2, references to "**the other amounts specified in Section 2(d)**" shall mean the shares of stock or other securities or property (including cash) attributable in the Fundamental Transaction to, or to be received in connection with the Fundamental Transaction with respect to, the shares of Common Stock issuable upon conversion of the shares of Series C Preferred, Series B Preferred or Series A Preferred, as the case may be, in accordance with Section 2(d)(i).

(iii) If upon any General Liquidation Event for Series C Preferred, the assets to be distributed to the holders of Series C Preferred shall be insufficient to permit the payment to such holders of the Series C Liquidation Preference, then all the net assets of the corporation available for distribution to its stockholders shall be distributed ratably (per share) to the holders of Series C Preferred. If upon any General Liquidation Event for Series B Preferred and Series A Preferred and after

payment in full of the Series C Liquidation Preference, the assets to be distributed to the holders of Series B Preferred and Series A Preferred shall be insufficient to permit the payment to such holders of their respective Liquidation Preferences in full, then all of the remaining net assets of the corporation available for distribution to its stockholders shall be distributed ratably (per share) to the holders of Series B Preferred and Series A Preferred on a *pari passu* basis. In either such event, no amounts shall be distributed to the holders of Common Stock.

(e) Valuation of Securities. Any securities to be delivered pursuant to this Section 2 shall be valued as follows:

(i) For securities not subject to investment letter or other similar restrictions on free marketability covered by Section 2(e)(ii):

(A) If traded on a securities exchange, the value shall be deemed to be the closing price of the securities on such exchange on the third trading day prior to the payment date set forth in the Notice (as defined in Section 2(f));

(B) If actively traded over-the-counter, the value shall be deemed to be the closing bid or sale price (whichever is applicable) on the third trading day prior to the payment date set forth in the Notice; and

(C) If there is no active public market, the value shall be the fair market value thereof, as determined in good faith by a majority of the Board.

(ii) The method of valuation of securities subject to investment letter or other restrictions on free marketability, other than restrictions arising solely by virtue of a stockholder's status as an affiliate or former affiliate of the corporation, shall be to make an appropriate discount from the market value determined as provided in Sections 2(e)(i)(A), (B) or (C) to reflect the adjusted fair market value thereof, such discount to be determined in good faith by a majority of the Board.

(iii) In the event that the holders of a majority of the outstanding shares of Series A Preferred and Series B Preferred, considered together as a single class on an as-converted basis, or the holders of at least sixty-five percent (65%) of the outstanding shares of Series C Preferred (in any case, a "**Disputing Party**") give prompt written notice to the corporation that they dispute the determination of the Board made pursuant to Section 2(e)(i)(C) or Section 2(e)(ii), a committee of the Board comprised of (A) at least one director who is not an employee of the corporation or a designee of a single holder, or a group of holders, of Series A Preferred, Series B Preferred or Series C Preferred, (B) at least one director who is a designee of a single holder, or a group of holders, of Series A Preferred or Series B Preferred and (C) at least one director who is a designee of a single holder, or a group of holders, of Series C Preferred shall select an investment banking firm or other expert of recognized standing

which shall determine conclusively the fair market value (in the case of Section 2(e)(i)(C)) or the discount (in the case of Section 2(e)(ii)). The cost of such firm or expert shall be divided equally between the Disputing Party (jointly and severally), on the one hand, and the corporation, on the other hand.

(f) Notice. Written notice (the "**Notice**") of any General Liquidation Event, which states the payment date, the place where said payments shall be made and the date on which Conversion Rights (as defined in Section 4) terminate as to such shares (which shall be not less than five (5) days after the date of such Notice), shall be given not less than fifteen (15) days prior to the payment date stated therein, to holders of record of each of the Preferred Series and Common Stock.

3. Voting Rights.

(a) Generally.

(i) Except as otherwise expressly provided herein or as required by law, the holder of each then outstanding share of Preferred Stock shall be entitled to the number of votes equal to the number of shares of Common Stock into which such share of Preferred Stock would be convertible on the appropriate record date and shall have voting rights and powers equal to the voting rights and powers of the Common Stock (except as otherwise expressly provided herein or as required by law, voting together with the Common Stock and the holders of all other Preferred Series as a single class and not as a separate voting group) and shall be entitled to notice of any stockholders' meeting in accordance with the bylaws of the corporation and applicable law. Fractional votes shall not be permitted and any fractional voting rights resulting from the above formula (after aggregating all shares of Common Stock into which shares of Preferred Stock held by each holder would be convertible) shall be rounded to the nearest whole number (with one-half being rounded upward).

(ii) Each holder of Common Stock shall be entitled to one vote per share of Common Stock owned by such holder.

(b) Series A Preferred Protective Covenants. From December 6, 2004 (the "**Series C Follow-On Issue Date**") until the earlier to occur of (i) a Qualified IPO (as defined in Section 4(b)) and (ii) the time that no shares of Series A Preferred remain outstanding, the corporation shall not, directly or indirectly, take any of the following actions without first obtaining the affirmative vote or the written approval of the holders of a majority of the then outstanding shares of Series A Preferred:

(i) only to the extent Section 3(d)(iii) does not apply, create, authorize, designate, reclassify, issue or sell any class or series of capital stock of the corporation, or rights, options, warrants or other securities convertible into or exercisable or exchangeable for any capital stock of the corporation, or any "**phantom**" equity or stock appreciation rights that rank as to payment of dividends, distribution of assets or redemption prior to or *pari passu* with the Series A Preferred or that in any manner

materially adversely affect the terms, designations, powers, preferences or other rights of the holders of Series A Preferred (other than shares of Series C Preferred issued as of the Series C Follow-On Issue Date under the Purchase Agreement, as defined in Section 3(d)(vi));

(ii) alter or modify the terms, rights, preferences or privileges of the shares of the Series A Preferred; or increase the authorized number of shares of Series A Preferred;

(iii) amend this Second Amended and Restated Certificate of Incorporation or the bylaws of the corporation if such amendment would be materially adverse to the holders of Series A Preferred;

(iv) agree or otherwise commit to take any of the actions set forth in the foregoing Sections 3(b)(i)-(iii).

(c) Series B Preferred Protective Covenants. From the Series C Follow-On Issue Date until the earlier to occur of (i) a Qualified IPO (as defined in Section 4(b)) and (ii) the time that no shares of Series B Preferred remain outstanding, the corporation shall not, directly or indirectly, take any of the following actions without first obtaining the affirmative vote or the written approval of the holders of at least two-thirds of the then outstanding shares of Series B Preferred:

(i) only to the extent Section 3(d)(iii) does not apply, create, authorize, designate, reclassify, issue or sell any class or series of capital stock of the corporation, or rights, options, warrants or other securities convertible into or exercisable or exchangeable for any capital stock of the corporation, or any "**phantom**" equity or stock appreciation rights that rank as to payment of dividends, distribution of assets or redemption prior to or *pari passu* with the Series B Preferred or that in any manner materially adversely affect the terms, designations, powers, preferences or other rights of the holders of Series B Preferred (other than shares of Series C Preferred issued as of the Series C Follow-On Issue Date under the Purchase Agreement, as defined in Section 3(d)(vi));

(ii) alter or modify the terms, rights, preferences or privileges of the shares of the Series B Preferred; or increase the authorized number of shares of Series B Preferred;

(iii) amend this Second Amended and Restated Certificate of Incorporation or the bylaws of the corporation if such amendment would be materially adverse to the holders of Series B Preferred;

(iv) agree or otherwise commit to take any of the actions set forth in the foregoing Sections 3(c)(i)-(iii).

(d) Additional Series A Preferred and Series B Preferred Protective Covenants. From the Series C Follow-On Issue Date until the earlier to occur of (i) a Qualified IPO (as defined in Section 4(b)) and (ii) the time that no shares of Series A Preferred or Series B Preferred remain outstanding, the corporation shall not, directly or indirectly, take any of the following actions without first obtaining the affirmative vote or the written approval of the holders of 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:

(i) voluntarily effect a General Liquidation Event;

(ii) consummate a Fundamental Transaction;

(iii) create, authorize, designate, reclassify, issue or sell any class or series of capital stock of the corporation, or rights, options, warrants or other securities convertible into or exercisable or exchangeable for any capital stock of the corporation, or any "**phantom**" equity or stock appreciation rights that rank as to payment of dividends, distribution of assets or redemption prior to, or *pari passu* with, both the Series A Preferred and the Series B Preferred or that in any manner materially adversely affect the terms, designations, powers, preferences or other rights of both the holders of Series A Preferred and the holders of Series B Preferred (other than shares of Series C Preferred issued as of the Series C Follow-On Issue Date under the Purchase Agreement, as defined in Section 3(d)(vi));

(iv) redeem, repurchase or otherwise acquire any outstanding shares of its capital stock or any other of its outstanding securities, except for (A) repurchases of shares pursuant to agreements entered into to evidence grants or awards under the corporation's 2000 Equity Incentive Plan, as amended and as may be further amended (the "**2000 Plan**"), or any other successor plan that is approved by the holders of at least 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 at least sixty-five percent (65%) of the then outstanding shares of Series C Preferred (together with the 2000 Plan, "**Plans**"), or (B) redemptions pursuant to Section 6;

(v) create, incur, assume or suffer to exist any indebtedness of the corporation for borrowed money (which shall include for purposes hereof capitalized lease obligations and guarantees or other contingent obligations for indebtedness for borrowed money) other than trade payables and accrued expenses incurred in the ordinary course of business and other debt not in excess at any point in time of $2,500,000 in the aggregate;

(vi) enter into any material transactions with any "affiliate" or "associate" (as such terms are defined under Rule 12b-2 under the Exchange Act) of the corporation, except as (x) expressly permitted by this Second Amended and Restated Certificate of Incorporation, (y) contemplated by the Series C Convertible Preferred Stock Purchase Agreement dated as of the Series C Follow-On Issue Date, as may be amended (the "**Purchase Agreement**"), or (z) approved by a majority of the members of

the Board excluding, solely for this purpose, any directors who are affiliates or associates of such affiliate or associates of the corporation; or

(vii) agree or otherwise commit to take any of the actions set forth in the foregoing Sections 3(d)(i)-(vi).

(e) Series C Preferred Protective Covenants. From the Series C Follow-On Issue Date until the earlier to occur of (i) a Qualified IPO (as defined in Section 4(b)) and (ii) the time that no shares of Series C Preferred remain outstanding, (1) the Board shall not be comprised of more than nine (9) members and (2) the corporation shall not, directly or indirectly, take any of the following actions, in each case without first obtaining the affirmative vote or the written approval of the holders of at least sixty-five percent (65%) of the then outstanding shares of Series C Preferred:

(i) create, authorize, designate, reclassify, issue or sell any class or series of capital stock of the corporation, or rights, options, warrants or other securities convertible into or exercisable or exchangeable for any capital stock of the corporation, or any "**phantom**" equity or stock appreciation rights that rank as to payment of dividends, distribution of assets or redemption prior to or *pari passu* with the Series C Preferred or that in any manner materially adversely affect the terms, designations, powers, preferences or other rights of the holders of Series C Preferred (other than shares of Series C Preferred issued as contemplated by the Purchase Agreement);

(ii) increase the authorized number of shares of Series C Preferred;

(iii) authorize, create or issue any capital stock of the corporation or securities exercisable or exchangeable for, or convertible into, capital stock of the corporation (collectively, "**Company Equity**"), except for Company Equity issued: (A) in connection with a joint venture, strategic alliance, licensing or other contractual arrangement with a third party that, together with all other issuances of Company Equity theretofore made in reliance on this Section 3(e)(iii)(A), represents (on a fully diluted, Common Stock equivalent basis) less than ten percent (10%) of the corporation's outstanding capital stock (on a fully diluted, Common Stock equivalent basis) immediately following the sale (or, if more than one as contemplated by the Purchase Agreement, the last sale) of shares of Series C Preferred under the Purchase Agreement; (B) upon conversion of shares of any Preferred Series; (C) upon exercise of options or warrants (1) outstanding as of the Series C Follow-On Issue Date or (2) if the approval contemplated by this Section 3(e)(iii) is either not required or obtained with respect to the issuance of such options or warrants, issued after the Series C Follow-On Issue Date; (D) pursuant to a Plan; or (E) upon conversion, exchange or exercise of any Company Equity issued as permitted under clauses (A) – (D) above;

(iv) consummate a Fundamental Transaction;

(v) redeem, repurchase or otherwise acquire any outstanding shares of its capital stock or any other of its outstanding securities, except for (A) repurchases of shares pursuant to agreements entered into to evidence grants or awards under Plans, or (B) redemptions pursuant to Section 6;

(vi) create, incur, assume or suffer to exist any indebtedness of the corporation for borrowed money (which shall include for purposes hereof capitalized lease obligations and guarantees or other contingent obligations for indebtedness for borrowed money) other than trade payables and accrued expenses incurred in the ordinary course of business and other debt not in excess at any point in time of $2,500,000 in the aggregate;

(vii) enter into any material transactions with any "**affiliate**" or "**associate**" (as such terms are defined under Rule 12b-2 under the Exchange Act) of the corporation, except as (x) expressly permitted by this Third Amended and Restated Certificate of Incorporation, (y) contemplated by the Purchase Agreement or (z) approved by a majority of the Board excluding, solely for this purpose, any directors who are affiliates or associates of such affiliate or associates of the corporation;

(viii) alter or modify the terms, rights, preferences or privileges of the shares of the Series C Preferred;

(ix) amend or waive any provision of this Third Amended and Restated Certificate of Incorporation or the bylaws of the corporation if such amendment or waiver would be adverse to the holders of Series C Preferred;

(x) agree or otherwise commit to take any of the actions set forth in the foregoing Sections 3(e)(i)-(ix).

(f) Quorum. Except as otherwise required by law, the presence in person or by proxy of the holders of at least fifty percent (50%) of the votes held by the outstanding shares of Common Stock and Preferred Stock, considered together as a single class on an as-converted basis, shall constitute a quorum, except that, in the case of matters voted on by a class or series of the corporation's capital stock voting separately as a class or series, the presence in person or by proxy of the holders of a majority of the votes held by the outstanding shares of such class or series shall constitute a quorum.

4. Conversion.

The holders of Preferred Stock shall have conversion rights as follows (the "**Conversion Rights**"):

(a) Right to Convert.

(i) Series A Preferred. Each outstanding share of Series A Preferred shall be convertible, at the option of the holder thereof, at any time after the date

of issuance of such share (but prior to the date that Conversion Rights terminate as set forth in the Notice issued pursuant to Section 2(f), if any), at the office of the corporation or any transfer agent for such stock, into fully paid and nonassessable shares of Common Stock. The number of shares of Common Stock into which each share of the Series A Preferred may be converted shall be determined by dividing $4.65 (the "**Series A Original Price**") by the Series A Conversion Price in effect at the time of conversion. The Series A Conversion Price shall, initially and as of the Series C Follow-On Issue Date, be equal to the Series A Original Price, and shall be subject to adjustment as provided pursuant to the other provisions of this Section 4.

(ii) Series B Preferred. Each outstanding share of Series B Preferred shall be convertible, at the option of the holder thereof, at any time after the date of issuance of such share (but prior to the date that Conversion Rights terminate as set forth in the Notice issued pursuant to Section 2(f), if any), at the office of the corporation or any transfer agent for such stock, into fully paid and nonassessable shares of Common Stock. The number of shares of Common Stock into which each share of the Series B Preferred may be converted shall be determined by dividing $4.65 (the "**Series B Original Price**") by the Series B Conversion Price in effect at the time of conversion. The Series B Conversion Price shall: (A) initially be equal to the Series B Original Price; (B) be adjusted to $1.95 as of March 14, 2003 and as of the Series C Follow-On Issue Date only for those holders of Series B Preferred as of November 26, 2002 (the "**Series C Original Issue Date**") that had not waived adjustments to the Series B Conversion Price resulting from the issuance of Series C Preferred at the Series C Original Price; and (C) be subject to adjustment pursuant to the other provisions of this Section 4.

(iii) Series C Preferred. Each outstanding share of Series C Preferred shall be convertible, at the option of the holder thereof, at any time after the date of issuance of such share (but prior to the date that Conversion Rights terminate as set forth in the Notice issued pursuant to Section 2(f), if any), at the office of the corporation or any transfer agent for such stock, into fully paid and nonassessable shares of Common Stock. The number of shares of Common Stock into which each share of the Series C Preferred may be converted shall be determined by dividing $1.21 (the "**Series C Original Price**") by the Series C Conversion Price in effect at the time of conversion. The Series C Conversion Price shall be, as of March 14, 2003 and as of the Series C Follow-On Issue Date, equal to $1.12, and shall be subject to adjustment pursuant to the other provisions of this Section 4. The Series C Conversion Price, Series B Conversion Price and Series A Conversion Price are sometimes referred to hereinafter collectively as the "**Conversion Prices**" and each, individually, as a "**Conversion Price**."

(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 Two Dollars and 15/100 ($2.15) (subject to adjustment for stock splits, stock dividends, reverse stock splits and other similar corporate reorganizations occurring after the Series C Follow-On Issue Date) or such lesser amount as is approved in writing after the Series C Follow-On Issue Date by the holders of (i) 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 (ii) 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 Fifty Million Dollars ($50,000,000) (a "**Qualified IPO**") (before the deduction of expenses and before applying any underwriter's discounts or commission).

(c) Mechanics of Voluntary Conversion. Before any holder of Preferred Stock shall be entitled to convert the same into shares of Common Stock, such holder shall surrender the certificate or certificates thereof, duly endorsed, at the office of the corporation or of any transfer agent for such stock, and shall give written notice to the corporation at such office that it elects to convert the same and shall state therein the name or names in which it wishes the certificate or certificates for shares of Common Stock to be issued. The corporation shall, as soon as practicable thereafter and at its expense, issue and deliver at such office to such holder a certificate or certificates for the number of shares of Common Stock to which it shall be entitled as aforesaid. Such conversion shall be deemed to have been made immediately prior to the close of business on the date of surrender of the shares of Preferred Stock to be converted, and the person or persons entitled to receive the shares of Common Stock issuable upon such conversion shall be treated for all purposes as the record holder or holders of such shares of Common Stock on such date.

(d) Adjustment for Stock Splits and Combinations. If the corporation shall at any time or from time to time after the Series C Follow-On Issue Date (as defined in Section 3(b)) effect a subdivision of the outstanding shares of Common Stock (by stock split or otherwise), the respective Conversion Prices then in effect immediately before the subdivision shall be proportionately decreased; conversely, if the corporation shall at any time or from time to time after the Series C Follow-On Issue Date reduce the outstanding shares of Common Stock by combination or otherwise, the respective Conversion Prices then in effect immediately before the combination shall be proportionately increased. Any adjustment under this Section 4(d) shall become effective at the close of business on the date the subdivision or combination becomes effective.

(e) Adjustment for Certain Dividends and Distributions. In the event the corporation at any time or from time to time after the Series C Follow-On Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable in additional shares of Common Stock, then and in each such event the respective Conversion Prices then in effect shall be decreased as of the time of such issuance or, in the event such a record date shall have been fixed, as of the close of

business on such record date, by multiplying the respective Conversion Prices then in effect by a fraction:

(i) the numerator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date; and

(ii) the denominator of which shall be the total number of shares of Common Stock issued and outstanding immediately prior to the time of such issuance or the close of business on such record date plus the number of shares of Common Stock issuable in payment of such dividend or distribution; provided, however, if such record date shall have been fixed and such dividend is not fully paid or if such distribution is not fully made on the date fixed therefor, the respective Conversion Prices shall be recomputed accordingly as of the close of business on such record date and thereafter the respective Conversion Prices shall be adjusted pursuant to this Section 4(e) as of the time of actual payment of such dividends or distributions.

(f) Adjustments for Other Dividends and Distributions. In the event the corporation at any time or from time to time after the Series C Follow-On Issue Date shall make or issue, or fix a record date for the determination of holders of Common Stock entitled to receive, a dividend or other distribution payable in securities of the corporation other than shares of Common Stock, then, and in each such event, provision shall be made so that the holders of Preferred Stock shall receive upon conversion thereof, in addition to the number of shares of Common Stock receivable thereupon, the amount of securities of the corporation that they would have received had their Preferred Stock been converted into Common Stock on the date of such event and had thereafter, during the period from the date of such event to and including the conversion date, retained such securities receivable by them as aforesaid during such period giving application to all adjustments called for during such period under this Section 4 with respect to the rights of the holders of the Preferred Stock.

(g) Adjustment for Reorganization, Reclassification or other Change. If the Common Stock issuable upon the conversion of the Preferred Stock shall be changed into the same or different number of shares of any class or classes of stock, whether by capital reorganization, reclassification or otherwise (other than a subdivision or combination of shares or stock dividend provided for above, or a reorganization, merger, consolidation or sale of assets provided for elsewhere in this Section 4), then and in each such event the holder of each share of Preferred Stock shall have the right thereafter to convert such share into the kind and amounts of shares of stock and other securities and property receivable upon such reorganization, reclassification or other change by holders of the number of shares of Common Stock into which such shares of Preferred Stock might have been converted immediately prior to such reorganization, reclassification or other change, all subject to further adjustment as provided herein.

(h) Mergers, etc. (i) In the event of a share exchange, consolidation, merger or other similar transaction in which (A) the corporation is a party and (B) the Series C Preferred, Series B Preferred or Series A Preferred is not canceled, exchanged, converted,

redeemed or otherwise retired, then provision shall be made so that the holders of Series C Preferred, Series B Preferred and Series A Preferred, as the case may be, shall thereafter be entitled to receive, upon conversion thereof, the number of shares of stock or other securities or property of the corporation to which a holder of that number of shares of Common Stock deliverable upon conversion thereof would have been entitled on such share exchange, consolidation, merger or other similar transaction. In any such case, appropriate adjustment shall be made in the application of the provisions of this Section 4 with respect to the rights of the holders of the Preferred Stock after the share exchange, consolidation, merger or other similar transaction to the end that the provisions of this Section 4 (including adjustment of the respective Conversion Prices then in effect and the number of shares into which such Preferred Stock is convertible) shall be applicable after that event as nearly equivalent as may be practicable.

(i) Sale of Shares Below Conversion Price.

(i) Unless waived as provided in Section 4(i)(vii), if at any time or from time to time after the Series C Follow-On Issue Date, the corporation shall issue or sell Additional Shares of Common Stock (as defined in Section 4(j)), other than as a dividend as provided in Section 4(e), and other than upon a subdivision or combination of shares of Common Stock as provided in Section 4(d), for a consideration per share less than the then existing Series C Conversion Price, then and in each case the Series C Conversion Price shall be reduced, as of the opening of business on the date of such issue or sale, to a price determined as follows: the new Series C Conversion Price shall be determined by multiplying the then-existing Series C Conversion Price by a fraction (A) the numerator of which shall be (1) the number of shares of Common Stock into which the outstanding shares of Series C Preferred immediately prior to such issue or sale are convertible based on the then-existing Series C Conversion Price plus (2) the number of shares of Common Stock that the aggregate consideration received by the corporation for the total number of Additional Shares of Common Stock so issued would purchase at such Series C Conversion Price, and (B) the denominator of which shall be (1) the number of shares of Common Stock into which the outstanding shares of Series C Preferred immediately prior to such issue or sale are convertible based on the then-existing Series C Conversion Price plus (2) the number of such Additional Shares of Common Stock so issued.

(ii) Unless waived as provided in Section 4(i)(vii), if at any time or from time to time after the Series C Follow-On Issue Date, the corporation shall issue or sell Additional Shares of Common Stock (as defined in Section 4(j)), other than as a dividend as provided in Section 4(e), and other than upon a subdivision or combination of shares of Common Stock as provided in Section 4(d), for a consideration per share less than the then existing Series C Conversion Price, then and in each case the Series B Conversion Price shall be reduced, as of the opening of business on the date of such issue or sale, to a price determined as follows: the new Series B Conversion Price shall be determined by multiplying the then-existing Series B Conversion Price by a fraction (A) the numerator of which shall be the Series C Conversion Price, as adjusted after giving effect to such issuance or sale of Additional Shares of Common Stock, and

(B) the denominator of which shall be the Series C Conversion Price immediately before giving effect to such issuance or sale of Additional Shares of Common Stock.

(iii) Unless waived as provided in Section 4(i)(vii), if at any time or from time to time after the Series C Follow-On Issue Date, the corporation shall issue or sell Additional Shares of Common Stock (as defined in Section 4(j)), other than as a dividend as provided in Section 4(e), and other than upon a subdivision or combination of shares of Common Stock as provided in Section 4(d), for a consideration per share less than the then existing Series C Conversion Price, then and in each case the Series A Conversion Price shall be reduced, as of the opening of business on the date of such issue or sale, to a price determined as follows: the new Series A Conversion Price shall be determined by multiplying the then-existing Series A Conversion Price by a fraction the numerator of which shall be (A) the Series C Conversion Price, as adjusted after giving effect to such issuance or sale of Additional Shares of Common Stock, and (B) the denominator of which shall be the Series C Conversion Price immediately before giving effect to such issuance or sale of Additional Shares of Common Stock.

(iv) For the purpose of the adjustments provided in Sections 4(i)(i), 4(i)(ii) and 4(i)(iii), the consideration received by the corporation for any issue or sale of securities shall:

(A) to the extent it consists of cash, be computed at the net amount of cash received by the corporation after deduction of any underwriting or similar commissions, concessions or compensation paid or allowed by the corporation in connection with such issue or sale;

(B) to the extent it consists of services or property other than cash, be computed at the fair value of such services or property as determined in good faith by a majority of the Board; and

(C) if Additional Shares of Common Stock, Convertible Securities (as hereinafter defined), or rights or options to purchase either Additional Shares of Common Stock or Convertible Securities are issued or sold together with other stock or securities or other assets of the corporation for a consideration that covers both, be computed as the portion of the consideration so received that may be reasonably determined in good faith by the Board to be allocable to such Additional Shares of Common Stock, Convertible Securities or rights or options.

(v) For the purpose of the adjustments provided in Sections 4(i)(i), 4(i)(ii) and 4(i)(iii), if at any time or from time to time, the corporation shall issue any rights or options for the purchase of, or stock or other securities convertible into, Additional Shares of Common Stock (such convertible stock or securities being hereinafter referred to as "**Convertible Securities**"), then, in each case, if the Effective Price (as hereinafter defined) of such rights, options or Convertible Securities shall be less than the then existing Series C Conversion Price, Series B Conversion Price or Series A

Conversion Price, as the case may be, the corporation shall be deemed to have issued at the time of the issuance of such rights or options or Convertible Securities the maximum number of Additional Shares of Common Stock issuable upon exercise or conversion thereof (determined as set forth in the instrument(s) relating thereto, but without regard to any provision contained therein designed to protect against dilution) and to have received as consideration for the issuance of such shares an amount equal to the total amount of the consideration, if any, received by the corporation for the issuance of such rights or options or Convertible Securities, plus, in the case of such options or rights, the minimum amounts of consideration, if any, payable to the corporation upon exercise or conversion of such options or rights (determined as set forth in the instrument(s) relating thereto, but without regard to any provision contained therein designed to protect against dilution). For purposes of the foregoing, "**Effective Price**" shall mean the quotient determined by dividing the total of all such consideration by such maximum number of Additional Shares of Common Stock. No further adjustment of the existing Series C Conversion Price, Series B Conversion Price or Series A Conversion Price adjusted upon the issuance of such rights, options or Convertible Securities shall be made as a result of the actual issuance of Additional Shares of Common Stock on the exercise of any such rights or options or the conversion of any such Convertible Securities.

If any such rights or options or the conversion privilege represented by any such Convertible Securities shall expire without having been exercised, the existing Series C Conversion Price, Series B Conversion Price or Series A Conversion Price, as the case may be, adjusted upon the issuance of such rights, options or Convertible Securities shall be readjusted to the existing Series C Conversion Price, Series B Conversion Price or Series A Conversion Price that would have been in effect had an adjustment been made on the basis that the only Additional Shares of Common Stock so issued were the Additional Shares of Common Stock, if any, actually issued or sold on the exercise of such rights or options, or rights of conversion of such Convertible Securities, and such Additional Shares of Common Stock, if any, were issued or sold for the consideration actually received by the corporation upon such exercise, plus the consideration, if any, actually received by the corporation for the granting of all such rights and options, whether or not exercised, plus the consideration received for issuing or selling the Convertible Securities actually converted plus the consideration, if any, actually received by the corporation on the conversion of such Convertible Securities.

(vi) For the purpose of the adjustments provided for in Sections 4(i)(i), 4(i)(ii) and 4(i)(iii), if at any time or from time to time, the corporation shall issue any rights or options for the purchase of Convertible Securities, then in each such case, if the Effective Price thereof is less than then existing Series C Conversion Price, Series B Conversion Price or Series A Conversion Price, as the case may be, the corporation shall be deemed to have issued at the time of the issuance of such rights or options the maximum number of Additional Shares of Common Stock issuable upon conversion of the total amount of Convertible Securities covered by such rights or options (determined as set forth in the instrument(s) relating thereto, but without regard to any provision contained therein designed to protect against dilution) and to have received as

consideration for the issuance of such Additional Shares of Common Stock an amount equal to the amount of consideration, if any, received by the corporation for the issuance of such rights or options, plus the minimum amounts of consideration, if any, payable to the corporation upon the conversion of such Convertible Securities (in each case determined as set forth in the instrument(s) relating thereto, but without regard to any provision contained therein designed to protect against dilution). For the purposes of the foregoing, "**Effective Price**" shall mean the quotient determined by dividing the total amount of such consideration by such maximum number of Additional Shares of Common Stock. No further adjustment of such Series C Conversion Price, Series B Conversion Price or Series A Conversion Price adjusted upon the issuance of such rights or options shall be made as a result of the actual issuance of the Convertible Securities upon the exercise of such rights or options or upon the actual issuance of Additional Shares of Common Stock upon the conversion of such Convertible Securities.

The provisions of Section 4(i)(v) for the readjustment of the Series C Conversion Price, Series B Conversion Price and Series A Conversion Price upon the expiration of rights or options or the rights of conversion of Convertible Securities, shall apply *mutatis mutandis* to the rights, options and Convertible Securities referred to in this Section 4(i)(vi).

(vii) Notwithstanding anything in this Section 4(i) to the contrary, the operation of, and any adjustment of the Series C Conversion Price, Series B Conversion Price and/or the Series A Conversion Price pursuant to this Section 4(i) may be waived with respect to any one or more of the Preferred Series, either prospectively or retroactively and either generally or in a particular instance, by a writing executed by (A) in the case of Series C Preferred, the holders of at least 65% of the then outstanding shares of Series C Preferred, (B) in the case of Series B Preferred, the holders of a majority of the then outstanding shares of Series B Preferred or (C) in the case of Series A Preferred, the holders of a majority of the then outstanding shares of such Series A Preferred. Any waiver pursuant to this Section 4(i)(vii) shall bind all future holders of shares of the Preferred Series for which such rights have been waived.

Notwithstanding anything in this Section 4(i) to the contrary, the operation of, and any adjustment of the Series B Conversion Price and/or the Series A Conversion Price pursuant to, this Section 4(i) may be waived with respect to any specific share or shares of Series B Preferred Stock and/or Series A Preferred Stock, either prospectively or retroactively and either generally or in a particular instance, by a writing executed by the record holder of such shares, including without limitation the corporation's Investor Rights Agreement dated as of August 22, 2000, as may be amended or restated; provided that no such waiver may be effected pursuant to this paragraph after March 14, 2003. Any waiver pursuant to this paragraph shall bind all future holders of such shares of Series B Preferred Stock and/or Series A Preferred Stock, as the case may be, for which such rights have been waived. In the event that a waiver of adjustment of the Series B Conversion Price and/or the Series A Conversion Price under this paragraph results in different Conversion Prices for shares of Series B Preferred Stock and/or shares of Series A Preferred Stock, the Secretary of the corporation shall maintain a written ledger

identifying the applicable Conversion Price for each such share, which ledger shall be available upon request. If different shares of Series B Preferred Stock and/or different shares of Series A Preferred Stock have different Conversion Prices as a result of application of this paragraph, the Conversion Price for triggering any future adjustment of the Conversion Price for the Series B Preferred Stock and/or Series A Preferred Stock, as the case may be, that have not waived such adjustment shall be the lowest Conversion Price in effect with respect to such shares of Series B Preferred Stock and/or Series A Preferred Stock, as the case may be.

(j) Definition. The term "**Additional Shares of Common Stock**" as used herein shall mean all shares of Common Stock issued or deemed issued by the corporation after the Series C Follow-On Issue Date, whether or not subsequently reacquired or retired by the corporation, other than (i) shares of Series C Preferred issued as contemplated by the Purchase Agreement, (ii) shares of Common Stock issued as a stock dividend or in a stock split subdivision, recapitalization and the like, (iii) shares of Common Stock issuable upon conversion of the Preferred Stock, (iv) 1,612,903 shares of Common Stock (as adjusted for all stock dividends, stock splits, subdivisions, combinations and the like), issuable to R.J. Reynolds Tobacco Holdings, Inc. ("**RJRH**") upon exercise of the Warrant to Purchase Common Stock dated as of August 22, 2000 originally issued by the corporation to RJRH's affiliate, (v) up to 7,721,772 shares of Common Stock (as adjusted for all stock dividends, stock splits, subdivisions, combinations and the like and as adjusted to reflect an increase in the number of shares subject to the 2000 Plan pursuant to any validly effected amendment thereto) issuable after the Series C Follow-On Issue Date to employees, officers, directors, consultants or other persons performing services for or on behalf of the corporation (if so issued solely because of any such person's status as an officer, director, employee, consultant or other person performing services for or on behalf of the corporation and not as part of any offering of the corporation's securities) pursuant to any Plan, (vi) securities issued in consideration of the acquisition by the corporation of the assets, capital stock or other equity interests of another entity (and any securities issued upon conversion or exercise thereof), and (vii) securities issued in connection with a joint venture, strategic alliance or licensing or other contractual arrangement with a third party (A) the issuance of which does not require the approval contemplated by Section 3(e)(iii) or (B) with (x) the consent contemplated by Section 3(e)(iii) and (y) the affirmative vote or written approval of the holders of 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, in either case, any securities issued upon conversion or exercise thereof).

(k) Certificate of Adjustment. In each case of an adjustment or readjustment of the respective Conversion Prices for the number of shares of Common Stock or other securities issuable upon conversion of the Preferred Stock, the corporation shall cause its Chief Financial Officer to compute, or, at the request of the holders of a majority of the shares of Preferred Stock (on an as-converted to Common Stock prior to such adjustment or readjustment basis), shall cause independent certified public accountants of recognized standing elected by the corporation (who may be the independent certified public accountants then auditing the books of the corporation) to compute, at the corporation's expense, such adjustment or readjustment in accordance herewith and prepare a certificate showing such adjustment or readjustment, and

shall mail such certificate, by first class mail, postage prepaid, to each registered holder of the Preferred Stock at the holder's address as shown in the corporation's books. The certificate shall set forth such adjustment or readjustment, showing in detail the facts upon which such adjustment or readjustment is based including a statement of (i) the consideration received or to be received by the corporation for any Additional Shares of Common Stock issued or sold or deemed to have been issued or sold, if applicable to such adjustment, (ii) the Conversion Prices at the time in effect for each such series of the Preferred Stock, and (iii) the number of Additional Shares of Common Stock and the type and amount, if any, of other property which at the time would be received upon conversion of the Preferred Stock.

(l) Notice of Certain Events. In the event of (i) any taking by the corporation of a record of the holders of any class or series of securities for the purpose of determining the holders thereof who are entitled to receive any dividend or other distribution or (ii) any reclassification or recapitalization of the capital stock of the corporation or (iii) any Fundamental Transaction, the corporation shall give notice to each holder of Preferred Stock at least ten (10) days prior to the record date specified therein (in the case of (i) and (ii)) or at least fifteen (15) days prior to the expected effective date thereof (in the case of (iii)), specifying, to the extent applicable, (A) the date on which any such record is to be taken for the purpose of such dividend or distribution, (B) the date on which any such reclassification, recapitalization or Fundamental Transaction is expected to become effective, and (C) the time, if any is to be fixed, as to when the holders of record of Common Stock (or other securities) shall be entitled to exchange their shares of Common Stock (or other securities) for securities or other property deliverable upon such reclassification, recapitalization or Fundamental Transaction; provided, that such notice may be waived by the holders of at least sixty-five percent (65%) of the then outstanding shares of Series C Preferred and the holders of a majority of the then outstanding shares of Series B Preferred and Series A Preferred, considered together as a single class on an as-converted basis.

(m) Fractional Shares. No fractional shares of Common Stock shall be issued upon conversion of shares of Preferred Stock. In lieu of any fractional shares to which the holder would otherwise be entitled, the corporation shall pay cash equal to the product of such fraction multiplied by the fair market value of one share of the corporation's Common Stock on the date of conversion, as determined in good faith by a majority of the Board. Whether or not fractional shares are issuable upon such conversion shall be determined on the basis of the total number of shares of Preferred Stock the holder is at the time converting into Common Stock and the number of shares of Common Stock issuable upon such aggregate conversion.

(n) Reservation of Stock Issuable Upon Conversion. The corporation shall at all times reserve and keep available out of its authorized but unissued shares of Common Stock, solely for the purpose of effecting the conversion of the shares of the Preferred Stock, such number of its shares of Common Stock as shall from time to time be sufficient to effect the conversion of all outstanding shares of the Preferred Stock. As a condition precedent to the taking of any action which would cause an adjustment to the Conversion Price, the corporation will take such corporate action as may, in the opinion of its counsel, be necessary to increase its authorized but unissued shares of Common Stock to such number of shares as shall be sufficient in order that it may validly and legally issue the shares of its Common Stock issuable based upon

such adjusted Conversion Price, including without limitation using its best efforts to obtain the requisite stockholder approval of any necessary amendment to this Third Amended and Restated Certificate of Incorporation.

(o) Reserved.

(p) Payment of Taxes. The corporation will pay all taxes and other governmental charges (other than taxes measured by the revenue or income of the holders of the Preferred Stock) that may be imposed in respect of the issue or delivery of shares of Common Stock upon conversion of the shares of the Preferred Stock.

(q) No Impairment. The corporation shall not, by amendment of this Third Amended and Restated Certificate of Incorporation or through any reorganization, transfer of assets, consolidation, merger, dissolution, issue or sale of securities or any other voluntary action, avoid or seek to avoid the observance or performance of any of the terms to be observed or performed hereunder by the corporation, but will at all times in good faith assist in the carrying out of all the provisions of this Section 4 and in taking of all such action as may be necessary or appropriate in order to protect the Conversion Rights of the holders of Preferred Stock against impairment.

5. No Preemptive Rights. Except as otherwise provided in any valid agreement between the corporation and one or more of its stockholders (including, without limitation, the Second Amended and Restated Investor Rights Agreement dated as of the Series C Original Issue Date among the corporation and certain of its stockholders, as may be amended or restated from time to time), the holders of Common Stock and Preferred Stock shall not have (solely by reason of the ownership of such stock) any rights to acquire shares of capital stock of the corporation (whether now authorized or not), which the corporation may, from time to time, propose to sell and issue, including without limitation rights, options or warrants to purchase capital stock, or securities of any type whatsoever that are, or may become, convertible into capital stock.

6. Mandatory Redemption.

(a) Redemption Election.

(i) So long as any Series C Preferred shall be outstanding, the corporation shall, at the written election (a "**Series C Mandatory Redemption Election**") of the holders of at least sixty-five percent (65%) of the outstanding shares of Series C Preferred at any time or from time to time after the sixth anniversary of the Series C Original Issue Date, redeem for cash at the Series C Mandatory Redemption Price (as hereinafter defined) all of the outstanding shares of Series C Preferred within sixty (60) days after receipt of such written election (the "**Series C Mandatory Redemption Date**").

(ii) So long as any Series A Preferred or Series B Preferred shall be outstanding, the corporation shall, at the written election (a "**Series A/B**

Mandatory Redemption Election and, together with a Series C Mandatory Redemption Election, a "Redemption Election") of the holders of a majority of the outstanding shares of Series A Preferred, or at the written election of the holders of a majority of the outstanding shares of Series B Preferred, at any time or from time to time after the later of (i) August 22, 2005 or (ii) the date on which no shares of Series C Preferred remain outstanding, redeem for cash at the Series A/B Mandatory Redemption Price (as hereinafter defined) the number of shares of Series A Preferred or Series B Preferred, as the case may be, elected to be redeemed within sixty (60) days after receipt of such written election (each a "**Series A/B Mandatory Redemption Date**" and, together with any Series C Redemption Date, a "**Redemption Date**").

(b) Mandatory Redemption Price.

(i) The Series C Mandatory Redemption Price for each share of Series C Preferred shall be an amount in cash equal to the Series C Original Price (subject to adjustment for stock splits, stock dividends, reverse stock splits and other similar corporate reorganizations) plus any previously declared or accumulated but unpaid dividends thereon, including without limitation the accrued but unpaid Series C Dividend (the "**Series C Mandatory Redemption Price**").

(ii) The Series A/B Mandatory Redemption Price for each share of Series A Preferred or Series B Preferred shall be an amount in cash equal to $4.65 (subject to adjustment for stock splits, stock dividends, reverse stock splits and other similar corporate reorganizations) plus (i) any previously declared or accumulated but unpaid dividends thereon and (ii) an amount equal to $0.081375 (subject to adjustment for stock splits, stock dividends, reverse stock splits and other similar corporate reorganizations) multiplied by the number of complete three-month periods that have elapsed from the date such share was originally issued to the Series A/B Mandatory Redemption Date (plus a prorated amount attributable to the period from the most recently completed three-month period to the Series A/B Mandatory Redemption Date) (the "**Series A/B Mandatory Redemption Price**" and, together with the Series C Mandatory Redemption Price, the "**Redemption Price**").

(c) Payment of Series A/B Mandatory Redemption Price. Notwithstanding anything in this Section 6 to the contrary, upon a Series A/B Mandatory Redemption Election pursuant to Section 6(a)(ii), the corporation may pay the aggregate Series A/B Mandatory Redemption Price as follows: (i) 33 1/3% in cash at the applicable Series A/B Mandatory Redemption Date and (ii) the remainder by execution and delivery of promissory notes that provide for (A) equal principal installments on each of the next two (2) successive annual anniversaries of the applicable Series A/B Mandatory Redemption Date (each an "**Anniversary Date**"), with the first installment payable on the first such Anniversary Date, (B) interest payable at the Prime Rate as of such Anniversary Date (as reported in the Wall Street Journal – Eastern Edition) and (C) the right at any time and from time to time to prepay all or any part of the remaining Series A/B Mandatory Redemption Price together with interest accrued thereon, without penalty. Compliance with this Section 6(c) shall constitute payment in full of the Series A/B Mandatory Redemption Price.

(d) Notice of Redemption. Not less than twenty (20) days prior to each Mandatory Redemption Date, written notice (the "**Redemption Notice**") shall be mailed, postage prepaid, to each holder of record of shares of Series A Preferred and Series B Preferred to be redeemed (in the case of a Series A/B Mandatory Redemption Election) and to each holder of record of shares of Series C Preferred (in the case of a Series C Mandatory Redemption Election) at its post office address last shown on the records of the corporation. The Redemption Notice shall state:

(i) the total number of shares of each Preferred Series subject to the Redemption Election;

(ii) the number of shares of each Preferred Series held by the holder that the corporation intends to redeem;

(iii) the applicable Redemption Date and the Redemption Price and, if permitted, whether the corporation intends to pay as provided in Section 6(c);

(iv) the date upon which the holder's Conversion Rights as to such Preferred Stock terminate; and

(v) that the holder is to surrender to the corporation, in the manner and at the place designated, his certificate or certificates representing the shares of each Preferred Series to be redeemed.

(e) Surrender of Certificates. On or before each Redemption Date, each holder of shares of Preferred Series to be redeemed, unless such holder has exercised his right to convert the shares as provided in Section 4, shall surrender the certificate or certificates representing such shares to the corporation, in the manner and at the place designated in the Redemption Notice, and thereupon the Redemption Price for such shares shall be payable to the order of the person whose name appears on such certificate or certificates as the owner thereof, and each surrendered certificate shall be cancelled and retired. If a holder fails to surrender its certificate or certificates within sixty (60) days after the Redemption Date, such holder shall thereafter have no right to the Redemption Price. In the event less than all of the shares represented by such certificate are redeemed, a new certificate shall be issued representing the unredeemed shares.

(f) Effect of Payment. If the Redemption Notice shall have been duly given, and if, on such Redemption Date, the Redemption Price shall have been paid (including, if permitted, payment as provided in Section 6(c)), then, notwithstanding that the certificates evidencing any of the shares of the Preferred Series so called for redemption shall not have been surrendered, all rights with respect to such shares thereafter shall terminate.

(g) Insufficient Funds. In the event that (i) there are insufficient funds legally available to pay in full the Redemption Price for shares of Series A Preferred, Series B Preferred or Series C Preferred, as the case may be, and (ii) if permitted, the corporation does not pay the applicable Redemption Price as provided in Section 6(c), at any time thereafter when

additional funds of the corporation become legally available, such funds will be used as soon as practicable thereafter to redeem the balance of the shares that the corporation has become obligated to redeem but that it has not redeemed. This Section 6(g) shall not limit or otherwise affect any right or remedy available to any holder of shares that the corporation has become obligated to redeem but that it has not redeemed.

7. No Reissuance of Preferred Stock. No share or shares of Preferred Stock acquired by the corporation by reason of redemption, purchase, conversion or otherwise shall be reissued as shares of Preferred Stock. All such shares shall be canceled and shall not be held as treasury shares.

8. Notices. Except to the extent otherwise expressly provided herein, all notices (including, without limitation, any Notice under Section 2(f)) required hereunder, whether to the holders of Preferred Stock or Common Stock or to the corporation, shall be deemed given or submitted: (i) when personally delivered to the recipient (if to the corporation, to the Chief Executive Officer); (ii) three (3) business days after such notice is sent by certified or registered mail, return receipt requested, postage prepaid (if to a stockholder, addressed to such stockholder at its record address appearing on the books of the corporation and, if to the corporation, addressed to the corporation at its principal offices to the attention of the Chief Executive Officer); or (iii) the next business day after deposit with a nationally recognized overnight courier or messenger for delivery at the applicable address referenced in clause (ii).

FIFTH: The corporation is to have perpetual existence.

SIXTH: Whenever a compromise or arrangement is proposed between this corporation and its creditors or any class of them and/or between this corporation and its stockholders or any class of them, any court of equitable jurisdiction within the State of Delaware may, on the application in a summary way of this corporation or of any creditor or stockholder thereof or on the application of any receiver or receivers appointed for this corporation under Section 291 of Title 8 of the Delaware Code or on the application of trustees in dissolution or of any receiver or receivers appointed for this corporation under Section 279 of Title 8 of the Delaware Code order a meeting of the creditors or class of creditors, and/or of the stockholders or class of stockholders of this corporation, as the case may be, to be summoned in such manner as the said court directs. If a majority in number representing three fourths in value of the creditors or class of creditors, and/or of the stockholders or class of stockholders of this corporation, as the case may be, agree to any compromise or arrangement and to any reorganization of this corporation as consequence of such compromise or arrangement, the said compromise or arrangement and the said reorganization shall, if sanctioned by the court to which the said application has been made, be binding on all the creditors or class of creditors, and/or on all the stockholders or class of stockholders, of this corporation, as the case may be, and also on this corporation.

SEVENTH: For the management of the business and for the conduct of the affairs of the corporation, and in further definition, limitation, and regulation of the powers of the corporation and of its directors and of its stockholders or any class thereof, as the case may be, it is further provided:

1. The management of the business and the conduct of the affairs of the corporation shall be vested in its Board of Directors. The number of directors which shall constitute the whole Board of Directors shall be fixed by, or in the manner provided in, the Bylaws. No election of directors need be by written ballot

2. After the original or other Bylaws of the corporation have been adopted, amended or repealed, as the case may be, in accordance with the provisions of Section 109 of the General Corporation Law of the State of Delaware, and, after the corporation has received any payment for any of its stock, the power to adopt, amend or repeal the Bylaws of the corporation may be exercised by the Board of Directors of the corporation; provided, however, that any provision for the classification of directors of the corporation for staggered terms pursuant to the provisions of subsection (d) of Section 141 of the General Corporation law of the State of Delaware shall be set forth in an initial Bylaw or in a Bylaw adopted by the stockholders entitled to vote of the corporation unless provisions for such classification shall be set forth in this Third Amended and Restated Certificate of Incorporation.

3. Whenever the corporation shall be authorized to issue only one class of stock, each outstanding share shall entitle the holder thereof to notice of, and the right to vote at, any meeting of stockholders. Whenever the corporation shall be authorized to issue more than one class of stock, no outstanding share of any class of stock which is denied voting power under the provisions of the Third Amended and Restated Certificate of Incorporation shall entitle the holder thereof to the right to vote at any meeting of stockholders except as the provisions of paragraph (2) of subsection (b) of Section 242 of the General Corporation Law of the State of Delaware shall otherwise require; provided, that no share of any such class which is otherwise denied voting power shall entitle the holder thereof to vote upon the increase or decrease in the number of authorized shares of said class.

EIGHTH: A director of the corporation shall not be personally liable to the corporation or its stockholders for monetary damages for breach of fiduciary duty as a director, except for liability (a) for any breach of the director's duty of loyalty to the corporation or its stockholders, (b) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (c) under Section 174 of the General Corporation Law of Delaware, or (d) for any transaction from which the director derived an improper personal benefit. If the General Corporation Law of Delaware is amended to authorize corporate action further eliminating or limiting the personal liability of directors, then the liability of a director of the corporation shall be eliminated or limited to the fullest extent permitted by the General Corporation Law of Delaware as so amended. Neither any amendment, repeal or modification of this article nor the adoption of any provision of this certificate of incorporation or the Bylaws of the corporation inconsistent with this article shall adversely affect any right or protection of a

director of the corporation existing at the time of such amendment, repeal, modification or adoption.

NINTH: The corporation shall, to the fullest extent permitted by the provisions of Section 145 of the General Corporation Law of the State of Delaware, as the same may be amended and supplemented, indemnify any person who is or was a director or officer of the corporation, or is or was serving at the request of the corporation as a director, officer or trustee of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, from and against any and all of the expenses, liabilities, or other matters referred to in or covered by said section, and the indemnification provided for herein shall not be deemed exclusive of any other rights to which such persons may be entitled under any Bylaw, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in his or her official capacity and as to action in another capacity while holding such office, and shall continue as to a person who has ceased to be a director or officer and shall inure to the benefit of the heirs, executors, and administrators of such a person. In addition, the corporation may, to the extent authorized from time to time by the Board, grant indemnification rights to other employees or agents of the corporation or other persons serving the corporation and such rights may be equivalent to, or greater or less than, those indemnification rights of directors and officers set forth in this article or the Bylaws. Neither any amendment, repeal or modification of this article nor the adoption of any provision of this certificate of incorporation or the Bylaws of the corporation inconsistent with this article shall adversely affect any right or protection of a director or officer of the corporation existing at the time of such amendment, repeal, modification or adoption.

TENTH: From time to time any of the provisions of this Third Amended and Restated Certificate of Incorporation may be amended, altered, or repealed and other provisions authorized by the laws of the State of Delaware at the time in force may be added or inserted in the manner and at the time prescribed by said laws and consistent with the terms of this Third Amended and Restated Certificate of Incorporation. All rights conferred upon stockholders of the corporation by this Third Amended and Restated Certificate of Incorporation are granted subject to the provisions of this Article TENTH.

Exhibit 4.2(b)

Amendment No. 1 to
Third Amended and Restated Investor Rights Agreement

THIS AMENDMENT NO. 1 to the Third Amended and Restated Investor Rights Agreement dated December 6, 2004 (this "**Amendment**") amends the Third Amended and Restated Investor Rights Agreement dated May 12, 2004 (the "**Future IRA**") by and among Targacept, Inc. (the "**Company**") and the holders of shares of the Company's Series C Convertible Preferred Stock, $0.001 par value per share ("**Series C Stock**"), Series B Convertible Preferred Stock, $0.001 par value per share ("**Series B Stock**"), or Series A Convertible Preferred Stock, $0.001 par value per share ("**Series A Stock**" and, together with the Series C Stock and Series B Stock, "**Preferred Stock**") party thereto. Capitalized terms used herein and not otherwise defined shall have the meanings ascribed to them in the Future IRA.

R E C I T A L S:

WHEREAS, the Future IRA was entered into in contemplation of an initial public offering of the Company's common stock in order to amend, effective as of the closing of such initial public offering, the Company's Second Amended and Restated Investor Rights Agreement dated November 26, 2002, as amended (the "**Current IRA**"), which is currently in effect; and

WHEREAS, by its terms, the Future IRA will not become effective or affect the Current IRA unless and until the prospective initial public offering is completed and will not become effective at all if such initial public offering is not completed on or before December 31, 2004 (the "**Trigger Date**"); and

WHEREAS, Section 3 of the Future IRA provides that the Future IRA may be amended only with the prior written consent of the Company and the holders of a majority of the outstanding Series A Registrable Securities and Series B Registrable Securities and at least 65% of the outstanding Series C Registrable Securities (collectively, the "**Required Investors**"); and

WHEREAS, the prospective initial public offering may not be completed on or before the Trigger Date, and the Company and the undersigned holders of Preferred Stock, constituting the Required Investors, desire to amend the Future IRA as provided herein to extend the Trigger Date;

NOW, THEREFORE, the undersigned parties agree as follows:

1. Section 2.1(a) of the Future IRA is hereby amended by deleting the first sentence in its entirety and replacing it with the following:

"Subject to the other provisions of this Section 2.1, Section 2.8 and Section 2.9, if, at any time or from time to time following the Eligibility Date (but in no event prior to (x) six months after the effective date of the first registration of the Company's securities on Form S-1 or (y) three months after the effective date of any other registration of the Company's securities, other than registrations on Form S-4, Form S-8 or comparable or successor forms and other than registrations for the account of selling stockholders on Form S-3 or a comparable or successor form), the Company shall receive a written

request (specifying that it is being made pursuant to this Section 2.1) from (i) Holders of at least a majority of the Series A Registrable Securities and Series B Registrable Securities, considered together, or (ii) Holders of Series C Registrable Securities that the Company file a registration statement under the Act covering the registration for offer and sale of (A) in the case of clause (i) above, at least thirty percent (30%) of all Series A Registrable Securities and Series B Registrable Securities, considered together, or (B) in the case of clause (ii) above, at least (1) thirty percent (30%) of all Series C Registrable Securities or (2) a number of Series C Registrable Securities for which the total gross proceeds in a public offering reasonably expected to be received by the requesting Holders is at least $7,500,000, then the Company shall, within ten (10) business days notify in writing all other Holders of such request."

2. Section 9 of the Future IRA is hereby amended by replacing "December 31, 2004" therein with "June 30, 2005."

3. As expressly amended hereby, the Future IRA shall continue in full force and effect.

4. For the avoidance of doubt, as used in the Future IRA and the Current IRA, the term "Series C Stock" shall include, without limitation, shares of Series C Stock issued and sold pursuant to the Series C Convertible Preferred Stock Purchase Agreement entered into on or about the date hereof.

[signature page follows]

IN WITNESS WHEREOF, this Amendment No. 1 to the Third Amended and Restated IRA is executed as of the day and year first above written.

TARGACEPT, INC.

By: /s/ J. Donald deBethizy
Name: J. Donald deBethizy
Title: President & CEO

R.J. REYNOLDS TOBACCO HOLDINGS, INC.

By: /s/ Charles A. Blixt
Name: Charles A. Blixt
Title: President

EUCLIDSR PARTNERS, L.P.

By: EuclidSr Associates, L.P.,
its general partner

By: /s/ Elaine V. Jones
Elaine V. Jones
General Partner

EUCLIDSR BIOTECHNOLOGY PARTNERS, L.P.

By: EuclidSr Biotechnology Associates, L.P.,
its general partner

By: /s/ Elaine V. Jones
Elaine V. Jones
General Partner

BURRILL BIOTECHNOLOGY CAPITAL FUND, L.P.

By: Burrill & Company (Biotechnology GP), LLC,
its General Manager

By: /s/ G. S. Burrill
G. Steven Burrill
Managing Member

[signatures continue on following page]

GENAVENT FUND

By: Société Générale Asset Management, S.A.,
its Manager

By: /s/ Ferriere
Corinne Ferriere
Deputy Head of Private Equity

FCPR SGAM AI BIOTECHNOLOGY FUND
Represented by SGAM Alternative Investments, its
management company with a share capital of 35 576
725 euros, having its registered office at 2, place de la Coupole,
92078 Paris – La Défense cedex France,
registered with the Nanterre Trade and Companies
registry under the number B 410 704 571

By: /s/ Ferriere
Corinne Ferriere
Deputy Head of Private Equity

FCPR CDC INNOVATION 2000, a venture
capital fund represented by CDC ENTREPRISES
INNOVATION, its management company
("Societe de gestion") with a share capital of
EUR 762,000

By: /s/ T. Laugel
Name: T. Laugel
Title: Director d'investissement

ADVENT PRIVATE EQUITY FUND II,
'A' LIMITED PARTNERSHIP
ADVENT PRIVATE EQUITY FUND II,
'B' LIMITED PARTNERSHIP
ADVENT PRIVATE EQUITY FUND II,
'C' LIMITED PARTNERSHIP
ADVENT PRIVATE EQUITY FUND II,
'D' LIMITED PARTNERSHIP

By: Advent Venture Partner, General Partner

By: /s/ Patrick Lee
Name: Patrick Lee
Title: General Partner

[signatures continue on following page]

NOMURA PHASE4 VENTURES LIMITED AS MANAGER ON BEHALF OF INTERNATIONAL PLC AND NOMURA PHASE4 VENTURES LP

By: /s/ Denise Pollard-Knight
Name: Denise Pollard-Knight
Title: Head of Nomura Phase4 Ventures Ltd.

NEW ENTERPRISE ASSOCIATES 10, LIMITED PARTNERSHIP

By: NEA Partners 10, Limited Partnership, General Partner

By: /s/ E. A. Trainor
Name: Eugene A. Trainor, III
Administrative General Partner & Chief Operating Officer

NEA VENTURES, 2002 LIMITED PARTNERSHIP

By: /s/ Pamela J. Clark
Pamela J. Clark
General Partner

CDIB BIOSCIENCE VENTURES I, INC.

By: /s/ Benny T. Hu
Name: Benny T. Hu
Title: Chairman

JAFCO G-9(A) VENTURE CAPITAL INVESTMENT LIMITED PARTNERSHIP

By: JAFCO CO., LTD., its general partner

By: /s/ Tomio Kezuka
Name: Tomio Kezuka
Title: Executive Vice President

[signatures continue on following page]

JAFCO G-9(B) VENTURE CAPITAL
INVESTMENT LIMITED PARTNERSHIP

By: /s/ Tomio Kezuka
Name: Tomio Kezuka
Title: Executive Vice President

Exhibit 4.4

THIS CONVERTIBLE PROMISSORY NOTE HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED. NO SALE OR DISPOSITION MAY BE EFFECTED EXCEPT IN COMPLIANCE WITH RULE 144 UNDER SAID ACT OR AN EFFECTIVE REGISTRATION STATEMENT RELATED THERETO OR AN OPINION OF COUNSEL FOR HOLDER REASONABLY SATISFACTORY TO PAYOR THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE ACT OR RECEIPT OF A NO-ACTION LETTER FROM THE SECURITIES AND EXCHANGE COMMISSION.

CONVERTIBLE PROMISSORY NOTE

$1,250,000 **December 15, 2004**

For value received TARGACEPT, INC., a Delaware corporation ("**Payor**"), promises to pay to the order of THE STANLEY MEDICAL RESEARCH INSTITUTE or its assigns ("**Holder**") the principal sum of $1,250,000, together with interest on the outstanding balance hereof at the rate of ten percent (10%) per annum, compounded annually as of each December 31 (beginning December 31, 2005) until paid. Interest shall commence with the date hereof and shall continue on the outstanding principal until paid in full or converted. Interest shall be computed on the basis of a year of 365 days for the actual number of days elapsed.

1. This note (this "**Note**") is issued pursuant to the terms of that certain Development Agreement between Holder and Payor (the "**Agreement**") of even date herewith (the "**Agreement Date**").

2. All payments of interest and principal shall be in lawful money of the United States of America and shall be made to Holder. All payments shall be applied first to accrued interest, and thereafter to principal.

3. In the event that Payor issues and sells shares of its common stock, $0.001 par value per share (the "**Common Stock**"), before January 1, 2007 (the "**Maturity Date**") in a firm commitment underwritten public offering registered pursuant to the Securities Act of 1933, as amended (the "**Initial Public Offering**"), and, as of the date such Initial Public Offering is closed this Note has not been paid in full, the outstanding principal balance of this Note, together with interest hereon through the date such Initial Public Offering is closed, shall automatically convert in whole without any further action by Holder into shares of Payor's Common Stock effective upon the closing of the Initial Public Offering at a conversion price equal to the price per share to the public of a share of Payor's Common Stock in the Initial Public Offering (rounded to the nearest whole share). For the avoidance of doubt, no fractional share would be issued.

4. Unless this Note has been converted in accordance with the terms of Section 3 above, the entire outstanding principal balance and all unpaid accrued interest shall become fully due and payable in cash on the Maturity Date.

5. Payor may prepay this Note, in whole or in part and at any time, or from time to time, prior to the Maturity Date without the consent of Holder.

6. If there is an Event of Default (as defined below), Payor shall pay all reasonable attorneys' fees and court costs incurred by Holder in enforcing and collecting this Note.

7. If there shall be any Event of Default hereunder, upon the declaration of Holder, this Note shall accelerate and all principal and unpaid accrued interest shall become due and payable. From and after the occurrence of an Event of Default, this Note shall bear interest at the rate of fifteen percent (15%) per annum, compounded annually. The occurrence of any one or more of the following shall constitute an Event of Default:

(a) Payor fails to pay any amount when due hereunder;

(b) Payor files any petition or action for relief under any bankruptcy, reorganization, insolvency or moratorium law or any other law for the relief of, or relating to, debtors, now or hereafter in effect, or makes any assignment for the benefit of creditors; or

(c) An involuntary petition is filed against Payor (unless such petition is dismissed or discharged within sixty (60) days, under any bankruptcy statute now or hereafter in effect, or a custodian, receiver, trustee, assignee for the benefit of creditors (or other similar official) is appointed to take possession, custody or control of any property of Payor.

8. Payor hereby waives demand, notice, presentment, protest and notice of dishonor.

9. This Note shall be governed by construed and under the laws of the State of Delaware, as applied to agreements among Delaware residents, made and to be performed entirely within the State of Delaware, without giving effect to conflicts of laws principles.

10. The indebtedness evidenced by this Note is subordinated in right of payment to the prior payment in full of any Senior Indebtedness in existence on the date of this Note. "**Senior Indebtedness**" shall mean, unless expressly subordinated to or made on a parity with the amounts due under this Note, all amounts due in connection with (a) indebtedness of Payor to banks, equipment lessors or other financial institutions and (b) any such indebtedness or any debentures, notes or other evidence of indebtedness issued in exchange for such Senior Indebtedness, or any indebtedness arising from the satisfaction of such Senior Indebtedness by a guarantor.

11. Any term of this Note may be amended or waived with the written consent of Payor and Holder.

Targacept, Inc.

By: /s/ J. Donald deBethizy

Name: J. Donald deBethizy
Title: President and CEO

[********] 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.

AMENDED AND RESTATED
COLLABORATIVE RESEARCH AND LICENSE AGREEMENT

between

TARGACEPT, INC.

and

AVENTIS PHARMA SA

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AMENDED AND RESTATED
COLLABORATIVE RESEARCH AND LICENSE AGREEMENT

This Amended and Restated Collaborative Research and License Agreement (this "Agreement") is made and entered into as of January 21, 2002, by and between **Targacept, Inc.**, a Delaware corporation having its principal place of business at 950 Reynolds Boulevard, Winston-Salem, North Carolina 27105 ("Targacept"), and **Aventis Pharma SA**, a corporation organized and existing under the laws of France having its principal place of business at 20, avenue Raymond Aron, 92160 Antony, France ("APSA") (each of Targacept and APSA a "Party" and collectively, the "Parties").

Recitals

Whereas, Targacept possesses proprietary technology and know-how related to the discovery, identification and/or synthesis of nicotinic agonists and has identified and applied for patents on certain nicotinic agonist compounds; and

Whereas, APSA is engaged in the research, development and marketing of products for the treatment of, among other things, central nervous system diseases and disorders; and

Whereas, Targacept and Aventis Pharmaceuticals Inc. (formerly known as Rhône-Poulenc Rorer Pharmaceuticals Inc. and Aventis Pharmaceutical Products Inc.), an Affiliate of APSA ("API"), are parties to a Collaborative Research and License Agreement dated December 30, 1998 (the "Original Agreement") under which they collaborate in the discovery, development and commercialization of certain nicotinic compounds for specified indications; and

Whereas, API desires to assign its rights and obligations under the Original Agreement to APSA with effect as of the date hereof, and Targacept is willing to consent to such assignment as contemplated by Section 14.2 of the Original Agreement; and

Whereas, Targacept and APSA have, as of the date hereof, entered into the Second Collaboration Agreement (as defined herein) under which they will collaborate in the discovery, development and commercialization of nicotinic compounds included in, or derived from, the Aventis Compound Library (as defined in the Second Collaboration Agreement) for specified indications; and

Whereas, in connection with the Second Collaboration Agreement, Targacept and APSA desire to amend and restate the Original Agreement in its entirety as provided herein.

Now, therefore, in consideration of the various promises and undertakings set forth herein, the Parties agree as follows:

ARTICLE 1

Definitions

Unless otherwise specifically provided herein, the following terms shall have the following meanings:

1.1 "Affiliate" means any Person that Controls, is Controlled by or is under common Control with a Party.

1.2 "Agreement" shall have the meaning assigned to such term in the preamble.

1.3 "APSA" shall have the meaning assigned to such term in the preamble.

1.3A "APSA Competitor" means a company (or affiliate thereof) that has total annual worldwide sales of pharmaceutical products exceeding $500 million, and that APSA regards in good faith as a competitor of APSA.

1.4 "APSA Indemnitees" shall have the meaning assigned to such term in Section 10.2.

1.5 "APSA Know-How" means all know-how, trade secrets, techniques, methods, developments, materials, compositions, inventions or data of any kind necessary or useful for the identification, pharmacological development, synthesis, characterization, optimization, assaying, formulation and/or use of Collaboration Compounds or Licensed Products that is Controlled by APSA or an Affiliate of APSA at any time during the Research Term or the Follow-Up Period (but excluding the APSA Patents, the Joint Patents, the Research Technology and any information that APSA is restricted from disclosing due to confidentiality obligations to a Third Party).

1.6 "APSA Patents" means all Patent Rights Controlled by APSA or an Affiliate of APSA that claim methods or materials used for discovering, identifying, assaying, characterizing or optimizing any Collaboration Compounds to the extent that such Patent Rights claim inventions made (x) prior to or during the Research Term or (y) during the Follow-Up Period.

1.6A "APSA Research Technology" means the Research Technology made, developed or discovered solely by employees or agents of APSA and/or its Affiliates, but excluding Targacept Technology.

1.7 "Back-Up Compound" means any Collaboration Compound that has been selected as such hereunder, or any salt, solvate, prodrug form, inclusion complex or metabolite thereof.

1.8 "Blocking Claim" shall have the meaning assigned to such term in Section 2.8(c).

1.9 "Blocking Patent" shall have the meaning assigned to such term in Section 2.8(c).

1.10 "Collaboration Compound" means any Targacept Compound, or any salt, solvate, prodrug form, inclusion complex or metabolite thereof.

For the avoidance of doubt, all Development Compounds and Back-Up Compounds shall be deemed to be Collaboration Compounds.

1.11 "Confidential Information" means (a) all information and data supplied by a Party under this Agreement, which, if disclosed in written, graphic or electronic form, is marked or otherwise designated as "confidential" or "proprietary" and, if disclosed orally, is summarized and designated as "confidential" or "proprietary" in a writing provided to the receiving Party not later than sixty (60) days after such disclosure; and (b) all other information expressly classified as **"Confidential Information"** hereunder.

1.12 "Control" means: (a) with respect to an item of information or an intellectual property right, possession of the ability, whether by ownership or license, to grant a license or sublicense as provided for herein with respect to such item or right without violating the terms of any agreement or other arrangements with any Third Party; and (b) with respect to a Person, (i) the possession, directly or indirectly, of the power to direct the management or policies of such Person, whether through the ownership of voting securities, by contract or otherwise, or (ii) the ownership, directly or indirectly, of more than 50% of the voting securities or other ownership interests of such Person.

1.12A "Derivative" means with respect to any compound, a derivative or other improvement of such compound.

1.13 "Development Committee" or **"DC"** means that committee to be formed pursuant to Section 6.15.

1.14 "Development Compound" means any Collaboration Compound that has been selected as such hereunder, or any salt, solvate, prodrug form, inclusion complex or metabolite thereof.

1.15 "Development Plan" shall have the meaning assigned to such term in Section 3.1.

1.16 "Effective Date" means December 30, 1998.

1.16A "Estimated Amount" shall have the meaning assigned to such term in Section 2.6(c).

1.17 [Intentionally Omitted]

1.18 [Intentionally Omitted]

1.19 "Executive Research Committee" or **"ERC"** means that committee to be formed pursuant to Section 6.1.

1.20 [Intentionally Omitted]

1.21 "FDA" means the United States Food and Drug Administration, or the successor federal agency thereto.

1.22 "Field" means the treatment or prevention in Humans of one or more Indications.

1.23 "First Commercial Sale" means, with respect to any Licensed Product in any country, the first sale for use or consumption by the general public of such Licensed Product in such country after all Regulatory Approvals have been obtained in such country.

1.23A "Follow-Up Period" means the period commencing immediately after the Research Term and ending: (a) with respect to activities conducted pursuant to Section 5.1(a)(i) after the Research Term, six (6) months after the Research Term; and (b) with respect to activities conducted pursuant to Section 5.1(a)(ii) after the Research Term, two (2) years after the Research Term. However, by written agreement the Parties may extend the Follow-Up Period with respect to specified joint endeavors in connection with this Agreement.

1.24 "FTE" means a full-time Targacept scientist or laboratory technician or any other employee of Targacept or its Affiliates specifically approved as an FTE by APSA, who is dedicated to the Research or support thereof, or in the case of a less than full-time dedicated person, a full-time, equivalent person year, based upon a total of forty-seven (47) weeks (*i.e.*, one thousand eight hundred eighty (1,880) hours) per year of scientific work on or directly related to the Research. Work on or directly related to the Research to be performed by such employees may include, without limitation, experimental laboratory work, recording and writing up results, reviewing literature and references, holding scientific discussions, and any other activities assigned to Targacept under the Research Plan.

1.24A "Full Royalty Term" shall have the meaning assigned to it in Section 7.3.

1.25 "IND" means an Investigational New Drug Application filed pursuant to the requirements of the FDA for approval to commence human clinical trials, and any equivalent application filed with any analogous regulatory authority in other countries or regulatory jurisdictions.

1.26 "Indication" means either of the following indications:

(a) Alzheimer's Disease (based upon ante mortem diagnostic evaluations in use as of the Effective Date); or

(b) Parkinson's Disease.

1.27 "Joint Patents" means all Patent Rights that claim or cover inventions within the Joint Research Technology.

1.28 "Joint Research Technology" means all Research Technology that is made, developed or discovered jointly by employees or agents of Targacept or its Affiliates and by employees or agents of APSA or its Affiliates, (a) prior to or during the Research Term or (b) during the Follow-Up Period, but excluding Targacept Technology.

1.29 "Key Employees" means J. Donald deBethizy; Merouane Bencherif; William S. Caldwell; and Patrick M. Lippiello.

1.30 "Know-How" means Targacept Know-How or APSA Know-How, as the case may be.

1.31 "Licensed Product" means any product, including any formulation thereof, containing or comprising a Development Compound.

1.32 "Losses" shall have the meaning assigned to such term in Section 10.1.

1.33 "Major Country" means each of France, Germany, Italy, Japan, Spain, the United Kingdom and the United States.

1.34 "Major Pharmaceutical Market" means each of the United States, the European Union (as it may be constituted from time to time) and Japan.

1.34A "Material Unexpected Technical Problem" shall have the meaning assigned to such term in Section 2.6(a).

1.35 "Materials" shall have the meaning assigned to such term in Section 2.9.

1.36 "Merger" shall have the meaning assigned to such term in Section 14.2.

1.37 "Milestone Event" shall have the meaning assigned to such term in Section 7.2.

1.38 "NDA" means a New Drug Application filed pursuant to the requirements of the FDA, as more fully defined in 21 C.F.R. § 314.50 *et seq*, and any equivalent application filed with any analogous regulatory authority in a Major Country (or, in the case of the centralized application process in the European Union, the European Medicines Evaluation Agency).

1.39 "Net Sales" means [********].

1.40 "Nicotinic Compound" means a chemical compound showing binding affinity for [********] receptors [********].

1.41 "Non-Filing Party" shall have the meaning assigned to it in Section 8.2(e).

1.41A "Non-Nicotinic Compound" means a compound having a binding affinity [********] to the [********] receptor [********].

1.41B "Other Metanicotine Compounds" means those compounds listed under the heading "Other Metanicotine Compounds" on Exhibit B.

1.41 [Intentionally Omitted]

1.41C "Partial Royalty Term" shall have the meaning assigned to it in Section 7.4

1.42 "Party" and **"Parties"** shall have the meaning assigned to such terms in the preamble.

1.43 "Patent Right" means rights under (a) any issued and existing letters patent, including any extensions, supplemental protection certificates, registration, confirmation, reissue, reexamination or renewal thereof, (b) pending applications, including any continuation, divisional, continuation-in-part application thereof, for any of the foregoing, and (c) all counterparts to any of the foregoing issued by or filed in any country or other jurisdiction.

1.43A "PCT" means the Patent Cooperation Treaty.

1.44 "Pentad Patents" means all Patent Rights Controlled by Targacept or an Affiliate of Targacept that claim the Pentad Technology.

1.45 "Pentad Technology" means proprietary know-how of Targacept and its Affiliates concerning structure activity, relationships of Nicotinic Compounds and nicotinic receptors, pharmacophore mapping of nicotinic receptors and computational and quantum mechanical methods for use in the design, synthesis and evaluation of pharmacologically active agents, including but not limited to Nicotinic Compounds.

1.46 "Person" means any natural person, corporation, firm, business trust, joint venture, association, organization, company, partnership or other business entity, or any government or agency or political subdivision thereof.

1.47 "Phase I" means that portion of the clinical development program which generally provides for the first introduction into humans of a product with the primary purpose of determining safety, metabolism and pharmacokinetic properties and clinical pharmacology of the product.

1.48 "Phase II" means that portion of the clinical development program which provides for small scale clinical trials primarily to determine efficacy of a product and certain other factors, such as dosing range.

1.49 "Phase III" means that portion of the clinical development program which provides for the pivotal trials of a product in sufficient numbers of patients to establish the safety and efficacy of a product for the desired label claims and indications.

1.50 "Phase Transition Criteria" shall have the meaning assigned to it in Exhibit A.

1.51 "Primary Screening" means conducting an assay, screen or other test on a Collaboration Compound under the Research to determine physical chemical profiles and *in vitro* pharmacological and toxicological profiles.

1.52 "Project Leaders" shall have the meaning ascribed to it in Section 6.14.

1.53 "Qualifying Offering" shall have the meaning ascribed to it in Section 13.1.

1.54 [Intentionally Omitted]

1.55 [Intentionally Omitted]

1.56 "Regulatory Approval" means any and all approvals (including price and reimbursement approvals), licenses, registrations, or authorizations of any federal, national, state, provincial or local regulatory agency, department, bureau or other government entity, necessary for the manufacture, use, storage, import, transport and sale of a Licensed Product in a country.

1.57 "Research" means the collaborative research program undertaken by the Parties pursuant to this Agreement to characterize, optimize and conduct research and development activities regarding Collaboration Compounds for use in the Field, in accordance with the Research and Development Plan.

1.58 "Research and Development Plan" shall have the meaning provided such term in Section 2.3.

1.59 "Research Technology" means all tangible and intangible know-how, trade secrets, inventions (whether or not patentable), discoveries, developments, data, clinical and preclinical results, information, and physical, chemical or biological material, compounds, and any replication of or any part of any of the foregoing, made by employees or agents of Targacept or its Affiliates or APSA or its Affiliates, either alone or jointly, (a) during the Research Term or (b) during the Follow-Up Period.

1.60 "Research Term" means the period during which the Parties shall conduct the Research, commencing on January 1, 1999 and terminating on December 31, 2002 or such later date as the Parties may mutually agree in writing.

1.61 "Screening Criteria" shall have the meaning assigned to such term in the Research and Development Plan.

1.61A "Second Collaboration Agreement" means the Collaborative Research and License Agreement between Targacept and APSA dated as of the date of this Agreement.

1.62 "Secondary Screening" means conducting any assay, screen or other test on a Collaboration Compound after the Primary Screening of such Collaboration Compound, for the purpose of confirming the results of the Primary Screening or determining additional physical chemical, pharmaceutical and process profiles and *in vivo* pharmacological and toxicological profiles.

1.62A "Semi-Annual Research Plan" shall have the meaning ascribed to it in Section 2.4.

1.63 "1734 Series" means those compounds listed under the heading "1734 Series" on Exhibit B.

1.64 "1767 Series" means those compounds listed under the heading "1767 Series" on Exhibit B.

1.65 "1768 Series" means those compounds listed under the heading "1768 Series" on Exhibit B.

1.65A "[********].

1.66 "Sublicensee" means any Third Party to which APSA has granted sublicense rights under the licenses granted APSA hereunder, which rights include at least the rights to make and sell Licensed Products. Third Parties that are permitted only to distribute and resell finished Licensed Products or that manufacture or finish Licensed Products for supply to APSA or its Affiliates are not "Sublicensees."

1.67 "Targacept" shall have the meaning assigned to such term in the preamble.

1.68 [Intentionally Omitted]

1.69 "Targacept Compounds" means (a) any compound from the 1734 Series, the 2429 Series, the 2563 Series, the 1767 Series or the 1768 Series, (b) any Other Metanicotine Compound, (c) as of the UK License Date, any UK Compound, and (d) any compound identified by Targacept or its Affiliates prior to the end of the Research Term and believed by Targacept to operate through the a4ß4 receptor, in each case together with any salt, solvate, prodrug form, inclusion complex, metabolite or Derivative thereof. No other compound, including without limitation RJR Compound No. 2403, shall be considered a Targacept Compound.

1.70 [Intentionally Omitted]

1.71 "Targacept Indemnitees" shall have the meaning assigned to such term in Section 10.1.

1.72 "Targacept Know-How" means all know-how, trade secrets, techniques, methods, developments, materials, compositions, inventions or data of any kind necessary or useful for the identification, pharmacological development, synthesis, characterization, optimization, assaying, formulation, manufacture and/or use of Collaboration Compounds or Licensed Products that is Controlled by Targacept or an Affiliate of Targacept at any time during the Research Term or the Follow-Up Period, but excluding the Pentad Technology, the Pentad Patents, the Targacept Patents, the Joint Patents, the Research Technology and any information that Targacept is restricted from disclosing due to confidentiality obligations to a Third Party.

1.73 "Targacept Patents" means all Patent Rights that are Controlled by Targacept or its Affiliates that claim (a) any Collaboration Compounds or Licensed Products (or pharmaceutical preparations containing the same), (b) the manufacture or use of any Collaboration Compounds or Licensed Products, (c) methods or materials used for discovering, identifying, assaying, characterizing or optimizing any Collaboration Compounds or (d) Targacept Compounds within the Research Technology, to the extent that such Patent Rights claim inventions made (x) prior to or during the Research Term or (y) during the Follow-Up Period.

1.73A "Targacept Research Technology" means both (i) the Research Technology made, developed or discovered solely by employees or agents of Targacept and/or its Affiliates and (ii) the Targacept Technology.

1.73B "Targacept Technology" means any Targacept Compounds (including, without limitation, Collaboration Compounds, Development Compounds, Back-Up Compounds, Terminated Compounds and Licensed Products) within the Research Technology made by employees

or agents of (i) APSA and/or its Affiliates, (ii) Targacept and/or its Affiliates or (iii) APSA and/or its Affiliates and Targacept and/or its Affiliates, jointly.

1.74 "Terminated Compound" means a Collaboration Compound that, pursuant to any provision of this Agreement, ceases to be a Collaboration Compound or a Licensed Product.

1.75 "Third Party" means a Person other than Targacept, APSA and Affiliates of either.

1.76 "Third Party License" shall have the meaning assigned to such term in Section 2.8(c).

1.76A "Threshold EU Market" means at any time any set of countries within the European Union which constituted during the prior calendar year at least 50% in dollar amount of all central nervous system related pharmaceutical sales in the European Union.

1.77 "2429 Series" means those compounds listed under the heading "2429 Series" on Exhibit B.

1.78 "2563 Series" means those compounds listed under the heading "2563 Series" on Exhibit B.

1.79 "UK Compounds" means those compounds listed under the heading "UK Compounds" on Exhibit B.

1.79A "UK License Date" shall have the meaning assigned to such term in Section 12.2(i).

1.79B "Valid Claim" means a claim of an issued and unexpired patent which has not been revoked or held unenforceable or invalid by a decision of a court or governmental agency of competent jurisdiction from which no appeal can be taken or, after mutual consultation and agreement between the Parties, an appeal is not taken within the time allowed for appeal, and which has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue or disclaimer or otherwise.

ARTICLE 2

Research

2.1 Collaborative Research. Commencing on the Effective Date, the Parties shall conduct the Research pursuant to the Research and Development Plan, with the goals of: (a) identifying and selecting those Collaboration Compounds that may be suitable for further scientific evaluation (immediately or at some future time during the Research Term) and those Collaboration Compounds that clearly do not warrant such further scientific evaluation and should instead be classified as Terminated Compounds; (b) further evaluating Collaboration Compounds; (c) identifying and selecting certain Collaboration Compounds for further development as Development Compounds; and (d) identifying and selecting certain Collaboration Compounds as Back-Up Compounds to the

Development Compounds. The Parties shall conduct the Research in accordance with this Agreement, the Research and Development Plan (as it may be amended hereunder from time to time), the Semi-Annual Research Plans established pursuant to the provisions of this Article 2 and the Phase Transition Criteria.

2.2 Screening of Collaboration Compounds and Selection of Development Compounds and Back-Up Compounds.

(a) *Primary and Secondary Screening of Collaboration Compounds.* Targacept and APSA shall conduct Primary Screening and Secondary Screening of Collaboration Compounds during the Research Term, as set forth in the Research and Development Plan and the Semi-Annual Research Plans, and shall inform the ERC of the progress and results thereof.

(b) *Rejection of Collaboration Compounds.* The ERC shall review the results of the Primary Screening and Secondary Screening of the Collaboration Compounds provided by the Parties pursuant to Section 2.2(a). Based upon the standards set forth in the Research and Development Plan and such other appropriate factors as the Parties mutually agree, the ERC shall determine whether any Collaboration Compounds clearly do not warrant further scientific evaluation and should instead be classified as Terminated Compounds. If a Collaboration Compound is classified as a Terminated Compound or is not selected as a Development Compound or Back-Up Compound within the time frames established hereunder, it shall automatically cease to be a Collaboration Compound and thereafter shall not be subject to research, development or commercialization by APSA or its Affiliates or Sublicensees pursuant to this Agreement.

(c) *Selection of Development Compounds and Back-Up Compounds; Rejection of Collaboration Compounds.*

(1) From time to time, the ERC shall review data relating to the Collaboration Compounds that is generated by the Research. Based upon standards set forth in the Research and Development Plan and such other appropriate factors as the ERC deems appropriate, the ERC (and after its term, the DC) shall identify and select the Development Compounds (and the Back-Up Compounds) for development (or potential development) in accordance with the Research and Development Plan. Up to **[********]** Collaboration Compounds may be classified at any time as Development Compounds and Back-Up Compounds for each Indication.

(2) If a Collaboration Compound (a) is classified as a Terminated Compound under Section 2.2(b), (b) is a UK Compound and does not undergo Primary Screening within six (6) months after the later of UK License Date or the date such compound is

available for screening, (c) is an Other Metanicotine Compound and does not undergo Primary Screening within nine (9) months after the date such compound is available for screening, (d) does not undergo Primary Screening prior to the expiration of the Research Term, (e) undergoes Primary Screening prior to the expiration of the Research Term but does not meet the Screening Criteria set forth in the Research and Development Plan or (f) is not selected as a Development Compound or a Back-up Compound under Section 2.2(c)(i) within six (6) months after the end of the Research Term, it shall automatically cease to be a Collaboration Compound and thereafter shall not be subject to research, development or commercialization by APSA or its Affiliates or Sublicensees pursuant to this Agreement.

2.3 Research and Development Plan. Attached hereto as Exhibit C is the initial version of the Research and Development Plan (as it may be modified from time to time, the "Research and Development Plan") that sets forth the plan for the Research activities expected to be performed by each Party pursuant to this Agreement. The Research and Development Plan may be amended by the ERC from time to time in accordance with the provisions of Article 6.

2.4 Semi-Annual Research Plans. On a semi-annual basis, the Parties shall establish a detailed research plan and budget, as may be modified from time to time (each a "Semi-Annual Research Plan") for the activities to be performed by APSA and Targacept as part of the Research during the following six (6) month period starting January 1 or July 1, as the case may be (or such longer period as may be set forth for certain tasks in the Semi-Annual Research Plan). Each Semi-Annual Research Plan may be amended by the ERC from time to time in accordance with the provisions of Article 6. Each Semi-Annual Research Plan shall be in accord with the Research and Development Plan and shall specify in reasonable detail:

(a) the objectives of the Research for the ensuing period(s);

(b) the specific research and other activities to be performed by APSA and Targacept during such period;

(c) the specific deliverables expected to be provided by APSA and Targacept, and the projected dates by which such deliverables will be provided;

(d) the FTEs to be devoted by Targacept to its tasks under the Semi-Annual Research Plan; and

(e) the total funding expected to be provided to Targacept for the ensuing six-month period to support Targacept's Research activities (which funding will be subject to adjustment as provided in Section 2.6).

2.5 Preparation and Approval of Semi-Annual Research Plans. Attached hereto as Exhibit D is the Semi-Annual Research Plan for the initial period of the Research Term. The ERC shall meet at the earliest reasonably practicable time to establish, by mutual agreement of the

Parties, the priority for performing the Primary Screening and Secondary Screening of the Collaboration Compounds and to amend the initial Semi-Annual Research Plan as required to reflect such agreement. It is intended that the Semi-Annual Research Plan for each subsequent period during the Research Term shall be approved by the ERC by May 1 and December 1 of each calendar year during the Research Term.

2.6 Targacept Research Efforts.

(a) Targacept agrees to commit such resources of Targacept and its Affiliates as are specified in the Semi-Annual Research Plans to perform its obligations set forth therein. Targacept agrees to commit such further resources as are reasonably necessary to perform its obligations set forth in each Semi-Annual Research Plan, ***provided, however***, that Targacept shall have the right to notify the ERC promptly upon becoming aware of an unanticipated scientific or technical problem which makes it likely to preclude Targacept from fulfilling any obligation set forth in a Semi-Annual Research Plan with the FTEs **[********]** budgeted to the performance of such obligation (a "Material Unexpected Technical Problem"). As part of such notification, Targacept shall provide the ERC with a reasonably detailed description of such Material Unexpected Technical Problem, together with its good faith estimate of the number of additional FTEs and time which will be required to perform such obligation in light of such Material Unexpected Technical Problem. Upon receipt of such notification, the ERC shall then meet to determine whether to modify the Semi-Annual Research Plan as it applies to such obligation to (i) refocus the remaining unused FTE resources allocated to such obligation to other obligations under the Plan, (ii) increase the funding to be provided by APSA to Targacept for such obligation, subject to the agreement of both Parties on the amount of such increased funding, (iii) terminate any further Targacept activities relating to such obligation, (iv) provide additional non-financial resources from APSA to support Targacept's activities, or (v) take such other action as may be mutually agreeable to the parties; ***provided, however,*** that, following notification of a Material Unexpected Technical Problem, Targacept shall not be required to perform activities related to an obligation after such notification unless and until the ERC acts to provide additional funding. In connection with the performance by Targacept of its obligations hereunder, Targacept shall maintain (or cause its Affiliates to maintain) and utilize such scientific staff, laboratories, offices and other facilities as are reasonably designed for such purposes. Targacept shall use personnel with such skills and experience as are reasonably designed to accomplish efficiently and expeditiously the objectives of the Research as set forth in the Research and Development Plan and each Semi-Annual Research Plan in good scientific manner and in compliance in all material respects with all applicable laws, rules, regulations, and all other requirements of applicable good laboratory practices; ***provided, however,*** that except as otherwise required by law, Targacept shall be required to comply only with general good laboratory practices as

practiced by like companies in the biotechnology industry in performing similar research and not with the requirements for Good Laboratory Practices prescribed by the FDA.

(b) APSA shall reimburse Targacept for all fully documented expenses incurred by Targacept in performing its obligations under the Semi-Annual Research Plans in accordance with the following procedures:

(c) Promptly following the commencement of the first calendar quarter covered by each Semi-Annual Research Plan, Targacept shall furnish APSA with an invoice in the amount of **[********]** of the product of (A) **[********]** (on an annualized basis) and (B) the total number of FTEs specified in such Semi-Annual Research Plan pursuant to Section 2.4(d). APSA shall advance Targacept such amount (the "Estimated Amount") within forty-five days after receipt of such invoice.

(1) No later than July 31 or February 28, as the case may be, immediately following the end of the six-month period covered by such Semi-Annual Research Plan, Targacept shall furnish APSA with a statement detailing the number of FTEs actually dedicated to the performance of each Research obligation set forth in such Semi-Annual Research Plan. However, for any obligation of Targacept set forth in such Semi-Annual Research Plan (as it may be amended from time to time pursuant to this Agreement), such statement (A) shall not state a number of FTEs less than **[********]** of the budgeted FTEs allocated to such obligation even if the number of FTEs actually dedicated to such performance was less than **[********]** of such budgeted amount; (B) shall not state a number of FTEs more than **[********]** of the budgeted FTEs allocated to such obligation even if the number of FTEs actually dedicated to such performance was more than **[********]** of such budgeted amount; and (C) absent authorization from the ERC, shall not include or request payment for any FTEs for any work performed on any obligation after the occurrence of a Material Unexpected Technical Problem related to such obligation.

(2) Within forty-five (45) days after the receipt of such statement from Targacept, APSA shall pay Targacept an amount equal to the difference between (A) the product of (I) **[********]** (on an annualized basis) and (II) the total number of FTEs properly set forth in such statement, and (B) the Estimated Amount for such Semi-Annual Research Plan paid to Targacept pursuant to subparagraph (i) above.

(3) Targacept shall keep complete and accurate books and financial records pertaining to its costs and expenses of performing the Research (in accordance with generally accepted accounting principles consistently applied), which books and financial

records shall be retained by Targacept until three (3) years after the end of the period to which such books and records pertain. APSA shall have the right, at its expense, to have certified public accountants, who shall be reasonably acceptable to Targacept, audit the books and financial records of Targacept relating to its costs and expenses during one or more six-month periods; ***provided, however,*** that APSA shall not have the right to audit a six-month period more than two (2) years after the end of such period, to conduct more than one such audit in any twelve-month period, or to audit any six-month period more than once.

2.7 APSA Research Efforts.

(a) APSA agrees to commit such resources as are specified in the Semi-Annual Research Plans to perform its obligations set forth in each Semi-Annual Research Plan. APSA agrees to commit such further resources as are reasonably necessary to perform its obligations set forth in each Semi-Annual Research Plan, provided that APSA shall have the right to notify the ERC promptly upon becoming aware of an unanticipated scientific or technical problem that would be likely to preclude APSA from completing an obligation set forth in a Semi-Annual Research Plan for a manpower expenditure **[********]** and shall be permitted to discontinue work on such obligation if the ERC does not modify the Semi-Annual Research Plan with respect to such obligation in a manner reasonably acceptable to APSA. In the performance of its obligations, APSA shall maintain and utilize such scientific staff, laboratories, offices and other facilities as are reasonably designed for such purposes. APSA shall use personnel with such skills and experience as are reasonably designed to accomplish efficiently and expeditiously the objectives of the Research as set forth in the Research and Development Plan and each Semi-Annual Research Plan in good scientific manner and in compliance in all material respects with all applicable laws, rules, regulations, and all other requirements of applicable good laboratory practices; ***provided, however,*** that except as otherwise required by law, APSA shall be required to comply only with general good laboratory practices as practiced by like companies in the pharmaceutical industry in performing similar research and not with the requirements for Good Laboratory Practices prescribed by the FDA.

(b) APSA shall be solely responsible for bearing the costs of any and all activities performed by APSA in connection with the Research.

2.8 Termination of Agreement During Research Term.

(a) *Termination for Material Breach of Research Obligations by Targacept or for Specified Change in Control.* In the event that Targacept materially fails to perform its obligations with respect to the Research,

APSA may give notice to Targacept specifying the nature of the default, requiring it to cure such default and stating APSA's intention to terminate Targacept's participation in the Research if such default is not cured within the period set forth below. If (i) such default is not cured within sixty (60) days after the receipt of such notice; or (ii) such default is not curable within such period and Targacept has not commenced reasonable actions to cure such default or does not diligently continue to perform such actions; APSA may elect (x) to terminate all, but not less than all, of those provisions of this Agreement that create any continuing right or obligation of Targacept to perform the Research or any obligation of APSA to fund any such activity by Targacept in the future and to disband the ERC and the DC and (y) to assume all rights and powers of the ERC and the DC, without prejudice to any other rights and obligations of the Parties under this Agreement, which election shall be effected by giving written notice to Targacept and shall be effective immediately upon delivery of such notice. In addition, if any APSA Competitor becomes an Affiliate of Targacept, APSA shall have the right to make the election described in the immediately preceding sentence. Upon the election of APSA described in either of the two preceding sentences, Targacept shall promptly transfer to APSA copies of all data, reports, records and other materials under Targacept's Control that relate to the Research and furnish to APSA all Materials developed or Controlled by Targacept that are used or useful in connection with the Research.

(b) *Termination for Material Breach of Research Obligations by APSA.* In the event that APSA materially fails to perform its obligations with respect to the Research, Targacept shall have the right to terminate this Agreement in accordance with Section 11.2(a) hereof.

(c) *Termination Due to Issuance of Third Party Patent Rights.* In the event that, prior to the end of the Research Term, (i) a Patent Right owned by a Third Party is either granted or published in a Major Pharmaceutical Market; (ii) such Patent Right (a "Blocking Patent") claims (A) methods of treating one of the Indications using Nicotinic Compounds, or (B) the composition of matter of a significant portion of the Collaboration Compounds identified by Targacept as of the Effective Date (each, a "Blocking Claim"); and (iii) in the opinion of patent counsel selected by APSA, (A) with respect to a published Blocking Patent, it is likely that enforceable letters patent will issue with at least one of such Blocking Claims covering the United States, Japan or a Threshold EU Market and (B) it is unlikely that the Parties will be able to avoid infringing such claims, then:

(x) if the Blocking Patent is held by **[********]**, then Targacept shall have the right, for a period of six (6) months, to use commercially reasonable, good faith efforts to negotiate and obtain a license under such Blocking Patent on commercially reasonable terms (for royalties not exceeding **[********]**% of

Net Sales or such higher amount agreed to by the Parties) that permits APSA, Targacept and their respective Affiliates (and, in the case of APSA, its Sublicensees) to continue to pursue the discovery, development, manufacture and commercialization of Licensed Products for use in the Field as provided hereunder (a "Third Party License") and thereafter APSA shall have the right to use commercially reasonable, good faith efforts to negotiate and obtain such Third Party License on commercially reasonable terms, in either case with the cost of such license (including without limitation license fees, milestone payments and royalties) to be set off against any payments owed to Targacept by APSA pursuant to Section 7.2 or Section 7.3; ***provided, however,*** that in no event shall the aggregate amount set off in any calendar quarter against royalties payable pursuant to Section 7.3 in such calendar quarter exceed **[********]** thereof;

(y) if the Blocking Patent is held by any Third Party other than **[********]**, APSA shall use commercially reasonable, good faith efforts to negotiate and obtain a Third Party License on commercially reasonable terms, except where APSA in good faith believes that such negotiation would be futile because such Third Party is an APSA Competitor, with the cost of such license (including without limitation license fees, milestone payments and royalties) to be borne equally by APSA and Targacept, with Targacept's share of such costs to be set off against any payments owed to Targacept by APSA pursuant to Section 7.2 or Section 7.3; ***provided, however,*** that in no event shall the aggregate amount set off in any calendar quarter against royalties payable under Section 7.3 in such calendar quarter exceed **[********]** thereof;

(z) If the Parties do not obtain a Third Party License from **[********]** or if APSA is unable, after commercially reasonable, good faith efforts, to obtain a Third Party License from any other Third Party holding a Blocking Patent or if APSA does not seek such a Third Party License because APSA in good faith believes that such negotiation would be futile because such Third Party is an APSA Competitor, then APSA shall have the right to terminate this Agreement pursuant to Section 11.3.

2.9 Material Transfer. In order to facilitate the Research, either Party may provide to the other Party certain biological materials or chemical compounds including, but not limited to Collaboration Compounds, receptors, reagents and screens (collectively, "Materials") owned by or licensed to the supplying Party (other than under this Agreement) for use by the other Party in furtherance of the Research, subject to a separate global Material Transfer Agreement if desired by the supplying Party, in a form to be mutually agreed by the Parties. Except as otherwise provided under this Agreement, all such Materials delivered to the other Party shall remain the sole property of the

supplying Party, shall be used only in furtherance of the Research and solely under the control of the other Party, shall not be used or delivered to or for the benefit of any Third Party (or in the case of APSA, any Sublicensee) without the prior written consent of the supplying Party, and shall not be used in research or testing involving human subjects. The Materials supplied under this Section 2.9 shall be used with prudence and appropriate caution in any experimental work, since not all of their characteristics may be known. SUBJECT TO SECTIONS 12.1 AND 12.2 HEREOF, THE MATERIALS ARE PROVIDED "AS IS" AND WITHOUT ANY REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION ANY IMPLIED WARRANTY OF MERCHANTABILITY OR OF FITNESS FOR ANY PARTICULAR PURPOSE OR ANY WARRANTY THAT THE USE OF THE MATERIALS WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY.

2.10 Liability. Except as otherwise set forth in Section 10.1, in connection with the conduct of the Research, each Party shall be responsible for, and hereby assumes, any and all risks of personal injury or property damage attributable to the negligent acts or omissions of that Party or its Affiliates, and their respective directors, officers, employees and agents.

2.11 Exclusivity of Research. During the Research Term, each Party agrees not to, and agrees to cause its Affiliates not to, (a) conduct any activity, either on its own, or for the benefit of, sponsored by, or pursuant to any type of corporate partnership with, any Third Party, that has as its goal or intent discovering, identifying, researching, developing or marketing Nicotinic Compounds (including without limitation any Collaboration Compounds) for use in the Field, except pursuant to this Agreement or the Second Collaboration Agreement, or (b) grant any license, either express or implied, or any option to license, to any Third Party to utilize any intellectual property Controlled by such Party or its Affiliates for the purpose of discovering, identifying, researching, developing or marketing Nicotinic Compounds for use in the Field, except to the extent expressly permitted by this Agreement or the Second Collaboration Agreement***; provided, however,*** that a Party may terminate the foregoing covenant as it applies to such Party, as one of its remedies and not to the exclusion of any other remedy such Party may have, if the other Party materially violates its obligations under the foregoing covenant.

2.12 Subcontractors. Either Party may subcontract to Affiliates or Third Parties portions of the Research to be performed by it, subject to the provisions of this Section 2.12. Any subcontractor shall enter into a confidentiality agreement with the contracting party, and shall be in compliance in all material respects with all requirements of applicable laws and regulations, together with all applicable good laboratory practices and good manufacturing practices. The contracting Party shall at all times be responsible for the performance of such subcontractor. Upon the reasonable request of the other Party, a Party shall provide a written list of all subcontractors other than Affiliates with whom such Party has subcontracted under this Section 2.12.

2.13 No Warranty of Success. Nothing contained in this Agreement shall be construed as a warranty on the part of either Party that any results will be achieved by such Party, or that any particular Patent Rights or Know-How developed during the Research will be commercially exploitable.

2.14 No Solicitation of Employees. During the Research Term and for a period of two (2) years thereafter, each Party agrees not to, and agrees to cause its Affiliates not to, without the consent of the other Party, solicit the employment of any person who during the course of employment with such other Party or any of such other Party's Affiliates was involved with activities related to or

conducted in furtherance of the Research. For purposes of this Section 2.14, "solicit" shall not be deemed to cover general solicitations of employment not specifically targeted at employees of the other party or any of its Affiliates. This provision shall not preclude either Party from soliciting the employment of any person whose employment with the other Party has terminated or any person who has announced his or her impending resignation or retirement from the other Party.

ARTICLE 3

Development and Commercialization

3.1 Development Plans. Within sixty (60) days after a Development Compound is selected for development in accordance with Section 2.2(c), APSA shall prepare a reasonably detailed plan for the initial development of such Development Compound in each Major Pharmaceutical Market for review and approval by the DC (each, a "Development Plan"). On a semi-annual basis, APSA shall apprise the DC of progress under each Development Plan and shall submit revisions to existing Development Plans to the DC for review and approval by the DC.

3.2 Development Responsibilities of APSA; Diligence. APSA shall be solely responsible for and shall have the sole right to develop the Development Compounds through preclinical development and all phases of clinical trials, and to make all applications for and obtain all Regulatory Approvals on a worldwide basis. For each Development Compound, APSA shall use commercially reasonable efforts, which efforts shall not be less than those used by APSA with respect to the development of its own compounds of comparable commercial significance, to develop such compound for the relevant Indication in each Major Pharmaceutical Market, subject to Section 3.3. For the purpose of assessing the commercial reasonableness of such efforts, the effect on other competitive products of APSA and its Affiliates of diverting resources to the development of the Development Compound shall not be considered. APSA shall be solely responsible for bearing all costs and expenses in connection with the development of each Development Compound.

3.3 Termination of Development of a Development Compound. APSA may terminate the development of any Development Compound at any time upon prior notice to the DC and may at that time designate such compound as a Back-Up Compound. If APSA terminates the development of any Development Compound and does not designate such compound as a Back-Up Compound, or if APSA does not act in accordance with the diligence obligations set forth in Section 3.2 with respect to a Development Compound, such compound shall be deemed to be a Terminated Compound. So long as APSA (or its Affiliates or Sublicensees) continues to act in accordance with the diligence obligations set forth in Section 3.2 to pursue the preclinical and clinical development of at least one Development Compound for use in an Indication (or so long as APSA has produced a Licensed Product for such Indication) APSA's cessation of development efforts with respect to one or more other Development Compounds or Back-Up Compounds in such Indication shall not be deemed to be a breach of APSA's diligence obligations hereunder with respect to such Indication. Further, if after the end of the Research Term, APSA has conducted development with respect to one or more Development Compounds in an Indication in accordance with the diligence obligations set forth in Section 3.2 and there is no reasonable additional preclinical or clinical work or investigation to pursue on any Development Compounds or Back-Up Compounds for such Indication, or alternatively APSA determines that it no longer desires to continue working on the Development Compounds in such Indication, then APSA may cease further work on the Development Compounds and Back-Up

Compounds in such Indication, without there being a breach of such diligence obligations, so long as APSA has produced a Licensed Product for such Indication or so long as APSA terminates the Agreement with respect to such Indication pursuant to Section 11.3 within sixty (60) days of ceasing such work.

3.4 Termination of Development of all Development Compounds. If after the Research Term APSA and its Affiliates or Sublicensees fail to use commercially reasonable efforts to pursue the preclinical and clinical development of at least one Development Compound for use in an Indication in the Major Pharmaceutical Markets and have not produced a Licensed Product for such Indication, and do not initiate and continue using such efforts within sixty (60) days after written notice from Targacept specifying such failure and the nature of such failure, then Targacept may terminate this Agreement under Section 11.2 as it applies to such Indication.

3.5 Breach of Development Diligence Obligations. If at any time Targacept determines that APSA is not meeting the standards set forth in Section 3.2, before taking any action with respect to such determination Targacept shall provide APSA with written notice specifying the basis for such determination and any underlying facts in support thereof, and APSA shall have the same cure rights (whether such failure applies to one or more Development Compounds or one or both Indications) that it would have for a default under Section 11.2(a).

3.6 Development Information and Reporting. From and after the commencement of the first Phase I trial covering a Development Compound, APSA shall prepare and maintain complete and accurate information regarding the worldwide clinical development of Development Compounds and shall make such information available to the DC in the form of reasonably detailed reports provided to the DC at least on a semi-annual basis. Such reports shall reasonably and accurately summarize the status and results of such development efforts. APSA also shall respond to reasonable requests by the DC for additional information regarding the development of Development Compounds. The DC shall provide comments to APSA regarding such development efforts, and APSA shall reasonably consider such comments.

3.7 [Intentionally Omitted]

3.8 Commercialization Responsibilities of APSA; Diligence. APSA shall be solely responsible for and shall have the sole right to commercialize each Licensed Product for each Indication. With respect to each Licensed Product, after receipt of Regulatory Approval APSA shall use commercially reasonable efforts, which efforts shall not be less than those used by APSA with respect to the commercialization of its own products of comparable commercial significance, to commercialize such Licensed Product for the relevant Indication in each Major Pharmaceutical Market. For the purpose of assessing the commercial reasonableness of such efforts, the effect on other competitive products of APSA and its Affiliates of diverting resources to the commercialization of the Licensed Product shall not be considered. APSA shall be solely responsible for bearing all costs and expenses in connection with such commercialization efforts.

3.9 Termination of Commercialization of a Licensed Product. APSA may terminate the commercialization of any Licensed Product at any time upon prior notice to the DC. If APSA terminates the commercialization of any Licensed Product containing a certain Collaboration Compound without undertaking the commercialization of another Licensed Product containing that same Collaboration Compound, then such Collaboration Compound shall be deemed to be a Terminated Compound.

3.10 Termination of Commercialization of all Licensed Products. If APSA and its Affiliates or Sublicensees fail to act in accordance with the diligence obligations imposed by Section 3.8 in commercializing a particular Licensed Product for an Indication in any of the Major Pharmaceutical Markets, then Targacept shall be entitled to terminate the license granted to APSA pursuant to Section 5.1(b) regarding such Licensed Product for such Indication in such Major Pharmaceutical Market. In the event that APSA is not acting in accordance with the diligence obligations imposed by Section 3.8 to commercialize at least one Licensed Product in a Major Pharmaceutical Market for a particular Indication, then Targacept shall be entitled to terminate the license granted to APSA pursuant to Section 5.1(b) with respect to such Indication in such Major Pharmaceutical Market. In the event that, with respect to an Indication, such license is terminated with respect to all Major Pharmaceutical Markets, then such Indication shall no longer be deemed to be part of the Field.

3.11 Breach of Commercialization Diligence Obligations. If at any time Targacept determines that APSA is not meeting the standards set forth in Section 3.8, before taking any action with respect to such determination Targacept shall provide APSA with written notice specifying the basis for such determination and any underlying facts in support thereof and APSA shall have the same cure rights (whether such failure applies to one or more Licensed Products or one or both Indications) that it would have for a default under Section 11.2(a).

3.12 Commercialization Information and Reporting. From and after the First Commercial Sale of a Licensed Product, APSA shall provide to Targacept on a semi-annual basis reasonably detailed reports regarding the worldwide commercialization of such Licensed Product. APSA also shall respond to reasonable requests by Targacept for additional information regarding the commercialization of Licensed Products.

ARTICLE 4

Information Exchange

4.1 Disclosure of Enabling Technology; Maintenance of Records Regarding Research and Inventions.

(a) During the Research Term, each Party shall disclose to the other the Know-How and Patent Rights of such Party for which letters patent have not yet been issued as the other Party reasonably needs to perform its obligations and assigned tasks under the Research and Development Plan; ***provided, however***, that in no event shall Targacept be required to disclose the Pentad Technology and ***provided, further,*** that all such disclosed Know-How and Patent Rights shall be considered Confidential Information.

(b) All work conducted by each Party in the course of the Research shall be thoroughly and accurately recorded, in detail and in good scientific manner and, to the extent reasonably practicable, in separate laboratory notebooks distinct from other work being conducted by such Party. On reasonable notice, and at reasonable intervals, each Party shall have the

right to inspect and copy all such records maintained by the other Party reflecting Research Technology or work done under the Research and Development Plan, to the extent reasonably required to carry out its obligations and to exercise its rights hereunder. Notwithstanding Section 1.11, all such records shall constitute Confidential Information and shall be deemed the property of the Party creating such records.

(c) In order to protect the Parties' patent rights under U.S. law in any inventions conceived or reduced to practice during or as a result of the Research, each Party agrees to establish and support a policy which requires its employees to record and maintain all data and information developed in performing the Research in such a manner as to enable the parties to use such records to establish the earliest date of invention and/or diligence to reduction to practice. At a minimum, the policy shall require such individuals to record all inventions generated by them in standard laboratory notebooks which are dated and corroborated by non-inventors on a regular, contemporaneous basis.

4.2 Information and Reports. Each Party shall disclose to the other Party from time to time during the Research Term any Know-How or Research Technology learned, acquired, discovered, invented or made by such Party, to the extent reasonably required by the other Party to carry out its obligations and to exercise its rights hereunder; *provided, however*, that in no event shall Targacept be required to disclose the Pentad Technology. Such Know-How and Research Technology will be promptly disclosed to the other Party, with meaningful discoveries or advances being communicated as promptly as practicable after such information is obtained or its significance is appreciated. Each Party will provide the other with copies of the raw data generated in the course of the Research, if reasonably necessary to the other Party's work under the Research.

ARTICLE 5

Licenses

5.1 Licenses to APSA.

(a) *Research License.* Subject to the other provisions of this Agreement, Targacept hereby grants to APSA and its Affiliates (i) during the Research Term (and for an additional six (6) months for those Collaboration Compounds that undergo Primary Screening prior to the end of the Research Term and meet the Screening Criteria set forth in the Research and Development Plan) an exclusive (except with regard to Targacept) world-wide, paid-up right and license under the Targacept Patents, the Targacept Know-How and Targacept Research Technology and under Targacept's rights in the Joint Patents and Joint Research Technology solely to conduct the Research and to characterize, optimize and develop and, in connection with the Research, make and use Collaboration Compounds for use in the Field; and (ii) effective as of the end of the Research Term and for a period of two (2) years thereafter, a non-exclusive, world-wide, paid-up right and license under

the Targacept Patents and Targacept Know-How to make Derivatives of Development Compounds and Back-Up Compounds, and to use such Derivatives solely to conduct research in order to determine whether to designate such Derivatives as Development Compounds or Back-Up Compounds.

(b) *Commercialization License.* Subject to the other provisions of this Agreement (including Section 5.1(a) hereof), Targacept hereby grants to APSA and its Affiliates an exclusive (including with regard to Targacept), world-wide, royalty-bearing right and license under the Targacept Patents, the Targacept Know-How and Targacept Research Technology, and under Targacept's rights in the Joint Research Technology and Joint Patents, to research and develop, and to make, have made and use Back-Up Compounds and Development Compounds for use in the Field and to make, have made, import, use, sell and offer for sale Licensed Products for use in the Field. For the avoidance of doubt, it is understood that APSA's and its Affiliates' right to sell Licensed Products shall include the right to sell such Licensed Products under the foregoing license through distributors.

5.2 License to Targacept. Subject to the other provisions of this Agreement:

(a) APSA hereby grants to Targacept and its Affiliates an exclusive (except with regard to APSA), world-wide, paid-up right and license under the APSA Patents, the APSA Know-How and APSA Research Technology and under APSA's rights in the Joint Patents and Joint Research Technology, to conduct the Research;

(b) APSA hereby grants to Targacept and its Affiliates the right to use, but not the right to disclose to Third Parties (except as provided in the immediately following sentence), free of charge, all regulatory and clinical documentation and data disclosed to Targacept under this Agreement, as reasonably necessary in connection with the development and commercialization of pharmaceutical products outside the Field. Further, upon Targacept's request, APSA shall grant to Targacept and its Affiliates the right to reference all such regulatory and clinical documentation and data as reasonably necessary in connection with the development and commercialization of pharmaceutical products outside the Field except for use in regulatory submissions for pharmaceutical products that would compete with a product commercialized or under clinical development by APSA or any Affiliate for use in the same indication.

(c) APSA hereby grants to Targacept and its Affiliates an exclusive (including with regard to APSA), world-wide, paid-up right and license under the APSA Patents, the APSA Research Technology and the APSA Know-How and APSA's rights in the Joint Patents and Joint Research Technology, covering the composition of matter or the use of the Terminated Compounds, solely to research, develop, make, have

made, import, use, sell and offer for sale the Terminated Compounds outside the Field, and APSA agrees to negotiate in good faith with Targacept and its Affiliates other royalty-bearing licenses under the APSA Patents, APSA Research Technology and the APSA Know-How and under APSA's rights in the Joint Patents and Joint Research Technology that may be useful to Targacept and its Affiliates in conducting research and development and commercializing the Terminated Compounds for use outside the Field. For the avoidance of doubt, it is understood that Targacept's and its Affiliates' right to sell Terminated Compounds shall include the right to sell such Terminated Compounds under the foregoing license through distributors.

5.3 Right to Sublicense. Each Party shall have the right to grant to Third Parties sublicenses under the licenses granted hereunder (except pursuant to Section 5.1(a) and Section 5.2(a)). Notwithstanding the foregoing, the grant of any such sublicenses shall not relieve the sublicensing Party of any of its obligations under this Agreement.

5.4 Negative Covenants and License Limitations.

(a) *Mutual Covenants.* Each Party covenants to the other Party that:

(i) It shall not practice, exercise or use any intellectual property rights licensed to it by the other Party under this Agreement, except as permitted expressly by the terms hereof; ***provided, however***, that this Section 5.4(a)(i) shall preclude a Party from practicing, exercising or using any intellectual property rights of the other Party only to the extent such practice, exercise or use would violate the intellectual property rights of the other Party.

(ii) APSA, Targacept and their respective Affiliates shall not during or after the term of this Agreement, research, develop, commercialize or license any Third Party to research, develop or commercialize, for use in or outside of the Field, any Collaboration Compound that the APSA designees to the ERC recommended for selection as a Development Compound or Back-Up Compound but that could not be so selected due to objection of the Targacept designees to the ERC.

(b) *Additional Negative Covenants of Targacept.* Targacept further covenants to APSA that:

(i) During the Research Term **[********]**, Targacept and its Affiliates shall not research, develop, commercialize, or license any Third Party to research, develop or commercialize, any Collaboration Compound other than a Terminated Compound for use outside the Field.

(ii) Targacept and its Affiliates shall not research, develop, commercialize, or license any Third Party to research, develop

or commercialize, any Development Compound, Back-Up Compound or Licensed Product except pursuant to this Agreement.

(iii) During the term of this Agreement, Targacept and its Affiliates shall not, other than pursuant to this Agreement or the Second Collaboration Agreement, (A) conduct any activity, either on their own, or with, for the benefit of, or sponsored by any Third Party, that has as its goal or intent discovering, identifying, researching, developing or commercializing Nicotinic Compounds for use in the Field, or (B) grant any license or other rights to any Third Party to utilize any intellectual property Controlled by Targacept or its Affiliates, including without limitation, any Collaboration Compounds (or Derivatives thereof), Targacept Patents, Joint Patents, Pentad Patents, Targacept Research Technology, Joint Research Technology, Pentad Technology and Targacept Know-How , for the express purpose of discovering, identifying, researching, developing or commercializing Nicotinic Compounds for use in the Field. During the term of this Agreement, in conducting any activity with, for the benefit of, or sponsored by any Third Party with respect to Nicotinic Compounds, Targacept and its Affiliates shall require the Third Party to agree in writing that (x) it will not make use of any intellectual property Controlled by Targacept or its Affiliates, including without limitation, any Collaboration Compounds (or Derivatives thereof), Targacept Patents, Joint Patents, Pentad Patents, Targacept Research Technology, Joint Research Technology, Pentad Technology and Targacept Know-How, with respect to any activity that has as its goal or intent discovering, identifying, researching, developing, marketing, commercializing or selling Nicotinic Compounds for use in the Field; and (y) APSA and its Affiliates shall be third party beneficiaries of such agreement.

(c) *Additional Negative Covenants of APSA.* APSA further covenants to Targacept that:

(i) During the term of this Agreement, APSA and its Affiliates shall not conduct any clinical development work, or license any Third Party to conduct any clinical development work, on any Nicotinic Compound (including without limitation any Collaboration Compound or Derivative thereof) for use in the Field unless and until such Nicotinic Compound has been selected as a Development Compound or a Back-Up Compound under this Agreement or as an “Alliance Development Compound” or “Alliance Back-Up Compound” (both as defined in the Second Collaboration Agreement) under the Second Collaboration Agreement, as applicable.

(ii) During the term of this Agreement, APSA and its Affiliates shall not commercialize, or sub-license any Third Party to commercialize, any Nicotinic Compound (including without limitation any Development Compound, Back-Up Compound or Derivative thereof) for use in the Field unless and until such Nicotinic Compound has been selected as a Licensed Product under this Agreement or as an "Alliance Product" (as defined in the Second Collaboration Agreement) under the Second Collaboration Agreement, as applicable.

(iii) During the term of this Agreement, APSA and its Affiliates shall not, other than pursuant to this Agreement, (A) conduct any activity, either on their own, or with, for the benefit of, or sponsored by any Third Party, that has as its goal or intent discovering, identifying, researching, developing or commercializing any Collaboration Compounds; or (B) grant any license or other rights to any Third Party to utilize any intellectual property Controlled by APSA or its Affiliates (including without limitation any APSA Patents, APSA Know-How, Joint Patents or Joint Research Technology) for the express purpose of discovering, identifying, researching, developing or commercializing any Collaboration Compounds for use in or outside of the Field.

(iv) APSA and its Affiliates will not during or after the term of this Agreement, research, develop, commercialize or license any Third Party to research, develop or commercialize, any Terminated Compound for use in or outside of the Field.

5.5 Understanding Regarding Exclusivity and Negative Covenants. The parties agree that, given the high costs and significant risks involved in discovering and developing pharmaceutical products, and given that the parties will be exchanging Confidential Information in order to perform the Research and to conduct the development and commercialization efforts, the exclusive relationship between them regarding the Research, development, commercialization and the Field, which is reflected herein, is a fair and efficient means to reach a satisfactory conclusion from their cooperative efforts.

ARTICLE 6

Management of Research, Development and Commercialization

6.1 Creation and Structure of the ERC. As of the Effective Date, the Parties shall create an Executive Research Committee of **[********]** to facilitate the Research and to manage and monitor the activities conducted by the Parties pursuant to the Research and Development Plan. The ERC shall consist of an equal number of representatives appointed by each Party, who shall include senior decision-makers of such Party.

6.2 Responsibilities of the ERC. The ERC shall be the primary vehicle for interaction between the Parties with respect to the Research. Without limiting the foregoing, the ERC shall: (a) formulate and review Research objectives; (b) manage and monitor progress in implementing the Research and Development Plan; (c) prepare and approve changes to the Research and Development Plan; (d) prepare and approve Semi-Annual Research Plans and modifications thereof; (e) approve the designation of Collaboration Compounds as Terminated Compounds, Development Compounds and Back-Up Compounds; and (f) maintain a current and complete list of Terminated Compounds.

6.3 Composition of the ERC. Within fifteen (15) days after the Effective Date, the Parties shall notify each other in writing of the names of their initial representatives on the ERC. Each Party may replace its ERC representatives at any time upon written notice to the other. A Party's representative on the ERC shall be authorized to act on behalf of such Party until written notice of the removal of such representative is received by the other Party. A Party's representative on the ERC may resign at any time upon written notice to the Parties. Such resignation shall take effect at the time specified therein, and unless otherwise specified therein, no acceptance of such resignation shall be necessary to make it effective. Upon the resignation of a Party's representative, that Party shall appoint a replacement representative. A chairperson for the ERC shall be selected from among the members of the ERC, who shall serve for a term of one year. The right to select the chairperson shall rotate between APSA and Targacept. Targacept shall select the first chairperson.

6.4 Duration of the ERC. The ERC shall exist until the termination of the Research Term.

6.5 Meetings of the ERC. During its existence, the ERC shall meet in person on scheduled dates three (3) times per year and upon thirty (30) days advance written notice from either Party to the other Party. Meetings shall alternate between the offices of Targacept and APSA. A quorum of the ERC shall exist whenever there is present at a meeting members appointed by each Party. An ERC member of the Party hosting the meeting shall serve as Secretary of that meeting. The Secretary of the meeting shall prepare and distribute to all members of the ERC minutes of the meeting sufficiently in advance of the next meeting to allow adequate review and comment prior to the meeting. Such minutes shall provide a description in reasonable detail of the discussions had at the meeting and a list of any actions, decisions or determinations approved by the ERC. Minutes of any meeting shall be approved or disapproved, and revised as necessary, at the next meeting. Final minutes of each meeting shall be distributed to the members of the ERC by the Chairperson. Each Party shall disclose to the other proposed agenda items in advance of each meeting of the ERC. The ERC may also convene, or be polled or consulted, from time to time by means of telecommunications, video conferencing or written correspondence, as deemed necessary or appropriate. Members of the ERC may be represented at any meeting by a designee appointed by such member for such meeting. The ERC may invite other representatives of the parties with special skills to attend meetings where appropriate. The ERC shall adopt such other rules as shall be necessary or convenient for its work.

6.6 Decisions of the ERC. All decisions of the ERC shall be made by the unanimous vote of all ERC members participating in the meeting. In the event that the members of the ERC cannot agree with respect to a particular issue, such issue shall be referred to the President of Targacept and the Senior Vice President, Research of APSA, who shall meet within thirty (30) days in a good faith effort to resolve the dispute. In the event such officers cannot agree on a resolution of the dispute within thirty (30) days: **[********]**; (f) if the dispute relates to APSA's request to select a Collaboration Compound (other than a Collaboration Compound that has already been designated as a

Back-Up Compound) as a Development Compound or Back-Up Compound and Targacept's opposition to such request, the Collaboration Compound in question shall be subject to Section 5.4(a)(ii); **[********]**.

6.7 [Intentionally Omitted]

6.8 [Intentionally Omitted]

6.9 [Intentionally Omitted]

6.10 [Intentionally Omitted]

6.11 [Intentionally Omitted]

6.12 [Intentionally Omitted]

6.13 Subcommittees and Working Groups of the ERC. From time to time, the ERC may establish one or more subcommittees or working groups to oversee particular projects or activities, and such subcommittees or working groups will be constituted as the ERC agrees.

6.14 Project Leaders. APSA and Targacept shall each appoint one or more persons to coordinate their respective activities under the Research ("Project Leaders"). In advance of each meeting of the ERC, the Project Leaders shall prepare and distribute to each member of the ERC a written report which shall (a) evaluate the work performed under the Research in relation to the goals of such program, and (b) state any recommendation of the Project Leaders to modify, alter the resources of, or revise the priorities of, the Research.

6.15 Creation and Structure of the DC. Upon the earlier of (a) the expiration of the Research Term and (b) the initiation by APSA of clinical development of any Development Compound, the Parties shall create a Development Committee of **[********]**. The DC shall consist of an equal number of representatives nominated by each Party.

6.16 Responsibilities of the DC. The DC shall serve as the primary vehicle for interaction between the Parties with respect to the development of Development Compounds. Without limiting the generality of the foregoing, the DC shall be responsible for: (a) reviewing and approving all Development Plans, and any updates thereto; (b) monitoring the progress of the development efforts; and (c) identifying and selecting Development Compounds and Back-up Compounds from among the Collaboration Compounds in accordance with Section 2.2(c), after the dissolution of the ERC).

6.17 Composition of the DC. Within fifteen (15) days of the creation of the DC, the Parties shall notify each other in writing of the names of their initial representatives on the DC. Each party may replace its DC representatives at any time upon written notice to the other. A Party's representative on the DC is authorized to act on behalf of such Party until written notice of the removal of such representative is received by the other Party. A Party's representative on the DC may resign at any time upon written notice to the Parties. Such resignation shall take effect at the time specified therein, and unless otherwise specified therein, no acceptance of such resignation shall be necessary to make it effective. Upon the resignation of a Party's representative, that Party shall appoint a

replacement representative. APSA shall select a chairperson for the DC from among its representatives on the DC.

6.18 Duration of the DC. The DC shall remain in existence so long as APSA continues to develop any Development Compound for any Indication, after which the DC shall dissolve, except that the DC shall automatically dissolve in the event that (a) APSA terminates the Agreement pursuant to Sections 11.2 or 11.3, or (b) Targacept terminates the Agreement pursuant to Section 11.2.

6.19 Meetings of the DC. During its existence, the DC shall meet in person on scheduled dates two (2) times per year and upon thirty (30) days advance written notice from either Party to the other Party. Meetings shall alternate between the offices of Targacept and APSA. A quorum of the DC shall exist whenever there is present at a meeting members appointed by each Party. A DC member of the Party hosting the meeting shall serve as Secretary of that meeting. The Secretary of the meeting shall prepare and distribute to all members of the DC minutes of the meeting sufficiently in advance of the next meeting to allow adequate review and comment prior to the meeting. Such minutes shall provide a description in reasonable detail of the discussions had at the meeting and a list of any actions, decisions or determinations approved by the DC. Minutes of any meeting shall be approved or disapproved, and revised as necessary, at the next meeting. Final minutes of each meeting shall be distributed to the members of the DC by the Chairperson. Each Party shall disclose to the other proposed agenda items in advance of each meeting of the DC. The DC may also convene, or be polled or consulted, from time to time by means of telecommunications, video conferencing or written correspondence, as deemed necessary or appropriate. Members of the DC may be represented at any meeting by a designee appointed by such member for such meeting. The DC may invite other representatives of the parties with special skills to attend meetings where appropriate. The DC shall adopt such other rules as shall be necessary or convenient for its work.

6.20 Decisions of the DC. All decisions of the DC shall be made by the unanimous vote of all DC members participating in the meeting. In the event that the members of the DC cannot agree with respect to a particular issue, such issue shall be referred to the President of Targacept and the Vice President, Clinical Research of APSA for resolution. In the event that such officers cannot agree on a resolution of the dispute within thirty (30) days, APSA's decision shall control.

6.21 Subcommittees of the DC. From time to time, the DC may establish one or more subcommittees to oversee particular projects or activities, and such subcommittees will be constituted as the DC agrees.

6.22 Expenses. Each Party shall be responsible for all travel and related costs for its representatives to attend meetings of, and otherwise participate on, the ERC and the DC.

ARTICLE 7

Payments to Targacept

7.1 License Fees. In consideration of the rights granted hereunder, APSA shall pay Targacept a non-refundable, non-creditable license fee of Two Million U.S. Dollars ($2,000,000) within ten (10) days after the Effective Date of this Agreement.

7.2 Milestone Payments. Subject to Sections 2.8(c) and 7.9, APSA shall make non-refundable payments to Targacept within thirty (30) days after the occurrence of each of the events listed below (each, a "Milestone Event"), in the amount provided:

(a) With respect to the Alzheimer's Disease Indication:

	Milestone Event	Payment Amount
1:	[********]	[********]
2:	[********]	[********]
3:	[********]	[********]
4:	[********]	[********]
5:	[********]	[********]
6:	[********]	[********]

For clarity, each Milestone Event, with the exception of Milestone Events 5 and 6, shall be payable only for the first Development Compound for the Alzheimer's Disease Indication to achieve the specified Milestone Event. Payment for Milestone Events 5 and 6 shall be made for each Development Compound that achieves such Milestone Event for the Alzheimer's Disease Indication.

(b) With respect to the Parkinson's Disease Indication:

	Milestone Event	Payment Amount
1:	[********]	[********]
2:	[********]	[********]
3:	[********]	[********]
4:	[********]	[********]
5:	[********]	[********]
6:	[********]	[********]

[********]

(c) As used in this Section 7.2, the following definitions apply:

(1) "Initiation", and its derivative forms, with respect to a particular phase, means when the first patient has been enrolled for the trials of such phase.

(2) “Completion”, and its derivative forms, with respect to a particular phase, means when all case report forms for all patients in the phase trials have been collected, and all queries have been resolved and the database for the phase trials has been locked.

(3) “Filing of NDA” means when the filing has been accepted for submission by the relevant regulatory authority.

7.3 Royalty Payments. Subject to the terms and conditions of this Agreement, APSA shall pay to Targacept royalties in an amount equal to **[********]** of the Net Sales of such Licensed Product during the Full Royalty Term in any country and **[********]** of the Net Sales of such Licensed Product during the Partial Royalty Term in any country. The Parties agree that the above royalty rates reflect an efficient and reasonable blended allocation of the values of the worldwide Know-How and Patent Rights licensed by Targacept hereunder.

7.4 Term of Royalty Obligation. The “Full Royalty Term” for a particular Licensed Product in a particular country shall commence with the First Commercial Sale of such Licensed Product in such country and shall terminate upon the later of (a) the expiration of the last-to-expire of (i) issued Targacept Patent Rights, (ii) issued APSA Patent Rights covering the composition of the Development Compound constituting or included in the Licensed Product, (iii) issued APSA Patent Rights covering inventions during the Research Term or (iv) Joint Patent Rights covering inventions during the Research Term, for which at least one Valid Claim exists covering the sale of such Licensed Product or its use in the Field, in such country, or (b) the **[********]** anniversary of the First Commercial Sale of such Licensed Product in such country. The “Partial Royalty Term” (if any) for a particular Licensed Product in a particular country shall commence immediately after the Full Royalty Term of such Licensed Product in such country and shall terminate upon the **[********]** anniversary of the First Commercial Sale of such Licensed Product in such country.

7.5 Timing of Payment of Royalties. Running royalties shall be payable on a quarterly basis, within sixty (60) days after the end of each calendar quarter, based upon the Net Sales during each calendar quarter, commencing with the calendar quarter in which the First Commercial Sale of a Licensed Product is made. Royalties shall be calculated in accordance with U.S. generally accepted accounting principles consistently applied and with the terms of this Agreement.

7.6 Obligation to Pay Royalties. APSA’s obligation to pay royalties to Targacept under this Article 7 is imposed only once with respect to the same unit of Licensed Product regardless of the number of Targacept Patents, APSA Patents or Joint Patents pertaining thereto.

7.7 Statement of Royalties. Each royalty payment to Targacept hereunder shall be accompanied by a statement showing the amounts of gross sales and Net Sales and the number of units of each Licensed Product sold by APSA on a country-by-country basis during such quarter and the amount of royalties due on such Net Sales.

7.8 Compulsory Licenses. If a court or a governmental agency in a particular country requires a Party (or its Affiliate) to grant a compulsory license to a Third Party permitting such Third Party to make and sell a Licensed Product in such country, and such compulsory license contains a royalty rate lower than the rates provided in Section 7.3 with respect to the sale of such Licensed Product, then the royalty rate to be paid by APSA based upon Net Sales of the Licensed Product in

such country shall automatically be reduced to the royalty rate under such compulsory license, during the time period when such compulsory license is in effect and being exercised.

7.9 Third Party Licenses. If any unexpired Third Party patent(s) claiming a Collaboration Compound or its manufacture or use in the Field exist(s) in a country where a Licensed Product including such Collaboration Compound is being manufactured, used or sold, and if it should prove in APSA's bona fide, good faith judgment impractical or impossible for it or its Affiliates or Sublicensees to commence or continue the manufacture, use or sale of such Licensed Product in such country without obtaining a Third Party License under such patent and if Targacept does not deliver to APSA an opinion without material qualifications from nationally recognized patent counsel in such country to the effect that such manufacture, use or sale does not and will not infringe such Third Party patent(s):

(a) if the Third Party patent is held by **[********]**, then Targacept shall have the right, for a period of six (6) months, to use commercially reasonable, good faith efforts to negotiate and obtain a Third Party License on commercially reasonable terms (for royalties not exceeding **[*********]** of Net Sales or such higher amount agreed to by the Parties) and thereafter APSA shall have the right to use commercially reasonable, good faith efforts to negotiate and obtain such Third Party License on commercially reasonable terms, in either case with the cost of such license (including without limitation license fees, milestone payments and royalties) to be set off against any payments owed to Targacept by APSA pursuant to Section 7.2 or Section 7.3; ***provided, however,*** that in no event shall the aggregate amount set off in any calendar quarter against royalties payable pursuant to Section 7.3 in such calendar quarter exceed **[*********]**;

(b) if the Third Party patent is held by any Third Party other than **[********]**, APSA shall have the right to use commercially reasonable, good faith efforts to negotiate and obtain a Third Party License on commercially reasonable terms, with the cost of such license (including without limitation license fees, milestone payments and royalties) to be borne equally by APSA and Targacept, with Targacept's share of such costs to be set off against any payments owed to Targacept by APSA pursuant to Section 7.2 or Section 7.3; ***provided, however,*** that in no event shall the aggregate amount set off in any calendar quarter against royalties payable under Section 7.3 in such calendar quarter exceed **[*********]**;

(c) if such Third Party License cannot be obtained on terms reasonably acceptable to APSA, APSA may terminate its license rights hereunder with respect to such Licensed Product in such country upon sixty (60) days written notice to Targacept, whereupon APSA, its Affiliates and Sublicensees shall have no further license rights in such country regarding such Licensed Product.

7.10 Mode of Payment. All payments to Targacept hereunder shall be made by deposit of United States Dollars in the requisite amount to such bank account as Targacept may from

time to time designate by notice to APSA. Payments shall be free and clear of any taxes (other than withholding and other taxes imposed on Targacept), fees or charges, to the extent applicable. With respect to sales outside the United States, payments shall be calculated based on currency exchange rates for the last calendar quarter for which remittance is made for royalties. For each quarter and each currency, such exchange rate shall equal the arithmetic average of the daily exchange rates during the calendar quarter obtained from the *Reuters Daily Rate Report* or, if such exchange rates are not available on any day, *The Wall Street Journal*, Eastern U.S. Edition, or, if such exchange rates are not available on any day, as otherwise agreed by the Parties.

7.11 Records Retention. For three (3) years after each sale of each Licensed Product, and for such longer period as may be required by law, APSA shall keep (and shall ensure that its Affiliates and Sublicensees shall keep) complete and accurate books and records pertaining to the sale of all Licensed Products in sufficient detail to confirm the accuracy of calculations of payments due to Targacept hereunder.

7.12 Audits.

(a) Upon the written request of Targacept and not more than once in each calendar year, APSA shall permit an independent certified public accounting firm of nationally recognized standing appointed by Targacept, at Targacept's expense, to have access during normal business hours, and upon reasonable prior written notice, to such of the records of APSA as may be reasonably necessary to verify the accuracy of the royalty reports hereunder for any calendar year ending not more than thirty-six (36) months prior to the date of such request. The accounting firm shall disclose to Targacept and APSA whether the royalty reports are correct or incorrect, the basis for its finding and the specific details concerning any discrepancies.

(b) If such accounting firm correctly concludes that additional royalties were owed during such period, APSA shall pay the additional royalties, with interest from the date originally due at the prime rate, as published in *The Wall Street Journal* (Eastern U.S. Edition) on the last business day preceding such date, within thirty (30) days after the date Targacept delivers to APSA such accounting firm's written report so correctly concluding. [********].

(c) APSA shall include in each sublicense granted by it pursuant to this Agreement a provision requiring the Sublicensee to make reports to APSA, to keep and maintain records of sales made pursuant to such sublicense and to grant access to such records by Targacept's independent accountant to the same extent required by APSA under this Agreement.

(d) Targacept shall treat all information subject to review under this Section 7.12 in accordance with the confidentiality provisions of Article 9 of this Agreement, and shall cause its accounting firm to enter into an acceptable confidentiality agreement with APSA obligating such firm to retain all such financial information in confidence pursuant to such

confidentiality agreement; ***provided, however,*** that in no event shall such confidentiality agreement prevent the accounting firm from disclosing to Targacept the information contemplated by Section 7.12(a).

7.13 Taxes. The Party receiving royalties and other payments under this Agreement shall pay any and all taxes levied on account of such payment. If any taxes are required to be withheld by the paying Party, it shall (a) deduct such taxes from the remitting payment, (b) timely pay the taxes to the proper taxing authority, and (c) send proof of payment to the other Party and certify its receipt by the taxing authority within sixty (60) days following such payment.

ARTICLE 8

Inventions and Patents

8.1 Title to Inventions and Documentation. Except as otherwise expressly provided in Article 5 and this Section 8.1:

(a) the Parties shall jointly own all right, title to and interest in all Joint Research Technology and the Patent Rights related to Joint Research Technology;

(b) Targacept shall own all right, title to and interest in all Targacept Research Technology and the Patent Rights related to Targacept Research Technology; and

(c) APSA shall own all right, title to and interest in all APSA Research Technology and the Patent Rights related to APSA Research Technology.

8.2 Patent Prosecution. The Parties expect that patent applications will be filed as required to secure suitable Patent Rights covering Collaboration Compounds and inventions that are within the Research Technology or are otherwise applicable to the Field. The Parties agree as follows with respect to the filing and prosecution of such applications.

(a) *Targacept Patents.* Subject to the provisions of this Section 8.2: Targacept shall be responsible for obtaining, prosecuting and/or maintaining throughout the world the Targacept Patents, including Patent Rights covering Targacept Research Technology solely owned by Targacept. In this regard, Targacept shall file, prosecute and/or maintain patent applications in the United States to secure Patent Rights for the Collaboration Compounds and any Research Technology solely owned by Targacept and other inventions claimed in the Targacept Patents. Within one year of filing any such United States patent application, Targacept shall file a counterpart International Application under the PCT designating all member countries and any additional counterpart national patent applications in non-PCT member countries as the parties shall mutually agree upon (subject to the provisions of

Subsection 8.3(e)). Targacept shall bear all costs for filing, prosecuting and/or maintaining Targacept Patents. Notwithstanding the foregoing, APSA shall reimburse Targacept for (i) **[********]** of the out-of-pocket costs incurred by Targacept for the filing, prosecuting and/or maintaining Targacept Patents which claim a Development Compound or a Back-Up Compound (or its manufacture or use); (ii) upon the designation of any Development Compound or Back-Up Compound as a Licensed Product, an additional **[********]** of such costs previously incurred for any Targacept Patents that claim such Development Compound or Back-Up Compound and (iii) thereafter, **[********]** of the out-of-pocket costs incurred by Targacept for the filing, prosecuting and/or maintaining Targacept Patents which claim such Licensed Product (or its manufacture or use); ***provided, however,*** that APSA may decline to pay costs for filing, prosecuting and/or maintaining any such Targacept Patent in one or more countries, in which case Targacept may elect to exclude such Targacept Patent from the licenses granted to APSA under Section 5.1 hereof in such countries.

(b) *APSA Patents.* APSA shall be responsible for obtaining, prosecuting and/or maintaining throughout the world Patent Rights covering APSA Research Technology solely owned by APSA. APSA shall bear all costs for filing, prosecuting and/or maintaining APSA Patents throughout the world.

(c) *Joint Patents.* Targacept shall be initially responsible for obtaining, prosecuting and/or maintaining throughout the world Patent Rights in the name of Targacept and APSA covering Joint Research Technology pertaining solely and directly to Nicotinic Compounds and APSA shall be initially responsible for obtaining, prosecuting and/or maintaining throughout the world Patent Rights in the name of Targacept and APSA covering all other Joint Research Technology. APSA and Targacept shall share equally the costs for filing, prosecuting and/or maintaining such Joint Patents. Notwithstanding the above, either Party may decline to pay its share of the costs for filing, prosecuting and/or maintaining any Joint Patent(s) in a particular country(ies), in which case the declining Party shall assign to the other Party all its right, title and interest to any such Joint Patent(s) in the relevant country and upon such assignment such Joint Patent(s) shall become a APSA Patent(s) or a Targacept Patent(s), as the case may be.

(d) *Cooperation.* Each 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. In addition, such filing Party shall provide the other Party and its patent counsel with an opportunity to consult with the Party and its patent counsel regarding the filing and contents of any such application, amendment, submission or response, and the advice and suggestions of the other

Party and its patent counsel shall be taken into reasonable consideration by such Party and its legal counsel in connection with such filing; ***provided, however,*** that with respect to the prosecution of Targacept Patents, Targacept shall give all due consideration to reasonable requests by APSA regarding the prosecution of such Patent Rights and ***provided further*** that with respect to the Joint Patents, the prosecuting Party shall give consideration to reasonable requests of the other Party regarding the prosecution of such Joint Patents. Each Party shall also provide the other Party with copies of any patentability search reports made by patent counsel with respect to inventions in the Research Technology, including patents located, a copy of each patent application, and each patent that issues thereon.

(e) *Election not to Prosecute*. If a Party elects not to pursue the initial filing of a potential Targacept Patent, APSA Patent or Joint Patent, as the case may be, or to support the PCT International filing or the continued prosecution or maintenance of any Targacept Patent, APSA Patent or Joint Patent, as the case may be, in a particular country for which it has the initial right or obligation to file pursuant to Section 8.2(a), (b) or (c) (such Party being referred to herein as the "Non-Filing Party"), then it shall notify the other Party promptly in writing and in good time to enable the other Party to meet any applicable deadlines. With respect to Targacept Patents, APSA Patents or Joint Patents scheduled for international filing with respect to such country, the Non-Filing Party shall notify the other Party in writing at least ninety (90) days before the date required for the convention year filing of such Targacept Patent, APSA Patent or Joint Patent application or within a reasonable time before any other deadline date by which an action must be taken to establish or preserve a Targacept Patent, APSA Patent or Joint Patent right in such country. The other Party shall then have the right, but not the obligation, to pursue the filing or support the continued prosecution or maintenance of such Targacept Patent, APSA Patent or Joint Patent, at its expense in such country. If the other Party does so elect to pursue such filing or continue such support, then it shall notify the Non-Filing Party of such election, and the Non-Filing Party shall (i) reasonably cooperate with the other Party in this regard, and (ii) promptly release or assign, as the case may be, to the other Party, without consideration, all right, title and interest in such Targacept Patent, APSA Patent or Joint Patent in such country. For the avoidance of doubt, in the event that the other Party supports a patent application that the Non-Filing Party declines to support, then such patent applications and patents that may result therefrom shall be considered a Targacept Patent (in the case APSA is the Non-Filing Party) or an APSA Patent (in the case Targacept is the Non-Filing Party), as applicable, for purposes of this Agreement.

8.3 Enforcement of Patents.

(a) If either Party considers that any Targacept Patent, APSA Patent or Joint Patent claiming a Collaboration Compound or Licensed Product, or the manufacture or use thereof, is being infringed by a Third Party's activities in the Field, it shall notify the other Party and provide it with any evidence of such infringement which is reasonably available. APSA shall have the first opportunity at its own expense to attempt to remove such infringement by commercially appropriate steps, including filing an infringement suit or taking other similar action. In the event that APSA fails to take commercially appropriate steps with respect to an infringement that is likely to have a material adverse effect on the sale of Licensed Products within **[********]** following notice of such infringement, Targacept shall have the right to do so at its expense; provided that if APSA has commenced negotiations with an alleged infringer of the patent for discontinuance of such infringement within such **[********]** period, APSA shall have an additional **[********]** to conclude its negotiations before the other Party may bring suit for such infringement. If required by law for the prosecuting Party to prosecute any suit referred to in this Section 8.3, the other Party shall join such suit as a party, at the prosecuting Party's expense. In no event shall either Party be required to enforce any Patent Right against more than one entity or in more than one country at any one time.

(b) The Party not enforcing the applicable Patent Rights shall provide commercially reasonable assistance to the other Party, including joining in infringement suits, providing access to relevant documents and other evidence, making employees available and seeking to obtain necessary Third Party consents, subject to the enforcing Party's reimbursement of any out-of-pocket expenses incurred by the non-enforcing Party.

(c) Any amounts recovered by APSA pursuant to Section 8.3(a), whether by settlement or judgment, shall be allocated in the following order: (i) to reimburse APSA and Targacept 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); and (ii) the portion of the award representing lost profits shall be allocated between APSA and Targacept so that the ratio of APSA's portion to Targacept's portion is equal to the ratio of APSA's historic profits on Net Sales in the Indication to Targacept's royalties in the Indication (or **[********]** of such royalties during the Partial Royalty Term), provided that if the infringement activity on which such recovery is based included actions outside the Field, then the Parties shall reasonably agree on an appropriate allocation of such recovery between activities in the Field and activities outside the Field (which will not bear a royalty). Any amounts recovered by Targacept pursuant to actions under Section 8.3(a) shall be allocated in the following order: (i) to reimburse Targacept and APSA 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); and (ii)

the remainder shall be divided **[********]** to Targacept and **[********]** to APSA.

(d) Except for Third Party infringement activities within the Field covered by the provisions of Section 8.3(a), each Party shall retain the sole and exclusive right to enforce its Patent Rights against all infringers at its sole cost and expense.

8.4 Third Party Patent Rights. If any warning letter or other notice of infringement is received by a Party, or action, suit or proceeding is brought against a Party, alleging infringement of a Patent Right of any Third Party in the manufacture, use or sale of a Licensed Product or in conducting the Research, the Parties shall promptly discuss and decide the best way to respond.

ARTICLE 9

Confidentiality

9.1 Confidentiality Obligations. Each Party agrees that, for the term of this Agreement and for five (5) years thereafter, such Party shall keep, and shall ensure that its officers, directors, employees and agents keep, completely confidential and shall not publish or otherwise disclose and shall not use for any purpose except as expressly permitted hereunder any Confidential Information furnished to it by the other Party pursuant to this Agreement (including, without limitation, Know-How or Research Technology of the disclosing Party) or any Joint Research Technology. The foregoing obligations shall not apply to any information to the extent that it can be established by such receiving Party that such information:

(a) was already known to the receiving Party, other than under an obligation of confidentiality, at the time of disclosure;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the receiving Party in breach of this Agreement;

(d) was subsequently lawfully disclosed to the receiving Party by a Third Party other than in contravention of a confidentiality obligation of such Third Party to the disclosing Party; or

(e) was developed or discovered by employees of the receiving Party or its Affiliates who had no access to the Confidential Information of the disclosing Party.

Each Party shall have, shall obtain or shall have assigned to it written agreements from each of its employees, agents, and consultants who perform substantial work on the Research or development, which agreements shall obligate such persons to similar obligations of confidentiality and to assign to such Party all inventions made by such persons during the course of performing the Research. Each

Party may disclose the other's Confidential Information to the extent such disclosure is reasonably necessary in filing or prosecuting patent applications, prosecuting or defending litigation or as otherwise required by legal process, complying with applicable governmental regulations, making a permitted sublicense of its rights hereunder or conducting clinical trials or otherwise in performing its obligations or exercising its rights hereunder, *provided that* if a Party is required to make any such disclosure of the other Party's Confidential Information, it will give reasonable advance notice to such other Party of such disclosure requirement, will cooperate with such other Party in the efforts of such other Party to secure confidential treatment of such Information prior to its disclosure, and, save to the extent inappropriate in the case of patent applications, will use all reasonable efforts to secure confidential treatment of such information prior to its disclosure (whether through protective orders or confidentiality agreements or otherwise). In addition, each Party shall have the right to disclose to its Affiliates Confidential Information of the other Party, provided that such Party shall ensure that its Affiliates maintain the confidentiality of such information in accordance with the provisions of this Section 9.1.

9.2 Publications.

(a) Neither Party shall publish or present the results of the Research or development studies carried out on any Development Compound or Back-Up Compound until after completion of Phase I clinical development with respect thereto. Subject to the foregoing and the restrictions provided below, either Party may publish or present the results of the Research or of development studies carried out by it on such Development Compound, subject to the prior review by the other Party for patentability and protection of such other Party's Confidential Information. Each Party shall provide to the other Party the opportunity to review any proposed abstracts, manuscripts or summaries of presentations which cover the results of the Research or of pre-Phase III clinical development of such Development Compound. Each party shall designate a person who shall be responsible for approving such publications. Such designated person shall respond in writing promptly and in no event later than sixty (60) days after receipt of the proposed material with either approval of the proposed material or a specific statement of concern, based upon either the need to seek patent protection or concern regarding competitive disadvantage arising from the proposal. In the event of concern, the submitting Party agrees not to submit such publication or to make such presentation that contains such information until the other Party is given a reasonable period of time (not to exceed ninety (90) days) to seek patent protection for any material in such publication or presentation which it believes is patentable or to resolve any other issues. This Section 9.2(a) shall cease to apply with respect to any Development Compound upon the commercial launch of a Licensed Product containing such Development Compound as an active ingredient. Furthermore, with respect to any proposed abstracts, manuscripts or summaries of presentations by investigators or other Third Parties, such materials shall be subject to review under this Section 9.2(a) to the extent that APSA or Targacept (as the case may be) has the right to do so.

(b) Each Party also agrees to delete from any such proposed publication any Confidential Information of the other Party upon its reasonable request.

(c) In any publication permitted under this Section 9.2, each Party shall acknowledge its collaboration with the other Party under this Agreement.

9.3 Press Releases. Except to the extent required by law or as otherwise permitted in accordance with this Section 9.3, neither Party shall make any public announcements concerning this Agreement or the subject matter hereof without the prior written consent of the other, which shall not be unreasonably withheld. Notwithstanding the foregoing, the Parties agree that each Party may desire or be required to issue press releases relating to the Agreement or activities thereunder, and the Parties agree to consult with each reasonably and in good faith with respect to the text and timing of such press releases prior to the issuance thereof, provided that a Party may not unreasonably withhold consent to such releases, and that either Party may issue such press releases as it determines, based on advice of counsel, are reasonably necessary to comply with laws or regulations or for appropriate market disclosure. The principles to be observed by Targacept and APSA in public disclosures with respect to this Agreement shall be: accuracy, compliance with applicable legal requirements, the requirements of confidentiality under this Article 9 and normal business practice in the pharmaceutical and biotechnology industries for disclosures by companies comparable to Targacept and APSA. In the event of a public announcement, the Party making such public announcement shall provide the other Party with a reasonable opportunity, judged in the light of the circumstances, and the right to approve the content of such announcement prior to its being made, which approval shall not be delayed or unreasonably withheld. Furthermore, each Party shall give the other Party a reasonable opportunity, to the extent practicable, to review all filings with the United States Securities and Exchange Commission describing the terms of this Agreement prior to submission of such filings, and shall give reasonable consideration to any comments received from the non-filing Party relating to such filing, including without limitation the provisions of this Agreement for which confidential treatment should be sought.

ARTICLE 10

Indemnification

10.1 Indemnification by APSA. APSA shall indemnify, defend and hold Targacept and its Affiliates and each of their respective agents, employees, officers and directors (the “Targacept Indemnitees”) harmless from and against any and all liability, damage, loss, cost or expense (including reasonable attorney’s fees) in connection with any and all suits, investigations, claims or demands by Third Parties (collectively, the “Losses”) arising from or occurring as a result of (a) any breach by APSA of this Agreement or (b) APSA’s performance of its obligations under this Agreement and/or (c) the manufacture, use or sale of any Collaboration Compound or any product containing a Collaboration Compound by APSA and its Affiliates, Sublicensees, distributors and agents, except for those Losses for which Targacept has an obligation to indemnify APSA pursuant to Section 10.2, as to which Losses each party shall indemnify the other to the extent of their respective liability for the Losses. Notwithstanding any provision hereof to the contrary, APSA shall have no obligation to indemnify any Targacept Indemnitee against any Losses in connection with any product liability claim arising out of the manufacture, use or sale of any product by Targacept and its Affiliates, Sublicensees, distributors

and agents, regardless of whether such claim sounds in tort, contract, strict liability, products liability or any other legal theory.

10.2 Indemnification by Targacept. Targacept shall indemnify, defend and hold APSA and its Affiliates and each of their respective agents, employees, officers and directors (the "APSA Indemnitees") harmless from and against any Losses arising from or occurring as a result of (a) any breach by Targacept of this Agreement, (b) Targacept's performance of its obligations under this Agreement and/or (c) the manufacture, use or sale of any Collaboration Compound or any product containing a Collaboration Compound by Targacept and its Affiliates, Sublicensees, distributors and agents, except for those Losses for which APSA has an obligation to indemnify Targacept pursuant to Section 10.1, as to which Losses each Party shall indemnify the other to the extent of their respective liability for the Losses. Notwithstanding any provision hereof to the contrary, Targacept shall have no obligation to indemnify any APSA Indemnitee against any Losses in connection with any product liability claim arising out of the manufacture, use or sale of any Licensed Product by APSA and its Affiliates, Sublicensees, distributors and agents, regardless of whether such claim sounds in tort, contract, strict liability, products liability or any other legal theory.

10.3 Notification of Claims; Conditions to Indemnification Obligations. As a condition to a Party's right to receive indemnification under this Article 10, it shall (a) promptly notify the other Party as soon as it becomes aware of a claim or action for which indemnification may be sought pursuant hereto, (b) cooperate with the indemnifying Party in the defense of such claim or suit, and (c) permit the indemnifying Party to control the defense of such claim or suit, including without limitation the right to select defense counsel. In no event, however, may the indemnifying party compromise or settle any claim or suit in a manner which admits fault or negligence on the part of the indemnified Party without the prior written consent of the indemnified party. The indemnifying Party shall have no liability under this Article 10 with respect to claims or suits settled or compromised without its prior written consent.

ARTICLE 11

Termination and Expiration

11.1 Term and Termination. This Agreement shall commence upon the Effective Date and, unless earlier terminated as provided herein, shall expire on the expiration of all royalty and other payment obligations hereunder. The obligation of APSA to pay royalties shall expire on a country-by-country basis as provided in Section 7.4. Upon expiration of all royalty obligations with respect to a particular Licensed Product, the licenses granted to APSA under Section 5.1(b) shall expire, and APSA shall automatically thereafter be granted a non exclusive, fully paid up license to make, have made, use, import, sell and offer for sale such Licensed Product worldwide. For the avoidance of doubt, if no Development Compound is selected prior to six months after the Research Term, the term of this Agreement shall terminate six months after the Research Term, unless earlier terminated in accordance with this Agreement or unless the parties otherwise agree in writing.

11.2 Termination of the Agreement upon Material Breach.

(a) Failure by a Party to comply with any of its material obligations contained herein shall entitle the Party not in default to give to the Party in default notice specifying the nature of the default, requiring it to

make good or otherwise cure such default, and stating its intention to terminate if such default is not cured. If such default is not cured within sixty (60) days after the receipt of such notice (or, if such default cannot be cured within such sixty (60) day period, if the Party in default does not commence and diligently continue actions to cure such default), the Party not in default 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; ***provided, however,*** that such right to terminate shall be stayed in the event that, during such sixty (60) day period, the Party alleged to have been in default shall have initiated dispute resolution in accordance with Section 14.10 with respect to the alleged default, which stay shall last so long as the initiating Party diligently and in good faith cooperates in the prompt resolution of such dispute resolution proceedings.

(b) The right of a Party to terminate this Agreement, as herein above provided, shall not be affected in any way by its waiver or failure to take action with respect to any prior default.

(c) In the event that APSA is developing or commercializing more than one Development Compound and/or Licensed Product for use in the Field, and APSA breaches this Agreement in connection with a particular Development Compound or Licensed Product, then Targacept shall be entitled to terminate this Agreement only with respect to such particular Development Compound or Licensed Product. Furthermore, in the event a breach relating to a particular Development Compound or Licensed Product is limited to a particular Major Pharmaceutical Market, then Targacept shall be entitled to terminate this Agreement only with respect to such Major Pharmaceutical Market.

11.3 Termination of the Agreement by APSA. APSA may terminate this Agreement in its entirety upon thirty (30) days prior written notice on or after the end of the Research Term, or as specified in Section 2.8; ***provided, however,*** that APSA shall not be discharged of its liability to Targacept under any previously approved Semi-Annual Research Plan.

11.4 Consequences of Termination.

(a) Upon termination of this Agreement (but not upon expiration of its term under Section 11.1), in case of partial termination of this Agreement with respect to the compound(s) and/or product(s) subject to such termination and in case of termination of this Agreement as a whole with respect to all compounds and products being subject to this Agreement, the following shall apply with respect to the compounds and/or products with respect to which the Agreement is being terminated: (i) each Party shall promptly return all relevant records and materials in its possession or control containing or comprising the other Party's Know-How and Confidential Information and to which the former Party does not retain rights hereunder (except one copy of which

may be retained in a Party's confidential files for archival purposes); (ii) all licenses granted by each Party to the other under Article 5 shall terminate except as expressly provided otherwise herein; (iii) each Party shall provide the other Party with copies of all reports and data, including preclinical data and reports, obtained by the former Party pursuant to this Agreement that relate to Collaboration Compounds and that have not otherwise been provided to such Party, within sixty (60) days after such termination; ***provided, however,*** that a Party shall not be obligated to provide the foregoing copies in the case where such Party terminates under Section 11.2 and that Targacept shall not be obligated to do so in the case where APSA terminates under Section 11.3 and ***provided further*** that the provision to a Party of the foregoing copies shall not be deemed to create any additional rights or licenses in any such copies or the intellectual property embodied therein, and such Party's rights to use or exploit such information and rights shall be solely as expressly granted elsewhere in this Agreement and, with respect to Joint Research Technology or Joint Patents, those rights of such Party as a joint owner); and (iv) any and all claims and payment obligations that accrued prior to the date of such termination shall survive such termination.

(b) In the event APSA terminates the Agreement under Section 11.3, APSA shall grant Targacept an exclusive, paid-up, worldwide license, with the right to sublicense, under (i) any Patent Rights Controlled by APSA which claim a Development Compound, Back-Up Compound or Licensed Product (or its manufacture or use in the Field), and (ii) any Know-How Controlled by APSA which is necessary to make and use Development Compounds, Back-Up Compounds or Licensed Products in the Field, solely to make, have made, import, use, sell and offer for sale Development Compounds, Back-Up Compounds and Licensed Products for use in the Field. APSA agrees to negotiate in good faith with Targacept any further royalty-bearing licenses under such other APSA Patents, APSA Know-How and APSA rights in the Joint Patents and Joint Research Technology as may be useful to Targacept in conducting research and development and commercializing such Compounds for use in the Field.

(c) In the event Targacept terminates the Agreement under Section 11.2, APSA shall grant Targacept an exclusive, paid-up, worldwide license, with the right to sublicense, under (i) any Patent Rights Controlled by APSA which claim a Development Compound, Back-Up Compound or Licensed Product (or its manufacture or use in the Field), and (ii) any Know-How Controlled by APSA which is necessary to make and use Development Compounds, Back-Up Compounds or Licensed Products in the Field, solely to make, have made, import, use, sell and offer for sale Development Compounds, Back-Up Compounds and Licensed Products for use in the Field. APSA agrees to negotiate in good faith with Targacept any further royalty-bearing licenses under such other APSA Patents, APSA Know-How and APSA rights in the Joint Patents

and Joint Research Technology as may be useful to Targacept in conducting research and development and commercializing such Compounds for use in the Field.

(d) In connection with the grant of a license pursuant to Section 11.4(b) or 11.4(c), APSA shall assign to Targacept any and all regulatory filings (including applications for Regulatory Approval) made by APSA covering Development Compounds, Back-Up Compounds and Licensed Products, and APSA shall provide appropriate notification of such assignment to applicable regulatory authorities within thirty (30) days after the request of Targacept.

(e) Notwithstanding the provisions of Section 11.5(b) hereof, in the event that Targacept terminates this Agreement pursuant to Section 11.2, then the restrictions imposed upon it pursuant to, and its obligations under, Sections 2.11 and 5.4 (other than Section 5.4(a)) shall terminate.

(f) Notwithstanding the provisions of Section 11.5(b) hereof, in the event that APSA terminates this Agreement pursuant to Section 11.2, then the restrictions imposed upon it pursuant to, and its obligations under, Sections 2.11 and 5.4 (other than Section 5.4(a)) shall terminate.

11.5 Accrued Rights; Surviving Obligations.

(a) Termination, relinquishment or expiration of this Agreement for any reason shall be without prejudice to any rights which shall have accrued to the benefit of a Party prior to such termination, or expiration. Such termination, relinquishment or expiration shall not relieve a Party from obligations which are expressly indicated to survive termination or expiration of this Agreement.

(b) Without limiting the foregoing, Sections 2.6(b), 2.6(c), 2.8(a), 2.9, 2.10, 2.14, 4.1(b), 4.1(c), 5.1(b) (in the event of expiration), 5.2(b) and (c) (unless APSA terminates this Agreement under Section 11.2), 5.3, 5.4(a), 5.4(b)(ii) (in the event of termination by APSA under Section 11.2), 5.4(c)(iv), 7.9, 7.10, 7.11, 7.12, 7.13, 14.3, 14.9, 14.10, 14.11 and 14.12 and Articles 1 (including, solely for purposes of interpreting a particular definition set forth therein, all provisions referenced in such definition), 8, 9, 10, and 11 of this Agreement shall survive the expiration or termination of this Agreement for any reason; provided that, in the event of a partial termination of this Agreement pursuant to Section 11.2(c), (i) the foregoing provisions shall survive and continue to apply in full force and effect with respect to the compound(s) and or product(s) subject to the partial termination and (ii) all of the provisions of this Agreement, including without limitation the foregoing provisions, shall continue to apply in full force and effect in all other respects (including, without limitation, to all compound(s) and/or product(s) that are not subject to the partial termination).

(c) Upon any termination of this Agreement as regards any particular Licensed Product, APSA shall be entitled, during the six (6) month period following the effective date of such termination, to finish any work-in-progress and to sell any inventory of the Licensed Product which remains on hand as of the date of the termination, so long as APSA pays to Targacept the royalties applicable to said subsequent sales in accordance with the terms and conditions set forth in this Agreement.

11.6 Rights in Bankruptcy. All rights and licenses granted under or pursuant to this Agreement by APSA or Targacept are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code, licenses of right to "intellectual property" as defined under Section 101 of the U.S. 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 U.S. Bankruptcy Code. The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against either Party under the U.S. Bankruptcy Code, the Party hereto which 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, and same, if not already in their possession, shall be promptly delivered to them (i) upon any such commencement of a bankruptcy proceeding upon their written request therefor, unless the Party subject to such proceeding elects to continue to perform all of its obligations under this Agreement or (ii) if not delivered under (i) above, following the rejection of this Agreement by or on behalf of the Party subject to such proceeding upon written request therefor by an non-subject Party.

ARTICLE 12

Representations and Warranties

12.1 Representations and Warranties. As of the Effective Date, each Party represented and warranted to the other Party that:

(a) Such Party is duly organized and validly existing under the laws of the state of its incorporation and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof;

(b) Such Party has taken all corporate action necessary to authorize the execution and delivery of this Agreement and the performance of its obligations under this Agreement;

(c) This Agreement is a legal and valid obligation of such Party, binding upon such Party and enforceable against such Party in accordance with the terms of this Agreement. The execution, delivery and performance of this Agreement by such Party does not conflict with any agreement, instrument or understanding, oral or written, to which such Party is a party or by which such Party may be bound, and does not violate any law or regulation of any court, governmental body or administrative or other agency having authority over such Party. All consents, approvals and authorizations from all governmental authorities or other Third

Parties required to be obtained by such Party in connection with this Agreement have been obtained;

(d) It has the full and exclusive right, power and authority to enter into this Agreement, to perform the Research and to grant the licenses granted under Article 5 hereof;

(e) All individuals who perform any activities on behalf of a Party or its Affiliates in connection with the Research will have assigned to such Party, directly or indirectly by assignment of another Person, the whole of their rights in any intellectual property conceived or reduced to practice by them as a result of the Research. No Third Party (other than a Sublicensee) will have any rights to any intellectual property which is conceived or developed by any individual who will perform any activities by or on behalf of a Party or its Affiliates in connection with the Research; and

(f) With respect to any Materials provided by it to the other Party, it has the full right to provide such Materials and has no reason to believe that the other Party's use of such Materials in accordance with this Agreement will infringe the intellectual property rights of any Third Party.

12.2 Additional Representations and Warranties of Targacept. As of the Effective Date, Targacept represented and warranted that:

(a) To the best knowledge of Targacept, the Targacept Patents or Targacept Know-How existing as of the Effective Date are not invalid or unenforceable, in whole or in part.

(b) To the best knowledge of Targacept, the inception, development and reduction to practice of the Targacept Patents and Targacept Know-How existing as of the Effective Date has not constituted or involved the misappropriation of trade secrets or other rights or property of any Third Party and APSA's practice of the Targacept Patents and Targacept Know-How as permitted herein will not infringe any intellectual property rights of any Third Party.

(c) As of the Effective Date, there are no agreements between Targacept and any Third Parties which would preclude or otherwise limit Targacept's ability to conduct its tasks and obligations under the Research and Development Plan or otherwise fulfill its obligations under this Agreement;

(d) As of the Effective Date, Targacept has not granted any license to any Third Party, either express or implied, or any option to license, to utilize any intellectual property owned or Controlled by Targacept (including under option) to discover, identify, research, develop or market any Nicotinic Compounds;

(e) As of the Effective Date, Targacept is the exclusive owner or assignee of the Patent Rights listed on Exhibit E(1) attached hereto. Such Patent Rights constitute all of the Patent Rights that Targacept and its Affiliates own, have under license or have a right to acquire (by option or otherwise) that are useful for the manufacture, use or sale of Targacept Compounds, other than the UK Compounds, in the Field. During the term of this Agreement, Targacept will use its best efforts not to encumber or diminish the rights granted to APSA hereunder, including without limitation, by not committing any acts or permitting the occurrence of any omissions which would cause the breach or termination of any Third Party License. Targacept will promptly provide APSA notice of any alleged breach of any Third Party License. As of the Effective Date, Targacept was not in breach of any Third Party License.

(f) As of the Effective Date, no Key Employee has given notice of any desire to retire, resign or otherwise terminate his employment and neither Targacept nor any Affiliate has given any notice of or has any intent of terminating the employment of any Key Employee.

(g) As of the Effective Date, Targacept's Affiliates have effectively transferred, assigned and licensed to Targacept all their right, title and interest in and to (i) the Targacept Compounds, (ii) the Targacept Patents, (iii) the Targacept Know-How, (iv) the Pentad Patents, (v) the Pentad Technology, (vi) the license agreements covering or relating to any of the foregoing and (vii) confidentiality and assignment of invention agreements. As of the Effective Date and, with respect to the UK Compounds, as of the UK License Date, Targacept has exclusive rights in the Field to the foregoing.

(h) To the best of Targacept's scientific judgment, the Targacept Compounds include all of the Nicotinic Compounds (other than the UK Compounds), created or developed at any time solely or jointly by Targacept or any Affiliate thereof, that show significant potential for development as a pharmaceutical product for use in the Field.

(i) Targacept shall obtain a license granting Targacept exclusive rights in the Field to the UK Compounds within ninety (90) days after the Effective Date (which date of license grant shall be referred to herein as the "UK License Date"). As of the UK License Date, Targacept shall be the exclusive licensee to the Patent Rights listed on Exhibit E(2) attached hereto and such Patent Rights shall constitute all of the Patent Rights that Targacept and its Affiliates own, have under license or have a right to acquire (by option or otherwise) that are useful for the manufacture, use or sale of the UK Compounds in the Field. During the term of this Agreement, Targacept will use its best efforts not to encumber or diminish the rights granted to Targacept under the UK License, including without limitation, by not committing any acts or

permitting the occurrence of any omissions which would cause the breach or termination of the UK License. Targacept will promptly provide APSA notice of any alleged breach of the UK License.

ARTICLE 13

[Reserved]

ARTICLE 14

Miscellaneous Provisions

14.1 Relationship of the Parties. Nothing in this Agreement is intended or shall be deemed to constitute a partnership, agency or employer-employee relationship between the Parties. Neither Party shall incur any debts or make any commitments for the other.

14.2 Assignments. Except as expressly provided herein, neither this Agreement nor any interest hereunder shall be assignable, nor any other obligation delegable, by a Party without the prior written consent of the other; ***provided, however,*** that (i) a Party may assign this Agreement to any Affiliate or to any successor in interest by way of merger or sale of all or substantially all of its assets in a manner such that the assignor shall remain liable and responsible for the performance and observance of all such Party's duties and obligations hereunder and (ii) API hereby assigns the Original Agreement, superseded by this Agreement as of the date hereof, to APSA and Targacept hereby consents to such assignment. This Agreement shall be binding upon the successors and permitted assigns of the Parties. Any assignment not in accordance with this Section 14.2 shall be void.

14.3 Disclaimer of Warranties. SUBJECT TO SECTIONS 12.1 AND 12.2, THE PARTIES EXPRESSLY DISCLAIM ALL WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR NON-INFRINGEMENT OF THIRD PARTY RIGHTS, UNLESS OTHERWISE EXPRESSLY PROVIDED IN THIS AGREEMENT.

14.4 Further Actions. Each Party agrees to execute, acknowledge and deliver such further instruments and to do all such other acts as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

14.5 Force Majeure. Neither Party shall be liable to the other for failure or delay in the performance of any of its obligations under this Agreement for the time and to the extent such failure or delay is caused by earthquake, riot, civil commotion, war, strike, flood, governmental acts or restrictions or any other reason which is beyond the control of the respective Party. The Party affected by force majeure shall provide the other Party with full particulars thereof as soon as it becomes aware of the same (including its best estimate of the likely extent and duration of the interference with its activities), and will use commercially reasonable efforts to overcome the difficulties created thereby and to resume performance of its obligations as soon as practicable. If the performance of any obligation under this Agreement is delayed owing to a force majeure for any continuous period of more

than six (6) months, the parties hereto shall consult with respect to an equitable solution, including the possibility of the mutual termination of this Agreement.

14.6 No Trademark Rights. No right, express or implied, is granted by this Agreement to a Party to use in any manner the name or any other trade name or trademark of a Party in connection with the performance of this Agreement.

14.7 Entire Agreement of the Parties; Amendments. This Agreement and the exhibits hereto constitute and contain the entire understanding and agreement of the Parties respecting the subject matter hereof and cancel and supersede any and all prior negotiations, correspondence, understandings and agreements between the Parties, whether oral or written, regarding such subject matter, including without limitation the Original Agreement. No waiver, modification or amendment of any provision of this Agreement shall be valid or effective unless made in writing and signed by a duly authorized officer of each Party.

14.8 Captions. The captions to this Agreement are for convenience only, and are to be of no force or effect in construing or interpreting any of the provisions of this Agreement.

14.9 Applicable Law. This Agreement shall be governed by and interpreted in accordance with the laws of the State of New York, USA, applicable to contracts entered into and to be performed wholly within the State of New York, excluding conflict of laws principles.

14.10 Disputes. In the event of any controversy or claim arising out of, relating to or in connection with any provision of this Agreement, or the rights or obligations of the Parties hereunder, the Parties shall try to settle their differences amicably between themselves. Either Party may initiate such informal dispute resolution by sending written notice of the dispute to the other Party, and within ten (10) days after such notice appropriate representatives of the Parties shall meet for attempted resolution by good faith negotiations. If such representatives are unable to resolve promptly such disputed matter, it shall be referred to the President of Targacept and such member of APSA's Executive Committee as APSA shall designate for discussion and resolution. If such personnel are unable to resolve such dispute within thirty (30) days of initiating such negotiations, the parties agree first to try in good faith to settle the dispute by mediation under the Commercial Mediation Rules of the American Arbitration Association, before resorting to litigation.

14.11 Notices and Deliveries. Any notice, request, delivery, approval or consent required or permitted to be given under this Agreement shall be in writing and shall be deemed to have been sufficiently given if delivered in person, transmitted by telecopier (receipt verified) or by express courier service (signature required) or five (5) days after it was sent by registered letter, return receipt requested (or its equivalent), to the Party to which it is directed at its address shown below or such other address or facsimile number as such party shall have last given by notice to the other Parties.

If to APSA, addressed to:

Aventis Pharma SA
20, avenue Raymond Aron
92160 Antony, France
Telecopier: (++33) 1 5571 3348
Attn.: Marie Christine Dubroeucq

With a copy to:

Aventis Pharma SA
20, avenue Raymond Aron,
92160 Antony, France
Telecopier: (++33) 1 5571 6431
Attn.: General Counsel

If to Targacept, addressed to:

Targacept, Inc.
Postal Mail Address:
P.O. Box 1487
Winston-Salem, NC 27102-1487
Street Address:
950 Reynolds Boulevard
Winston-Salem, NC 27105
Telecopier: (336) 741-2638
Attn.: President

14.12 No Consequential Damages. SUBJECT TO SECTIONS 10.1 AND 10.2, IN NO EVENT SHALL EITHER PARTY OR ANY OF ITS RESPECTIVE AFFILIATES BE LIABLE TO THE OTHER PARTY OR ANY OF ITS AFFILIATES FOR SPECIAL, INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES, WHETHER IN CONTRACT, WARRANTY, TORT, NEGLIGENCE, STRICT LIABILITY OR OTHERWISE, INCLUDING, BUT NOT LIMITED TO, LOSS OF PROFITS OR REVENUE, OR CLAIMS OF CUSTOMERS OF ANY OF THEM OR OTHER THIRD PARTIES FOR SUCH OR OTHER DAMAGES.

14.13 Waiver. A waiver by either Party of any of the terms and conditions of this Agreement in any instance shall not be deemed or construed to be a waiver of such term or condition for the future, or of any subsequent breach hereof. All rights, remedies, undertakings, obligations and agreements contained in this Agreement shall be cumulative and none of them shall be in limitation of any other remedy, right, undertaking, obligation or agreement of either party.

14.14 Severability. When possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be prohibited by or invalid under applicable law, such provision will be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of this Agreement. The parties shall make a good faith effort to replace the invalid or unenforceable provision with a valid one which in its economic effect is most consistent with the invalid or unenforceable provision.

14.15 Counterparts. This Agreement may be executed simultaneously in any number of counterparts, any one of which need not contain the signature of more than one Party but all such counterparts taken together shall constitute one and the same agreement, each copy of which shall for all purposes be deemed to be an original.

14.16 Patent Due Diligence. Targacept shall make available all reasonably necessary records and employees of Targacept and its Affiliates and otherwise cooperate fully in all reasonable inquiries, investigations and due diligence conducted by APSA after the Effective Date concerning the intellectual property status of the Collaboration Compounds, and APSA shall have a period of ninety (90) days after the Effective Date unilaterally to classify any Collaboration Compound as a Terminated Compound if APSA is not satisfied in its discretion with the intellectual property status or protection of such Collaboration Compound.

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their respective duly authorized officers as of the day and year first above written.

Targacept, Inc.

By: /s/ J. Donald deBethizy
J. Donald deBethizy
President and CEO

Aventis Pharma SA

By: /s/ E. Canet
Emmanuel Canet
Senior Vice President DIA France

Executing this Agreement solely to effect the assignment of its rights and obligations to Aventis Pharma SA:

Aventis Pharmaceuticals Inc.

By: /s/ Charles D. Dalton
Vice President, Legal Corporate Development

Exhibit A: Phase Transition Criteria

[********]

[Entire 16-page document has been redacted.]

Exhibit B: Targacept Compounds

[********]

[Entire table has been redacted.]

Exhibit C: Research and Development Plan

[********]

[Entire eight-page document has been redacted.]

Exhibit D: First Semi-Annual Research Plan

[********]

[Entire table has been redacted.]

Exhibit E(1): Patent Rights

[********]

[Entire table has been redacted.]

Exhibit E(2): UK Compound Patent Rights

[********]

Exhibit 10.14

[********] 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, DEVELOPMENT AND LICENSE AGREEMENT

between

TARGACEPT, INC.

and

DR. FALK PHARMA GmbH

TABLE OF CONTENTS

COLLABORATIVE RESEARCH, DEVELOPMENT AND LICENSE AGREEMENT

This Collaborative Research, Development and License Agreement (this "Agreement") is made and entered into as of January 26, 2001, by and between **Targacept, Inc.**, a Delaware corporation having its principal place of business at 950 Reynolds Boulevard, Winston-Salem, North Carolina 27105 ("Targacept"), and **Dr. Falk Pharma GmbH**, a corporation organized and existing under the laws of Germany having its place of business at Leinenweberstrasse 5, 79041 Freiburg, Germany ("Dr. Falk") (each of Targacept and Dr. Falk, a "Party" and, collectively, the "Parties").

Recitals:

WHEREAS, Targacept possesses proprietary technology and know-how related to the discovery, identification and synthesis of nicotinic agonists and has identified and applied for patents on certain nicotinic agonist compounds; and

WHEREAS, Dr. Falk is engaged in the research, development and marketing of products for the treatment of, among other things, ulcerative colitis; and

WHEREAS, Targacept and Dr. Falk desire to collaborate in the research, development and commercialization of nicotinic therapeutics for use in the prevention or treatment of ulcerative colitis.

NOW, THEREFORE, in consideration of the various promises and undertakings set forth herein, the Parties agree as follows:

ARTICLE 1

Definitions

Unless otherwise specifically provided herein, the following terms shall have the following meanings:

1.1 "Affiliate" with respect to any Person, means any Person that directly, or indirectly through one or more intermediaries, controls, is controlled by or is under common control with such Person or with the same group of Persons controlling such Person. For the purposes of this Section 1.1 only, "control" refers to (a) the possession, directly or indirectly, of the power to direct the management or policies of a Person, whether through the ownership of voting securities, by contract or otherwise, or (b) the ownership, directly or indirectly, of at least 50% (or, if less, the maximum ownership interest permitted by law) of the voting securities or other ownership interests of a Person (without regard to contractual rights that vest certain special voting rights in certain parties).

1.2 "Agreement" shall have the meaning ascribed to it in the preamble.

1.3 "Back-Up Compound" means any Collaboration Compound that has been selected as such hereunder, or any salt, solvate, prodrug form, inclusion complex, metabolite or other formulation thereof.

1.4 "Blocking Patent" shall have the meaning ascribed to it in Section 7.9.

1.5 "Collaboration Compound" means any compound, or any salt, solvate, prodrug form, inclusion complex, metabolite or other formulation thereof, that is a Targacept Compound, Development Compound or Back-Up Compound.

1.6 "Confidential Information" means (a) all information and data supplied by a Party under this Agreement, which, if disclosed in written, graphic or electronic form, is marked or otherwise designated as "confidential" or "proprietary" and, if disclosed orally, is summarized and designated as "confidential" or "proprietary" in a writing provided to the receiving Party not later than sixty (60) days after such disclosure; and (b) all other information expressly classified as "**Confidential Information**" hereunder.

1.7 "Control" means, with respect to an item of information or an intellectual property right, possession of the ability, whether by ownership or license, to grant a license or sublicense as provided for herein under such item or right without violating the terms of any agreement or other arrangements with any Third Party.

1.8 "Cost of Goods Sold" means with respect to any Licensed Product, **[********]**.

1.9 "Derivative" means with respect to any compound, a derivative or other improvement of such compound or any salt, solvate, prodrug form, inclusion complex, metabolite or other formulation thereof.

1.10 "Development Compound" means any Collaboration Compound that has been selected as such hereunder, or any salt, solvate, prodrug form, inclusion complex, metabolite or other formulation thereof.

1.11 "Dr. Falk" shall have the meaning ascribed to it in the preamble.

1.12 "Dr. Falk Indemnitees" shall have the meaning ascribed to it in Section 10.2.

1.13 "Dr. Falk Know-How" means all know-how, trade secrets, techniques, methods, developments, materials, compositions, inventions or data of any kind necessary or useful for the identification, pharmacological development, synthesis, characterization, optimization, assaying, formulation or use of Collaboration Compounds or Licensed Products (but excluding the Dr. Falk Patents, the Joint Patents, the Joint Know-How and any information that Dr. Falk is restricted from disclosing due to confidentiality obligations to a Third Party) that is Controlled by Dr. Falk or an Affiliate of Dr. Falk at any time during the term of this Agreement.

1.14 "Dr. Falk Patents" means all Patent Rights Controlled by Dr. Falk or an Affiliate of Dr. Falk that claim (a) Collaboration Compounds (or pharmaceutical preparations containing the same), or (b) the manufacture or use of any Collaboration Compounds, to the

extent that such Patent Rights claim inventions made prior to or during the term of this Agreement.

1.15 "Effective Date" means January 26, 2001.

1.16 "Executive Management Committee" or **"EMC"** means that committee to be formed pursuant to Section 6.8.

1.17 "Fair Market Value" means the cash consideration that the selling party would receive from an unaffiliated, unrelated buyer in an arms' length sale of an identical item sold in the same quantity and at the same time and place of the transaction.

1.18 "FDA" means the United States Food and Drug Administration, or the successor federal agency thereto.

1.19 "Field" means the treatment or prevention in humans of one or more Indications.

1.20 "First Commercial Sale" means, with respect to any Licensed Product in any country, the first sale for use or consumption by the general public of such Licensed Product in such country after all Regulatory Approvals have been obtained in such country.

1.21 "FTE" means a full-time Targacept scientist or laboratory technician or any other employee of Targacept or its Affiliates specifically approved as an FTE by Dr. Falk, or a full-time Dr. Falk scientist or laboratory technician or any other employee of Dr. Falk or its Affiliates specifically approved as an FTE by Targacept, in each case to the extent dedicated to the research and development of Collaboration Compounds or support thereof, or in the case of a less than full-time dedicated person, a full-time, equivalent person year, based upon a total of forty-seven (47) weeks (*i.e.*, one thousand eight hundred eighty (1,880) hours) per year of scientific or other work on or directly related to the research and development of Collaboration Compounds. Work on or directly related to the research and development of Collaboration Compounds to be performed by such employees may include, without limitation, experimental laboratory work, recording and documenting results, reviewing literature and references, holding scientific discussions, work on preclinical and clinical development activities, work on preparation and prosecution of applications seeking Regulatory Approvals and any other activities assigned to Targacept or Dr. Falk, as the case may be, under the Research and Development Plan or any Semi-Annual R&D Plan.

1.22 "Full Royalty Term" shall have the meaning ascribed to it in Section 7.4.

1.23 "Indication" means:

(a) ulcerative colitis; and

(b) other gastrointestinal and liver diseases.

1.24 "Joint Know-How" means all know-how, trade secrets, techniques, methods, developments, materials, compositions, inventions or data of any kind (but excluding

the Joint Patents) made jointly by employees or agents of Dr. Falk or its Affiliates and by employees or agents of Targacept or its Affiliates at any time during the R&D Term.

1.25 "Joint Patents" means all Patent Rights that claim or cover inventions within the Research Technology that are made jointly by employees or agents of Targacept or its Affiliates and by employees or agents of Dr. Falk or its Affiliates and name as inventors one or more employees or agents of Targacept or its Affiliates together with one or more employees or agents of Dr. Falk or its Affiliates, made during the R&D Term.

1.26 "Joint Research Technology" means all Research Technology that is made, developed or discovered jointly by employees or agents of Targacept or its Affiliates and by employees or agents of Dr. Falk or its Affiliates, but excluding the Joint Patents, made during the R&D Term.

1.27 "JRDT" means the Joint Research and Development Team to be formed pursuant to Section 6.1.

1.28 "Know-How" means Targacept Know-How or Dr. Falk Know-How, as the case may be.

1.29 "Licensed Product" means any product, including any formulation thereof, containing or comprising a Development Compound.

1.30 "Losses" shall have the meaning ascribed to it in Section 10.1.

1.31 "Major Country" means each of France, Germany and the United Kingdom.

1.32 "Material Unexpected Technical Problem" shall have the meaning ascribed to it in Section 2.6(a).

1.33 "Materials" shall have the meaning ascribed to it in Section 2.11.

1.34 "Net Profit" means the Net Sales invoiced, received or realized by Dr. Falk or its Affiliates or its Sublicensees, as the case may be, from the sale of Licensed Products in the Territory, less **[********]**.

1.35 "Net Sales" means [********].

1.36 "Nicotinic Compound" means a compound [********].

1.37 "Non-FilingParty" shall have the meaning ascribed to it in Section 8.2(e).

1.38 "Partial Royalty Term" shall have the meaning ascribed to it in Section 7.4.

1.39 "Party" and **"Parties"** shall have the meaning ascribed to it in the preamble.

1.40 "Patent Right" means rights under (a) any issued and existing letters patent, including any extensions, supplemental protection certificates, registration, confirmation, reissue, reexamination or renewal thereof, (b) pending applications, including any continuation, divisional, continuation-in-part application thereof, for any of the foregoing, and (c) all counterparts to any of the foregoing issued by or filed in any country or other jurisdiction.

1.41 "PCT" means the Patent Cooperation Treaty.

1.42 "Pentad Patents" means all Patent Rights Controlled by Targacept or an Affiliate of Targacept that claim the Pentad Technology.

1.43 "Pentad Technology" means proprietary know-how of Targacept and its Affiliates concerning structure activity, relationships of Nicotinic Compounds and nicotinic receptors, pharmacophore mapping of nicotinic receptors and computational and quantum mechanical methods for use in the design, synthesis and evaluation of pharmacologically active agents, including but not limited to Nicotinic Compounds.

1.44 "Person" means any natural person, corporation, firm, business trust, joint venture, association, organization, company, partnership or other business entity, or any government or agency or political subdivision thereof.

1.45 "Phase I" means that portion of the clinical development program that generally provides for the first introduction into humans of a product with the primary purpose of determining safety, metabolism and pharmacokinetic properties and clinical pharmacology of the product.

1.46 "Phase II" means that portion of the clinical development program which provides for small scale clinical trials primarily to determine efficacy of a product and certain other factors, such as dosing range.

1.47 "Phase III" means that portion of the clinical development program which provides for the pivotal trials of a product in sufficient numbers of patients to establish the safety and efficacy of a product for the desired label claims and indications.

1.48 "Regulatory Approval" means any and all approvals (including price and reimbursement approvals), licenses, product registrations, or authorizations of any federal, national, state, provincial or local regulatory agency, department, bureau or other government entity, necessary for the manufacture, use, storage, import, transport and sale of a Licensed Product in a country.

1.49 "Research" means the collaborative research program undertaken by the Parties pursuant to this Agreement to characterize, optimize and conduct research and development activities regarding Collaboration Compounds for use in the Field, in accordance with the Research and Development Plan.

1.50 "Research and Development Plan" shall have the meaning provided it in Section 2.3.

1.51 "Research Technology" means all tangible and intangible know-how, trade secrets, inventions (whether or not patentable), discoveries, developments, data, clinical and preclinical results, information, and physical, chemical or biological material, and any replication of or any part of any of the foregoing, made by employees or agents of Targacept or its Affiliates or Dr. Falk or its Affiliates, either alone or jointly prior to or during the R&D Term.

1.52 "Rest of World" means all countries throughout the world other than those included in the Territory.

1.53 "R&D Term" means the period commencing on January 1, 2001 and terminating on the earlier of: (a) the receipt of Regulatory Approval by Dr. Falk in the last country in the Territory; (b) the date that this Agreement is terminated pursuant to the terms hereof; or (c) on December 31, 2008, or such later date as the Parties may mutually agree in writing.

1.54 "Semi-Annual R&D Plan" shall have the meaning ascribed to it in Section 2.4.

1.55 "Shares" shall have the meaning ascribed to it in Article 13.

1.56 "Sublicensee" means any Third Party to which Dr. Falk or Targacept has granted sublicense rights under the licenses granted Dr. Falk or Targacept (as the case may be) hereunder, which rights include at least the rights to distribute and sell Licensed Products. Third Parties that are permitted only to manufacture or finish Licensed Products for supply to Dr. Falk, Targacept or their respective Affiliates or Sublicensees are not "Sublicensees."

1.57 "Targacept" shall have the meaning ascribed to it in the preamble.

1.58 "Targacept Compounds" means (a) TC 240312 and a second compound to be finally selected by the JRDT **[********]** and (b) any other compound identified by Targacept or its Affiliates prior to the end of the R&D Term and jointly selected by the Parties on the basis of mutually agreed upon criteria together with any salt, solvate, prodrug form, inclusion complex, metabolite or other formulation thereof, together with any Derivative of a Collaboration Compound made solely by Targacept. No other compound shall be considered a Targacept Compound.

1.59 "Targacept Indemnitees" shall have the meaning ascribed to it in Section 10.1.

1.60 "Targacept Know-How" means all know-how, trade secrets, techniques, methods, developments, materials, compositions, inventions or data of any kind necessary or useful for the identification, pharmacological development, synthesis, characterization, optimization, assaying, formulation, manufacture or use of Collaboration Compounds or Licensed Products that is Controlled by Targacept or an Affiliate of Targacept at any time during the term of this Agreement, but excluding the Pentad Technology, the Pentad Patents, the

Targacept Patents, the Joint Patents, the Joint Know-How and any information that Targacept is restricted from disclosing due to confidentiality obligations to a Third Party.

1.61 "Targacept Patents" means all Patent Rights that are Controlled by Targacept or its Affiliates that claim (a) any Collaboration Compounds or Licensed Products (or pharmaceutical preparations containing the same), (b) the manufacture or use of any Collaboration Compounds or Licensed Products, or (c) methods or materials used for discovering, identifying, assaying, characterizing or optimizing any Collaboration Compounds, to the extent that such Patent Rights claim inventions made prior to or during the term of this Agreement.

1.62 "Terminated Compound" means a Targacept Compound that ceases to be a Collaboration Compound or a Licensed Product pursuant to Sections 2.2(b), 2.8 and 3.3.

1.63 "Territory" means those countries listed on Exhibit A hereto.

1.64 "Third Party" means a Person other than Targacept, Dr. Falk or their respective Affiliates.

1.65 "Third Party License" shall have the meaning ascribed to it in Section 7.9.

1.66 "Valid Claim" means a claim of an issued and unexpired patent which has not been revoked or held unenforceable or invalid by a decision of a court or governmental agency of competent jurisdiction from which no appeal can be taken or, after mutual consultation and agreement between the Parties, an appeal is not taken within the time allowed for appeal, and which has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue or disclaimer or otherwise.

ARTICLE 2

Research and Development

2.1 Research. Commencing on the Effective Date, the Parties shall conduct the Research pursuant to the Research and Development Plan, with the goals of: (a) completing the selection of a second Targacept Compound and completing all preclinical research on the two Targacept Compounds in order to position them for further development as Development Compounds; and (b) identifying and selecting certain Collaboration Compounds as Back-Up Compounds to the Development Compounds. The Parties shall conduct the Research in accordance with this Agreement, the Research and Development Plan (as it may be amended hereunder from time to time) and the Semi-Annual R&D Plans established pursuant to the provisions of this Article 2.

2.2 Completion of Preclinical Research and Selection of Back-Up Compounds.

(a) *Completion of Preclinical Research.* Targacept shall complete preclinical chemical and pharmaceutical characterization and *in vivo* pharmacological and toxicological profiles for the two initial Targacept Compounds as set forth in the Research and Development Plan and shall inform the JRDT of the progress and results thereof.

(b) *Selection and Rejection of Targacept Compounds.* The Parties currently expect that both Targacept Compounds will initially be selected as Development Compounds. The JRDT shall review the results of the preclinical research concerning the two Targacept Compounds provided by Targacept pursuant to Section 2.2(a). Based upon the standards set forth in the Research and Development Plan and such other appropriate factors as the Parties mutually agree, the JRDT shall confirm the selection of the Targacept Compounds as Development Compounds or determine whether either Targacept Compound clearly does not warrant further scientific evaluation and should instead be classified as Terminated Compounds. Based upon standards set forth in the Research and Development Plan and such other factors as the JRDT deems appropriate, the JRDT from time to time shall also identify and select the Back-Up Compounds for development (or potential development) in accordance with the Research and Development Plan. A Collaboration Compound may be selected as a Back-Up Compound and a Back-Up Compound may be selected as a Development Compound at any time during the term of this Agreement. If a Targacept Compound is classified as a Terminated Compound or is not selected as a Development Compound or Back-Up Compound within the time frames established in the Research and Development Plan, it shall automatically cease to be a Collaboration Compound and thereafter shall not be subject to research, development or commercialization by Dr. Falk or its Affiliates or Sublicensees pursuant to this Agreement.

2.3 Research and Development Plan. Attached hereto as Exhibit B is the initial version of the Research and Development Plan (as it may be modified from time to time, the "Research and Development Plan") that sets forth the overall general plan for the Research activities expected to be performed by Targacept pursuant to this Agreement and the clinical development plan for the development of Development Compounds through all phases of clinical trials and Regulatory Approvals. The Research and Development Plan may be amended by the JRDT from time to time in accordance with the provisions of Article 6.

2.4 Semi-Annual Research and Development Plans. On an annual basis for the year ending December 31, 2001 and on a semi-annual basis commencing January 1, 2002, the Parties shall jointly establish a detailed research and development plan and budget, as may be modified from time to time (each a "Semi-Annual R&D Plan") for the research and development activities to be performed by Dr. Falk and Targacept in the Territory during the following six (6) month period starting January 1 or July 1, as the case may be (or such longer period as may be set forth for certain tasks in the Semi-Annual R&D Plan). Each Semi-Annual R&D Plan may be amended by the JRDT from time to time in accordance with the provisions of Article 6. Each Semi-Annual R&D Plan shall be in accord with the Research and Development Plan and shall specify in reasonable detail:

(a) the objectives of the research and development for the ensuing period(s);

(b) the specific research and development and other activities to be performed by Dr. Falk, Targacept and Third Parties during such period;

(c) the specific deliverables expected to be provided by Dr. Falk, Targacept and Third Parties, and the projected dates by which such deliverables will be provided;

(d) the FTEs to be devoted by each Party to its tasks under the Semi-Annual R&D Plan; and

(e) the total funding and financial support expected to be provided by both Parties for the ensuing six-month period to support the activities covered by the Semi-Annual R&D Plan (which funding will be subject to adjustment as provided in Section 2.6) and the mechanisms and procedures for funding such activities on a joint basis.

2.5 Preparation and Approval of Semi-Annual R&D Plans. Attached hereto as Exhibit C is the Semi-Annual R&D Plan for the first year of the R&D Term ending December 31, 2001. It is intended that the Semi-Annual R&D Plan for each subsequent semi-annual period during the R&D Term shall be approved by the JRDT by May 1 and December 1 of each calendar year during the R&D Term. Each budget included in a Semi-Annual R&D Plan shall be set forth in United States Dollars. For Third Party expenditures to be made by a Party outside the United States, the Parties shall agree on a contract-by-contract basis who is responsible for paying such amounts, in what currency amounts are to be paid and what procedures will be used to reconcile amounts paid to budgeted items as a result of currency fluctuations. Unless otherwise agreed by the Parties, budgeted items for expenditures outside the United States shall be calculated based on the arithmetic average of the daily currency exchange rates in effect as of the thirty (30) days preceding the period to which the budget relates and actual expenditures made by a Party under a Semi-Annual R&D Plan in a currency other than United States Dollars shall be reconciled for each currency based on the arithmetic average of the daily exchange rates during the period covered by the Semi-Annual R&D Plan. All exchange rates for these purposes shall be obtained from the *Reuters Daily Rate Report* or, if such exchange rates are not available on any day, *The Wall Street Journal*, Eastern U.S. Edition, or, if such exchange rates are not available on any day, as otherwise agreed by the Parties.

2.6 Research Efforts.

(a) Each Party agrees to commit such resources of such Party and its Affiliates as are specified in the Semi-Annual R&D Plans to perform its obligations set forth therein, ***provided, however***, that either Party shall have the right to notify the JRDT promptly upon becoming aware of an unanticipated scientific or technical problem which makes it likely to preclude such Party from fulfilling any obligation set forth in a Semi-Annual R&D Plan with the FTEs budgeted to the performance of such obligation (a "Material Unexpected Technical Problem"). As part of such notification, the affected Party shall provide the JRDT with a reasonably detailed description of such Material Unexpected Technical Problem, together with its good faith estimate of the number of additional FTEs and other expenses which will be required to perform such obligation in light of such Material Unexpected Technical Problem. Upon receipt of such notification, the JRDT shall determine whether to modify the Semi-Annual R&D Plan as it applies to such obligation to (i) refocus the remaining unused FTE resources

allocated to such obligation to other obligations under the Plan, (ii) increase the funding to be provided by both Parties for such obligation, subject to the agreement of both Parties on the amount of such increased funding, (iii) terminate any further activities relating to such obligation, or (iv) take such other action as may be mutually agreeable to the Parties; ***provided, however,*** that, following notification of a Material Unexpected Technical Problem, the affected Party shall not be required to perform activities related to an obligation after such notification unless and until the JRDT acts to provide additional funding. In connection with the performance by each Party of its obligations hereunder, each Party shall maintain (or cause its Affiliates to maintain) and utilize such scientific staff, laboratories, offices and other facilities as are reasonably designed for such purposes. Each party shall use personnel with such skills and experience as are reasonably designed to accomplish efficiently and expeditiously the objectives of the Research as set forth in the Research and Development Plan and each Semi-Annual R&D Plan in good scientific manner and in compliance in all material respects with all applicable laws, rules, regulations, and all other requirements of applicable good laboratory practices; ***provided, however,*** that except as otherwise required by law, each Party shall be required to comply only with general good laboratory practices as practiced by like companies in the biotechnology industry in performing similar research and not with the requirements for Good Laboratory Practices prescribed by the FDA.

The Parties shall equally bear all costs and expenses in connection with the Research in the Territory. FTEs dedicated by Targacept to research and development tasks under a Semi-Annual R&D Plan in 2001 shall be credited at the rate of **[********]**, which amount shall be subject to automatic adjustment each year. FTEs dedicated by Dr. Falk to research and development tasks under a Semi-Annual R&D Plan in 2001 shall be credited at the rate of **[********]**, which amount shall be subject to automatic adjustment each year. The FTE reimbursement rate charged by Targacept shall be increased automatically on an annual basis as of January 1 by an amount equal to the percentage increase (if any) in the CPI (as defined below) in effect in December of the immediately preceding year for the relevant year for which the adjustment is to be calculated, over the CPI in effect in December of the prior year. The FTE reimbursement rate charged by Dr. Falk shall be increased automatically on an annual basis as of January 1 by an amount equal to the percentage increase (if any) in the CPI-G (as defined below) in effect in December of the immediately preceding year for the relevant year for which the adjustment is to be calculated, over the CPI-G in effect in December of the prior year. Such adjustments are to be calculated by each Party as soon as the CPI and the CPI-G for December are published and then retroactively applied to all expenditures made by Targacept (in the case of changes to the CPI) and Dr. Falk (in the case of changes to the CPI-G) since the corresponding January 1. For the purpose of this provision, “CPI” means the Consumer Price Index for U.S. City Averages for all Urban Customers, All Items, as compiled and published by the United States Bureau of Labor Statistics (1984 = 100), and the “CPI-G” means the Price Index for Cost of Living for Private Households in Germany, as compiled and published in the monthly report of the German Bundesbank. If the Bureau of Labor Statistics or the German Bundesbank substantially revises the manner in which either the CPI or the CPI-G is determined, an adjustment shall be made in the revised index that will produce results equivalent, as nearly as possible, to those that would be obtained if the CPI or the CPI-G, as the case may be, had not been so revised. If either the CPI or the CPI-G specified in this Section is no longer available, the JRDT shall substitute a comparable index based upon changes in the cost of living or purchasing power of the consumer dollar published by another United States governmental agency (in the case of the CPI) or by another German governmental agency or financial institution (in the case of the CPI-G).

(b) If the costs and expenses (including allocated FTEs) to be borne by one Party under a Semi-Annual R&D Plan exceed the costs and expenses (including allocated FTEs) to be borne by the other Party under such Semi-Annual R&D Plan, the Parties shall set forth in the Semi-Annual R&D Plan the agreed procedures for reimbursement by the other Party of its share of the excess costs and expenses. Unless otherwise agreed by the Parties in a Semi-Annual R&D Plan, the Party incurring such excess costs and expenses shall be reimbursed by the other Party in advance on a quarterly basis for **[********]** of such excess costs and expenses. No later than July 31 or February 28, as the case may be, immediately following the end of the six-month period covered by a Semi-Annual R&D Plan, a Party that has been paid in advance under such Plan shall furnish the other Party with a statement detailing the costs and expenses incurred by it, including the number of FTEs actually dedicated to the performance of each Research obligation set forth in such Semi-Annual R&D Plan. However, for any obligation set forth in such Semi-Annual R&D Plan (as it may be amended from time to time pursuant to this Agreement), such statement (A) shall not state a number of FTEs more than **[********]** of the budgeted FTEs allocated to such obligation even if the number of FTEs actually dedicated to such performance was more than **[********]** of such budgeted amount; and (B) absent authorization from the JRDT, shall not include or request payment for any FTEs for any work performed on any obligation after the occurrence of a Material Unexpected Technical Problem related to such obligation. Within forty-five (45) days after the receipt of such statement, the Parties shall reconcile the actual authorized expenditures made and costs incurred by each Party under the Semi-Annual R&D Plan and based on such reconciliation, shall reimburse each other as appropriate for any under- or over-payments of amounts previously advanced pursuant to this Section 2.6(b).

(c) Each Party shall keep complete and accurate books and financial records pertaining to its costs and expenses of performing the Research (in accordance with generally accepted accounting principles consistently applied), which books and financial records shall be retained by the Parties until three (3) years after the end of the period to which such books and records pertain. Each Party shall have the right, at its expense, to have certified public accountants, who shall be reasonably acceptable to the other Party, audit the books and financial records of the other Party relating to its costs and expenses during one or more six-month periods; ***provided, however,*** that a Party shall not have the right to audit a six-month period more than two (2) years after the end of such period, to conduct more than one such audit in any twelve-month period, or to audit any six-month period more than once.

2.7 Development Responsibilities of the Parties. The Parties shall be jointly responsible for and shall jointly make all decisions through the JRDT regarding development of the Development Compounds in the Territory through preclinical development and all phases of clinical trials, while Targacept shall be solely responsible for development of the Development Compounds through preclinical development and all phases of clinical trials in the Rest of World. The Parties, acting through the JRDT, shall jointly make all decisions regarding, make all applications for and obtain all Regulatory Approvals (including price and reimbursement approvals) in the Territory, while Targacept shall make all decisions regarding, make all applications for and obtain all Regulatory Approvals (including price and reimbursement approvals) in its name in the Rest of World. All Regulatory Approvals in the Territory will be

prosecuted and obtained in the name of Dr. Falk with joint participation by Targacept in all decisions regarding the same and the joint right to attend all meetings with regulatory authorities. In the event that the laws or regulations of a country in the Territory do not allow the Licensed Products to be registered solely in the name of Dr. Falk, Dr. Falk shall register the Licensed Products at its discretion (i) jointly in the name of Dr. Falk and any applicable Affiliate or Sublicensee or (ii) solely in the name of any applicable Affiliate or Sublicensee. The Parties shall equally bear all costs and expenses in connection with the development of each Development Compound in the Territory and the obtaining of Regulatory Approvals in the Territory. Targacept shall bear all costs and expenses in connection with the development of each Development Compound and the obtaining of Regulatory Approvals in the Rest of World. The Parties shall fund their obligations under the Research and Development Plan and each Semi-Annual R&D Plan in accordance with the funding requirements and reimbursement mechanisms and procedures set forth therein and in Section 2.6(b).

2.8 Termination of Development of a Development Compound. The Parties may jointly terminate the development of any Development Compound at any time. Dr. Falk may terminate the development of any Development Compound at any time in its sole discretion after completion of Phase II clinical trials for such Development Compound upon prior notice to Targacept. The Parties may at that time jointly designate a former Development Compound as a Back-Up Compound. If the Parties or Dr. Falk terminate the development of any Development Compound and the Parties do not jointly designate such compound as a Back-Up Compound, such compound shall be deemed to be a Terminated Compound. In the event no Development Compounds or Back-Up Compounds remain under development, either Party may terminate this Agreement under Section 11.3.

2.9 Termination of Development of all Development Compounds. If upon expiration of the R&D Term, the Parties shall have failed to obtain Regulatory Approval of at least one Development Compound in at least one Major Country in the Territory, then Targacept may terminate this Agreement under Section 11.3; ***provided, however,*** that if an application for Regulatory Approval in a Major Country in the Territory has been made prior to the expiration of the R&D Term and is then pending, then the right to terminate this Agreement shall be tolled until no later than **[*********]**, after which Targacept may terminate this Agreement under Section 11.3 unless such Regulatory Approval has been obtained, in which case Targacept shall have no such right.

2.10 Development Information and Reporting. From and after the commencement of the first Phase I trial covering a Development Compound in the Territory, Dr. Falk shall prepare and maintain complete and accurate information regarding the clinical development of Development Compounds in the Territory and shall make such information (including raw data) available to Targacept through the JRDT in the form of reasonably detailed reports in electronic and paper form as specified by the JRDT that summarize the status and results of such development efforts provided to the JRDT at least on a semi-annual basis. Dr. Falk shall also provide Targacept with prompt adverse event reporting regarding clinical development of the Development Compounds in the Territory in the form and at the times as are required by the applicable regulatory authorities (including all requirements of the FDA to which Targacept is subject and of which Dr. Falk is advised in writing by Targacept). From and after the commencement of the first Phase I trial covering a Development Compound in the Rest of World, Targacept shall prepare and maintain complete and accurate information regarding the

clinical development of Development Compounds in the Rest of World and shall make such information (including raw data) available to Dr. Falk through the JRDT in the form of reasonably detailed reports in electronic and paper form as specified by the JRDT that summarize the status and results of such development efforts provided to the JRDT at least on a semi-annual basis. All Targacept know-how arising from development of the Development Compounds in the Rest of World shall be covered by the license granted by Targacept to Dr. Falk in Section 5.1 hereof and shall be available for reference and use by Dr. Falk for regulatory, sales and marketing purposes in the Territory. All Dr. Falk Know-How arising from development of the Development Compounds in the Territory shall be considered Joint Know-How, shall be jointly owned by the Parties, and shall be available for reference and use by Targacept for regulatory, sales and marketing purposes in the Rest of World. Each Party also shall respond to reasonable requests by JRDT for additional information regarding the development of Development Compounds in their respective territories. The JRDT may provide comments to either Party regarding development efforts, and such Party shall take appropriate action to respond to such comments.

2.11 Material Transfer. In order to facilitate the performance of research and development activities, either Party may provide to the other Party certain biological materials or chemical compounds including, but not limited to Collaboration Compounds, receptors, reagents and screens (collectively, "Materials") owned by or licensed to the supplying Party (other than under this Agreement) for use by the other Party in furtherance of such activities, subject to a separate global Material Transfer Agreement if desired by the supplying Party, in a form to be mutually agreed by the Parties. Except as otherwise provided under this Agreement, all such Materials delivered to the other Party shall remain the sole property of the supplying Party, shall be used only in furtherance of research and development activities under this Agreement in accordance with the Research and Development Plan and any Semi-Annual R&D Plan, shall be maintained solely under the control of the other Party, shall not be used or delivered to or for the benefit of any Third Party (or in the case of Dr. Falk, any Sublicensee) without the prior written consent of the supplying Party, and shall not be used in research or testing involving human subjects except in strict compliance with the Research and Development Plan or any Semi-Annual R&D Plan. The Materials supplied under this Section 2.11 shall be used with prudence and appropriate caution in any experimental work, since not all of their characteristics may be known. SUBJECT TO SECTIONS 12.1 AND 12.2 HEREOF, THE MATERIALS ARE PROVIDED "AS IS" AND WITHOUT ANY REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION ANY IMPLIED WARRANTY OF MERCHANTABILITY OR OF FITNESS FOR ANY PARTICULAR PURPOSE OR ANY WARRANTY THAT THE USE OF THE MATERIALS WILL NOT INFRINGE OR VIOLATE ANY PATENT OR OTHER PROPRIETARY RIGHTS OF ANY THIRD PARTY.

2.12 Liability. Except as otherwise set forth in Section 10.1, in connection with the conduct of activities under the Research and Development Plan and each Semi-Annual R&D Plan, each Party shall be responsible for, and hereby assumes, any and all risks of personal injury or property damage attributable to the negligent acts or omissions of that Party or its Affiliates, and their respective directors, officers, employees and agents.

2.13 Subcontractors. Either Party may subcontract to Affiliates or Third Parties portions of the research and development activities to be performed by it under any

Semi-Annual R&D Plan, subject to the provisions of this Section 2.13 and the consent of the other Party, which consent shall not be unreasonably withheld. Any subcontractor shall enter into a confidentiality agreement with the contracting party, and shall be in compliance in all material respects with all requirements of applicable laws and regulations, together with all applicable good laboratory practices and good manufacturing practices. The contracting Party shall at all times be responsible for the performance of such subcontractor. Upon the reasonable request of the other Party, a Party shall provide a written list of all subcontractors other than Affiliates with whom such Party has subcontracted under this Section 2.13.

2.14 No Warranty of Success. Nothing contained in this Agreement shall be construed as a warranty on the part of either Party that any results will be achieved by such Party, or that any particular Patent Rights or Know-How developed during the R&D Term will be commercially exploitable.

2.15 No Solicitation of Employees. During the R&D Term and for a period of two (2) years thereafter, each Party agrees not to, and agrees to cause its Affiliates not to, without the consent of the other Party, solicit the employment of any person who during the course of employment with such other Party or any of such other Party's Affiliates was involved with activities related to or conducted in furtherance of the performance of the Research and Development Plan. For purposes of this Section 2.15, "solicit" shall not be deemed to cover general solicitations of employment not specifically targeted at employees of the other Party or any of its Affiliates. This provision shall not preclude either Party from soliciting the employment of any person whose employment with the other Party has terminated or any person who has announced his or her impending resignation or retirement from the other Party.

ARTICLE 3

Commercialization

3.1 Commercialization Responsibilities of the Parties.

(a) *General.* Subject to the terms of this Section 3.1, the Parties shall be jointly responsible for and shall jointly make all decisions through the JRDT regarding commercialization of each Licensed Product in the Territory. Targacept shall retain the sole right to make all decisions regarding commercialization of each Licensed Product in the Rest of World.

(b) *Selection of Manufacturer.* The Parties shall jointly select a Third Party to manufacture Licensed Products for sale in the Territory on terms that are acceptable to the Parties; ***provided***, that such Third Party shall manufacture Licensed Products at facilities and using manufacturing practices that have been approved by the FDA unless **[********]**.

(c) *Approval of Commercialization Plans.* At least **[********]** prior to the anticipated receipt of the first Regulatory Approval for a Licensed Product in a country in the Territory, Dr. Falk shall submit to the JRDT for its review, input and approval an overall commercialization strategy and plan for commercialization of the Licensed Product in the Territory, which shall, *inter alia*, take into consideration the global product commercialization strategy for such Licensed Product presented by Targacept to the JRDT to the extent possible

under the particular requirements of the individual markets in the Territory. In connection with this submission, Dr. Falk shall respond to reasonable questions from the JRDT members regarding such strategy and, subject to Section 6.6 hereof, shall revise its plans to the extent required until the commercialization plan is finally approved by the JRDT.

(d) *Distribution Arrangements.* Following approval of a commercialization plan under Section 3.1(c), Dr. Falk shall be solely responsible for identifying and selecting one or more Third Parties as Sublicensees to distribute, market and resell such Licensed Product in each country in the Territory and for negotiating the terms and conditions of such distribution relationships. All proposed contracts, agreements and other arrangements with distributors of Licensed Products other than Affiliates of Dr. Falk shall be in writing and shall be submitted to the JRDT for review at least ten (10) days prior to execution by Dr. Falk. Such contracts, agreements or other arrangements may be executed by Dr. Falk upon the expiration of such 10-day period without further approval of the JRDT or Targacept; ***provided, however,*** such distributorship contract, agreement or arrangement shall be subject to the approval of Targacept, which approval shall not be unreasonably withheld or delayed, if such distributorship contract, agreement or arrangement (i) conflicts with any material term of the commercialization plan previously approved by the JRDT for such Licensed Product and Targacept notifies Dr. Falk of that conflict prior to the expiration of such 10-day period; (ii) does not obligate the distributor to use commercially reasonable efforts to commercialize the Licensed Product in the territory covered by the contract, agreement or arrangement; or (iii) in the good faith judgement of Targacept, contains one or more provisions that disadvantage the distribution of Licensed Products versus Dr. Falk's other products by providing a material economic advantage or incentive to distributors to commercialize Dr. Falk's other products that is not provided for the distribution of Licensed Products or by imposing a material economic disadvantage or disincentive to commercialization of the Licensed Products that is not imposed on the distribution of Dr. Falk's other products, and Targacept notifies Dr. Falk of the potential conflict of interest resulting therefrom prior to the expiration of such 10-day period; ***provided, however,*** that if Targacept identifies such a conflict of interest, Dr. Falk will be provided a reasonable opportunity to demonstrate that it has sound business reasons based on the particular circumstances affecting the distribution of Dr. Falk's other products and the Licensed Products to justify bona fide differences in the economic terms of distribution for such products. In lieu of obtaining the approval of Targacept, Dr. Falk may modify the proposed contract, agreement or arrangement to eliminate all applicable matters under clauses (i) – (iii) above and resubmit the modified contract to the JRDT for its review in accordance with the two preceding sentences of this Section.

(e) *Commercialization Obligations.* Dr. Falk and its Affiliates and Sublicensees shall use commercially reasonable efforts to commercialize each Licensed Product in each country in the Territory while Targacept and its Affiliates and Sublicensees shall use commercially reasonable efforts to commercialize each Licensed Product in the United States and Japan. In each case, such commercially reasonable efforts shall not be less than those used by a Party with respect to the commercialization of its own products of comparable commercial significance, however, Dr. Falk may elect not to commercialize a Licensed Product in any country in the Territory and Targacept may elect to delay commercialization of a Licensed Product in the United States or Japan for sound business or commercial reasons by providing prompt written notice of such election, together with a detailed explanation of the Party's reasoning, to the JRDT.

3.2 Trademarks. Dr. Falk shall have the sole right and responsibility for developing trademarks for the Licensed Products in the Territory, including product names and distinctive artwork and logos, and seeking registration or other protection of such trademarks in each country in the Territory. The Parties shall jointly share all costs and expenses associated with the development, preparation, registration, maintenance and enforcement of trademarks for the Licensed Products in the Territory and shall jointly own such trademarks. All packaging and printed literature for all Licensed Products offered for sale in the Territory shall display the trademark of Targacept in such size, form and location as is determined by Dr. Falk after consultation with the JRDT, subject to applicable legal requirements. Absent the prior consent of a Party, the other Party shall have no right to use the name or any other trademark of such Party.

3.3 Termination of Commercialization of a Licensed Product. The Parties may terminate the commercialization of any Licensed Product in any country in the Territory at any time if mutually agreed and thereafter Targacept shall be free to develop and commercialize such Licensed Product in such country in the Territory without any obligation to Dr. Falk. If the Parties terminate the commercialization of any Licensed Product in all countries in the Territory (without undertaking the commercialization of another Licensed Product with the same Targacept Compound), such Targacept Compound shall be deemed to be a Terminated Compound and Targacept thereafter shall be free to develop and commercialize such Terminated Compound in the Territory without any obligation to Dr. Falk.

3.4 Termination of Commercialization of all Licensed Products. If Dr. Falk and its Affiliates or Sublicensees fail to use commercially reasonable efforts, consistent with Section 3.1 hereof, to commercialize a particular Licensed Product in any country in the Territory, then subject to compliance with Section 3.5 and if Dr. Falk has not provided the JRDT with sound business or commercial reasons for not commercializing the Licensed Product in such country as provided in Section 3.1, Targacept shall be entitled to terminate the license granted to Dr. Falk pursuant to Section 5.1(b) regarding such Licensed Product in such country without any further obligation to Dr. Falk. In the event that, with respect to a Licensed Product, such license is terminated with respect to all Major Countries, then such Licensed Product shall no longer be deemed to be subject to this Agreement and Targacept shall be free to develop and commercialize such Licensed Product in the Territory without any obligation to Dr. Falk. In the event no Development Compounds or Back-Up Compounds remain under development and no Licensed Products are being commercialized in the Territory, either Party may terminate this Agreement under Section 11.3.

3.5 Breach of Commercialization Diligence Obligations. If at any time either Party determines that the other Party is not meeting the commercialization standards set forth in Section 3.1 (including any dispute by either Party regarding the other Party's election not to commercialize a Licensed Product in a country for sound business reasons), before taking any action with respect to such determination such Party shall provide the other Party with written notice specifying the basis for such determination and any underlying facts in support thereof and such matter shall be submitted to the JRDT for possible resolution in accordance with the procedures in Section 6.6. If the Parties are unable to resolve the matter after exhausting the procedures in Section 6.6, the Party claimed to be in breach shall have the same cure rights (whether such failure applies to one or more Licensed Products or one or more countries) that it would have for a default under Section 11.2(a). If Targacept is found to have failed to use

commercially reasonable efforts to commercialize a Licensed Product in either Japan or the United States, the royalty rates payable to Targacept under Section 7.2 shall be equitably adjusted by the JRDT to reflect Dr. Falk's loss of anticipated royalty revenue under Section 7.3 as a result of such failure.

3.6 Commercialization Information and Reporting. From and after the First Commercial Sale of a Licensed Product in the Territory, Dr. Falk shall provide to Targacept on a semi-annual basis for the first three years and on an annual basis thereafter with reasonably detailed reports regarding the commercialization of such Licensed Product in each country in the Territory. Dr. Falk also shall respond to reasonable requests by Targacept for additional information regarding the commercialization of Licensed Products in the Territory.

ARTICLE 4

Information Exchange

4.1 Disclosure of Enabling Technology; Maintenance of Records Regarding Research and Inventions.

(a) During the R&D Term, each Party shall disclose to the other the Know-How and Patent Rights of such Party for which letters patent have not yet been issued as the other Party reasonably needs to perform its obligations and assigned tasks under the Research and Development Plan; ***provided, however***, that in no event shall Targacept be required to disclose the Pentad Technology and ***provided, further,*** that all such disclosed Know-How and Patent Rights shall be considered Confidential Information.

(b) All work conducted by each Party in the course of performing research and development hereunder shall be thoroughly and accurately recorded, in detail and in good scientific manner and, to the extent reasonably practicable, in separate laboratory notebooks distinct from other work being conducted by such Party. On reasonable notice, and at reasonable intervals, each Party shall have the right to inspect and copy all such records maintained by the other Party reflecting Research Technology or work done under the Research and Development Plan, to the extent reasonably required to carry out its obligations and to exercise its rights hereunder. All such records shall constitute Confidential Information under Section 1.6(b) and shall be deemed the property of the Party creating such records.

(c) In order to protect the Parties' patent rights in all countries in any inventions conceived or reduced to practice during or as a result of the Research, each Party agrees to establish and support a policy which requires its employees to record and maintain all data and information developed in performing the Research in such a manner as to enable the parties to use such records to establish the earliest date of invention and/or diligence to reduction to practice. At a minimum, the policy shall require such individuals to record all inventions generated by them in standard laboratory notebooks which are dated and corroborated by non-inventors on a regular, contemporaneous basis.

4.2 Information and Reports. Each Party shall disclose to the other Party from time to time during the R&D Term any Know-How or Research Technology learned, acquired, discovered, invented or made by such Party, to the extent reasonably required by the

other Party to carry out its obligations and to exercise its rights hereunder; *provided*, *however*, that in no event shall Targacept be required to disclose the Pentad Technology. Such Know-How and Research Technology will be promptly disclosed to the other Party, with meaningful discoveries or advances being communicated as promptly as practicable after such information is obtained or its significance is appreciated. Each Party will provide the other with copies of the raw data generated in the course of performance of work under this Agreement, if reasonably necessary to the other Party's work under this Agreement.

ARTICLE 5

Licenses

5.1 Licenses to Dr. Falk.

(a) *Research and Development License.* Subject to the other provisions of this Agreement, Targacept hereby grants to Dr. Falk and its Affiliates during the R&D Term a co-exclusive (with Targacept) paid-up right and license in the Territory under the Targacept Patents and the Targacept Know-How and Research Technology and under Targacept's rights in the Joint Patents, Joint Research Technology and Joint Know-How, solely to conduct the Research, to characterize, optimize, research and develop the Development Compounds into Licensed Products in the Field and to make, have made and use Collaboration Compounds in the Field solely for research and development purposes in accordance with the Research and Development Plan and each Semi-Annual R&D Plan. "Co-exclusive" shall mean that Dr. Falk shall have no right to exercise its license rights under this Section 5.1(a) except jointly with Targacept under the terms of this Agreement.

(b) *Commercialization License.* Subject to the other provisions of this Agreement (including Section 5.1(a) hereof), effective upon the selection of the first Development Compound for development under this Agreement, Targacept hereby grants to Dr. Falk and its Affiliates (i) a co-exclusive (with Targacept), royalty-bearing right and license in the Territory under the Targacept Patents and the Targacept Know-How and Research Technology, and under Targacept's rights in the Joint Know-How, Joint Research Technology and Joint Patents, to make, have made, import and use Licensed Products for use in the Field; and (ii) an exclusive (including with regard to Targacept) royalty-bearing right and license in the Territory under the Targacept Patents and the Targacept Know-How and Research Technology, and under Targacept's rights in the Joint Know-How, Joint Research Technology and Joint Patents, to sell and offer for sale Licensed Products for use in the Field. "Co-exclusive" shall mean that Dr. Falk shall have no right to exercise its license rights under Section 5.1(b)(i) except jointly with Targacept under the terms of this Agreement. For the avoidance of doubt, it is understood that Dr. Falk's and its Affiliates' exclusive right to sell Licensed Products in the Territory shall include the right to sell such Licensed Products through Sublicensees that have been selected by Dr. Falk in accordance with the procedures in Section 3.1(d) hereof.

5.2 License to Targacept. Subject to the other provisions of this Agreement:

(a) Dr. Falk hereby grants to Targacept an exclusive (except with regard to Dr. Falk), world-wide, paid-up right and license under the Dr. Falk Patents and the Dr. Falk Know-How and Dr. Falk's rights in the Joint Patents, Joint Know-How and Joint Research

Technology, to conduct the Research. For the avoidance of doubt, nothing in this Section 5.2(a) is intended to restrict Dr. Falk's right to use the Dr. Falk Patents and the Dr. Falk Know-How for research and development activities outside the field of nicotinics.

(b) Dr. Falk hereby grants to Targacept the exclusive right to use and to disclose to Third Parties all regulatory and clinical documentation and data developed by or on behalf of Dr. Falk in the Territory in connection with this Agreement and required to be disclosed to Targacept under this Agreement, as reasonably necessary or desirable in connection with the development and commercialization of pharmaceutical products in the Field in the Rest of World or outside the Field throughout the world. The foregoing right of Targacept includes the right to reference all such regulatory and clinical documentation and data as reasonably necessary or desirable in connection with the development and commercialization of pharmaceutical products in the Field in the Rest of World or outside the Field throughout the world.

(c) At the request of Targacept, Dr. Falk agrees to negotiate in good faith with Targacept concerning the terms of a license under the Dr. Falk Patents and the Dr. Falk Know-How covering the composition of matter or the use of the Terminated Compounds, to permit Targacept to research, develop, make, have made, import, use, sell and offer for sale the Terminated Compounds outside the Field throughout the world.

(d) Dr. Falk hereby grants to Targacept an exclusive (including with regard to Dr. Falk) royalty-bearing right and license in the Rest of World under the Dr. Falk Patents and the Dr. Falk Know-How and under Dr. Falk's rights in the Joint Patents, Joint Know-How and Joint Research Technology, to research and develop, and to make, have made, import, use, sell and offer for sale pharmaceutical products (including Licensed Products) in the Field.

5.3 Right to Sublicense. Each Party shall have the right to grant to Third Parties sublicenses under the licenses granted hereunder (except pursuant to Section 5.1(a) and Section 5.2(a); ***provided, however***, that the grant of any sublicense by Dr. Falk shall be subject to compliance with the procedures set forth in Section 3.1(d). Notwithstanding the foregoing, the grant of any such sublicenses shall not relieve the sublicensing Party of any of its obligations under this Agreement.

5.4 Negative Covenants and License Limitations.

(a) *Mutual Covenants*. Each Party covenants to the other Party that it shall not practice, exercise or use any intellectual property rights licensed to it by the other Party under this Agreement, except as permitted expressly by the terms hereof; ***provided, however***, that this Section 5.4(a) shall preclude a Party from practicing, exercising or using any intellectual property rights of the other Party only to the extent such practice, exercise or use would violate the intellectual property rights of the other Party.

(b) *Additional Negative Covenant of Targacept.* Targacept further covenants to Dr. Falk that Targacept and its Affiliates shall not research, develop, commercialize, or license any Third Party to research, develop or commercialize, any Nicotinic Compound in the Field in the Territory or any Licensed Product in the Territory except pursuant to this Agreement.

(c) *Additional Negative Covenants of Dr. Falk.* Dr. Falk further covenants to Targacept that during the term of this Agreement, Dr. Falk and its Affiliates shall not, other than pursuant to this Agreement or with the prior written consent of Targacept, (A) conduct any activity, either on their own, or with, for the benefit of, or sponsored by any Third Party, that has as its goal or intent discovering, identifying, researching, developing or commercializing any Nicotinic Compounds; or (B) grant any license or other rights to any Third Party to utilize any intellectual property Controlled by Dr. Falk or its Affiliates (including without limitation any Dr. Falk Patents, Dr. Falk Know-How, Joint Patents or Joint Research Technology) for the express purpose of discovering, identifying, researching, developing or commercializing any such Nicotinic Compounds for use within or outside of the Field.

5.5 Understanding Regarding Exclusivity and Negative Covenants. The Parties agree that, given the high costs and significant risks involved in discovering and developing pharmaceutical products, and given that the Parties will be exchanging Confidential Information in order to perform the Research and to conduct the development and commercialization efforts, the exclusive relationship between them regarding the research, development and commercialization of Licensed Products in the Field, which is reflected herein, is a fair and efficient means to reach a satisfactory conclusion from their cooperative efforts.

ARTICLE 6

Management of Research, Development and Commercialization

6.1 Creation and Structure of the JRDT. As of the Effective Date, the Parties shall create a Joint Research and Development Team of **[********]** to facilitate the research and development of Licensed Products in the Territory and to manage and monitor the activities conducted by the Parties pursuant to the Research and Development Plan. The JRDT shall consist of an equal number of representatives appointed by each Party, who shall include senior decision-makers of such Party.

6.2 Responsibilities of the JRDT. The JRDT shall be the primary vehicle for interaction between the Parties with respect to the collaborative research, development and commercialization of Licensed Products in the Territory. Without limiting the foregoing, the JRDT shall: (a) formulate and review Research objectives; (b) decide upon the allocation of preclinical and clinical development activities between the Parties; (c) manage, review and monitor progress in implementing the Research and Development Plan; (d) prepare and recommend changes to the Research and Development Plan and submit such changes to the Parties for their approval; (e) prepare and approve Semi-Annual R&D Plans and modifications thereof; (f) approve the mechanism and criteria for the designation of Collaboration Compounds as Terminated Compounds and the designation of Development Compounds and Back-Up Compounds; (g) approve all preclinical development, clinical development and commercialization plans for Licensed Products in the Territory; (h) establish, monitor, review and change all development timelines to be adhered to by the Parties for all preclinical and clinical development and Regulatory Approval activities; (i) approve all contracts, agreements, commitments and undertakings with Third Parties regarding research and development activities in the Territory; (j) coordinate the preparation, filing and prosecution of all applications for Regulatory Approvals in the Territory, including all communications with regulatory authorities;

and (k) make all other decisions within the co-exclusive license rights of the Parties under Section 5.1 hereof.

6.3 Composition of the JRDT. Within fifteen (15) days after the Effective Date, the Parties shall notify each other in writing of the names of their initial representatives on the JRDT. Each Party may replace its JRDT representatives at any time upon written notice to the other. A Party's representative on the JRDT shall be authorized to act on behalf of such Party until written notice of the removal of such representative is received by the other Party. A Party's representative on the JRDT may resign at any time upon written notice to the Parties. Such resignation shall take effect at the time specified therein, and unless otherwise specified therein, no acceptance of such resignation shall be necessary to make it effective. Upon the resignation of a Party's representative, that Party shall appoint a replacement representative. A Team Leader for the JRDT shall be selected by Targacept from among the members of the JRDT, who shall coordinate all activities of the JRDT.

6.4 Duration of the JRDT. The JRDT shall exist until the termination of this Agreement.

6.5 Meetings of the JRDT. During its existence, the JRDT shall meet on scheduled dates four (4) times per year, at least two (2) of which shall be in person (or such other number of times as the Parties may agree) and upon ten (10) days advance written notice from either Party to the other Party. Meetings shall alternate between the offices of Targacept and Dr. Falk. A quorum of the JRDT shall exist whenever there is present at a meeting members appointed by each Party. An JRDT member of the Party hosting the meeting shall serve as Secretary of that meeting. The Secretary of the meeting shall prepare and distribute to all members of the JRDT minutes of the meeting in electronic and printed format sufficiently in advance of the next meeting to allow adequate review and comment prior to the meeting. Such minutes shall provide a description in reasonable detail of the discussions had at the meeting and a list of any actions, decisions or determinations approved by the JRDT. Minutes of any meeting shall be approved or disapproved, and revised as necessary, at the next meeting. Final minutes of each meeting shall be distributed to the members of the JRDT by the Team Leader. Each Party shall disclose to the other proposed agenda items in advance of each meeting of the JRDT. The JRDT may also meet, convene, or be polled or consulted, from time to time by means of telecommunications, video conferencing, e-mail or written correspondence, as deemed necessary or appropriate. Telephonic meetings (including video conferencing) may be called by either Party on two (2) business days notice. Members of the JRDT may be represented at any meeting by a designee appointed by such member for such meeting. The JRDT may invite other representatives of the Parties with special skills to attend meetings where appropriate. The JRDT shall adopt such other rules as shall be necessary or convenient for its work.

6.6 Decisions of the JRDT. All decisions of the JRDT shall be made by the unanimous vote of all JRDT members participating in the meeting. In the event that the members of the JRDT cannot agree with respect to a particular issue, such issue shall be referred to the President of Targacept and the President of Dr. Falk, who shall meet as soon as possible, but not later than thirty (30) days, in a good faith effort to resolve the dispute. In the event such officers cannot agree on a resolution of the dispute within thirty (30) days: (a) if the dispute relates solely and directly to matters of discovery and screening of Nicotinic Compounds, Targacept's decision shall control; (b) if the dispute relates solely and directly to the approval of

a commercialization plan for a Licensed Product in the Territory under Section 3.1(c), Dr. Falk's decision shall control; and (c) if the dispute relates to any other matter or issue within the authority of the JRDT, neither Party's decision shall control, but either Party may submit the dispute to arbitration for resolution under Section 14.10.

6.7 Subcommittees and Working Groups of the JRDT. From time to time, the JRDT may establish one or more subcommittees or working groups to oversee particular projects or activities, and such subcommittees or working groups will be constituted as the JRDT agrees.

6.8 Creation and Structure of the EMC. As of the Effective Date, the Parties shall create an Executive Management Committee of **[********]**. The EMC shall consist of an equal number of representatives nominated by each Party, including senior management members authorized to act on behalf of each Party.

6.9 Responsibilities of the EMC. The EMC shall serve as the primary vehicle for interaction between the Parties with respect to managing the overall collaborative effort of the Parties regarding research, development and commercialization of Licensed Products throughout the world. Without limiting the generality of the foregoing, the EMC shall be responsible for: (a) reviewing all Semi-Annual R&D Plans, and any updates thereto; and (b) monitoring the overall progress of the Parties' research, development and commercialization efforts.

6.10 Composition of the EMC. Within fifteen (15) days of the Effective Date, the Parties shall notify each other in writing of the names of their initial representatives on the EMC. Each Party may replace its EMC representatives at any time upon written notice to the other. A Party's representative on the EMC is authorized to act on behalf of such Party until written notice of the removal of such representative is received by the other Party. A Party's representative on the EMC may resign at any time upon written notice to the Parties. Such resignation shall take effect at the time specified therein, and unless otherwise specified therein, no acceptance of such resignation shall be necessary to make it effective. Upon the resignation of a Party's representative, that Party shall appoint a replacement representative. The Parties shall select a chairperson for the EMC from among the members of the EMC, who shall serve for a term of one year. The right to select the chairperson shall rotate between the Parties. Targacept shall select the first chairperson.

6.11 Duration of the EMC. The EMC shall remain in existence until the termination of this Agreement.

6.12 Meetings of the EMC. During its existence, the EMC shall meet in person on scheduled dates two (2) times per year (or such lesser number of times as the Parties may agree) and upon ten (10) days advance written notice from either Party to the other Party. Meetings shall alternate between the offices of Targacept and Dr. Falk. A quorum of the EMC shall exist whenever there is present at a meeting members appointed by each Party. An EMC member of the Party hosting the meeting shall serve as Secretary of that meeting. The Secretary of the meeting shall prepare and distribute to all members of the EMC minutes of the meeting in electronic and printed format sufficiently in advance of the next meeting to allow adequate review and comment prior to the meeting. Such minutes shall provide a description in

reasonable detail of the discussions had at the meeting and a list of any actions, decisions or determinations approved by the EMC. Minutes of any meeting shall be approved or disapproved, and revised as necessary, at the next meeting. Final minutes of each meeting shall be distributed to the members of the EMC by the Chairperson. Each Party shall disclose to the other proposed agenda items in advance of each meeting of the EMC. The EMC may also meet, convene, or be polled or consulted, from time to time by means of telecommunications, video conferencing, e-mail or written correspondence, as deemed necessary or appropriate. Telephonic meetings (including video conferencing) may be called by either Party on two (2) business days notice. Members of the EMC may be represented at any meeting by a designee appointed by such member for such meeting. The EMC may invite other representatives of the parties with special skills to attend meetings where appropriate. The EMC shall adopt such other rules as shall be necessary or convenient for its work.

6.13 Decisions of the EMC. All decisions of the EMC shall be made by the unanimous vote of all EMC members participating in the meeting. In the event that the members of the EMC cannot agree with respect to a particular issue, such issue shall be referred to the President of Targacept and the President of Dr. Falk, who shall meet as soon as possible, but not later than thirty (30) days, in a good faith effort to resolve the dispute. In the event that such officers cannot agree on a resolution of the dispute within thirty (30) days, neither Party's decision shall control, but either Party may submit the dispute to arbitration for resolution under Section 14.10.

6.14 Subcommittees of the EMC. From time to time, the EMC may establish one or more subcommittees to oversee particular projects or activities, and such subcommittees will be constituted as the EMC agrees.

6.15 Expenses. Each Party shall be responsible for all travel and related costs for its representatives to attend meetings of, and otherwise participate on, the JRDT and the EMC.

ARTICLE 7

Payments to Targacept and Dr. Falk

7.1 License Fees. In consideration of the rights granted hereunder, Dr. Falk shall pay Targacept a non-refundable, non-creditable license fee of One Million U.S. Dollars ($1,000,000) on the Effective Date of this Agreement.

7.2 Royalty and Sublicense Payments to Targacept. Subject to the terms and conditions of this Agreement, Dr. Falk shall pay to Targacept royalties in an amount equal to **[********]** of the Net Profit derived by Dr. Falk and its Affiliates from the sale of Licensed Products in any country in the Territory until the expiration of the Full Royalty Term. In addition to the royalty payments described above, Dr. Falk shall pay to Targacept **[********]** of all license fees paid in a fixed sum and not properly characterized as royalties, milestone payments, trademark fees, registration fees and other monies which are not royalties (regardless of how the same are characterized) received by Dr. Falk and its Affiliates from any Sublicensee with respect to the sale or offer for sale of any Licensed Product in the Territory until the expiration of the Full Royalty Term other than (i) bona fide payments from Sublicensees at

customary rates for periodic safety update reports and marketing support for services rendered by Dr. Falk after the First Commercial Sale of a Licensed Product; and (ii) bona fide payments from Sublicensees for the use of Dr. Falk's name and other trademarks solely owned by Dr. Falk, which shall in no event exceed during the Full Royalty Term **[********]**. The Parties agree that the above royalty rates reflect an efficient and reasonable blended allocation of the values of the Know-How and Patent Rights licensed by Targacept in the Territory hereunder.

7.3 Royalty Payments to Dr. Falk. Subject to the terms and conditions of this Agreement, Targacept shall pay to Dr. Falk royalties in an amount equal to **[********]** of the Net Sales of any Licensed Product during the Full Royalty Term in the United States and Japan and **[********]** of the Net Sales of such Licensed Product during the Partial Royalty Term in the United States and Japan. The Parties agree that the above royalty rates reflect an efficient and reasonable blended allocation of the values of the Know-How and Patent Rights licensed by Dr. Falk hereunder.

7.4 Term of Royalty Obligations. The "Full Royalty Term" for a particular Licensed Product in a particular country shall commence with the First Commercial Sale of such Licensed Product in such country and shall terminate upon the earlier of (a) the later of the expiration of the last-to-expire of (i) issued Targacept Patent Rights covering the composition of the Development Compound constituting or included in the Licensed Product or any method of preparation or use thereof in such country, (ii) issued Dr. Falk Patent Rights covering the composition of the Development Compound constituting or included in the Licensed Product or any method of preparation or use thereof in such country, (iii) issued Dr. Falk Patent Rights covering inventions during the R&D Term or (iv) Joint Patent Rights covering inventions during the R&D Term, in each case for which at least one Valid Claim exists covering the manufacture, importation, sale or offering for sale of such Licensed Product or its use in the Field, in such country, or (b) the twelfth anniversary of the First Commercial Sale of such Licensed Product in such country. The "Partial Royalty Term" (if any) for a particular Licensed Product in a particular country shall commence immediately after the Full Royalty Term of such Licensed Product in such country and shall terminate upon the twelfth anniversary of the First Commercial Sale of such Licensed Product in such country.

7.5 Timing of Payment of Royalties. Running royalties shall be payable by the Parties to each other under Sections 7.2 and 7.3 on a quarterly basis, within sixty (60) days after the end of each calendar quarter, based upon the Net Sales, Cost of Goods Sold and Net Profit (as applicable) during each calendar quarter, commencing with the calendar quarter in which the First Commercial Sale of a Licensed Product is made.

7.6 Obligation to Pay Royalties. Each Party's obligation to pay royalties to the other Party under this Article 7 is imposed only once with respect to the same unit of Licensed Product regardless of the number of Patent Rights pertaining thereto.

7.7 Statement of Royalties. Each quarterly royalty payment to either Party hereunder shall be accompanied by a statement showing the amounts of gross sales, Net Sales, Costs of Good Sold, Net Profit (as applicable) and the number of units of each Licensed Product sold by the Party on a country-by-country basis during such quarter and the amount of royalties due on such Net Sales or Net Profit (as applicable).

7.8 Compulsory Licenses. If a court or a governmental agency in a particular country requires a Party (or its Affiliate) to grant a compulsory license to a Third Party permitting such Third Party to make and sell a Licensed Product in such country, and such compulsory license contains a royalty rate lower than the rates provided in Section 7.2 or 7.3 (as applicable) with respect to the sale of such Licensed Product, then the royalty rate to be paid by a Party based upon Net Sales or Net Profit from sales (as applicable) of the Licensed Product in such country shall automatically be reduced to the royalty rate under such compulsory license, during the time period when such compulsory license is in effect and being exercised.

7.9 Third Party Licenses. If any Third Party holds a Patent Right (a "Blocking Patent") that claims a Collaboration Compound or its manufacture or use in the Field in the United States or Japan or in a country in the Territory where a Licensed Product including such Collaboration Compound is being manufactured, used or sold, and if it should prove in Dr. Falk's (in the case of the Territory) or Targacept's (in the case of the United States or Japan) bona fide, good faith judgment impractical or impossible for it or its Affiliates or Sublicensees to commence or continue the manufacture, use or sale of such Licensed Product in such country without obtaining a license under such Blocking Patent (a "Third Party License") and if the other Party does not deliver to the licensee Party an opinion without material qualifications from nationally recognized patent counsel in such country to the effect that such manufacture, use or sale does not and will not infringe such Blocking Patent:

(a) if the Blocking Patent is held in the Territory, then Targacept shall have the right, for a period of **[********]**, to use commercially reasonable, good faith efforts to negotiate and obtain a Third Party License on commercially reasonable terms acceptable to the Parties and thereafter Dr. Falk shall have the right to use commercially reasonable, good faith efforts to negotiate and obtain such Third Party License on commercially reasonable terms acceptable to the Parties, in either case with (i) the cost of obtaining such license (including any up-front license fees or other up-front payments) to be borne equally by the Parties, and (ii) royalties or other amounts payable in the future and Dr. Falk's share of the costs of obtaining such license, amortized over the term of the Third Party License, to be added to the Cost of Goods Sold for purposes of calculating Net Profit from the sale of Licensed Products payable pursuant to Section 7.2;

(b) if the Blocking Patent is held by any Third Party in the United States or Japan, Targacept shall have the right to use commercially reasonable, good faith efforts to negotiate and obtain a Third Party License on commercially reasonable terms, with the cost of obtaining such license (including any up-front license fees or other up-front payments) to be borne solely by Targacept, and any royalties or other amounts payable in the future to be allocated between the Parties so that the ratio of Targacept's portion to Dr. Falk's portion is equal to the ratio of Targacept's historic (or, if sales of such Licensed Product have not commenced, based on Targacept's good faith projection of) net profits on Net Sales of the Licensed Products in the United States or Japan (as the case may be) to Dr. Falk's royalties from the sale of Licensed Products in such country during the Full Royalty Term (or **[********]** of such royalties during the Partial Royalty Term), with Dr. Falk's share of such costs to be set off against any payments owed to Dr. Falk by Targacept pursuant to Section 7.3; ***provided, however,*** that in no event shall the aggregate amount set off in any calendar quarter against royalties payable under Section 7.3 in such calendar quarter exceed **[********]** thereof;

(c) if such Third Party License for a Blocking Patent in any country in the Territory cannot be obtained on terms reasonably acceptable to Dr. Falk, Dr. Falk may terminate its license rights hereunder with respect to such Licensed Product in such country upon sixty (60) days written notice to Targacept, whereupon Dr. Falk, its Affiliates and Sublicensees shall have no further license rights in such country regarding such Licensed Product and Targacept shall have no further obligations to Dr. Falk regarding commercialization of such Licensed Product in such country; and

(d) the provisions of this Section 7.9 do not apply to Blocking Patents, the existence of which constitute a breach by Targacept of its representations and warranties under Section 12.2 (a) or (b).

7.10 Mode of Payment. All payments to either Party hereunder shall be made by deposit of United States Dollars in the requisite amount to such bank account as such Party may from time to time designate by notice to the other Party. Payments shall be free and clear of any taxes (other than withholding and other taxes imposed on the receiving Party), fees or charges, to the extent applicable. With respect to sales outside the United States, payments shall be calculated based on currency exchange rates for the last calendar quarter for which remittance is made for royalties. For each quarter and each currency, such exchange rate shall equal the arithmetic average of the daily exchange rates during the calendar quarter obtained from the *Reuters Daily Rate Report* or, if such exchange rates are not available on any day, *The Wall Street Journal*, Eastern U.S. Edition, or, if such exchange rates are not available on any day, as otherwise agreed by the Parties.

7.11 Records Retention. For seven (7) years after each sale of each Licensed Product, and for such longer period as may be required by law, each Party shall keep (and shall ensure that its Affiliates and Sublicensees shall keep) complete and accurate books and records pertaining to the sale of all Licensed Products in sufficient detail to confirm the accuracy of calculations of payments due to the other Party hereunder.

7.12 Audits.

(a) Upon the written request of either Party and not more than once in each calendar year, the other Party shall permit an independent certified public accounting firm of nationally recognized standing appointed by the requesting Party, at the requesting Party's expense, to have access during normal business hours, and upon reasonable prior written notice, to such of the records of the other Party as may be reasonably necessary to verify the accuracy of the royalty reports hereunder for any calendar year ending not more than thirty-six (36) months prior to the date of such request. The accounting firm shall disclose to Targacept and Dr. Falk whether the royalty reports are correct or incorrect, the basis for its finding and the specific details concerning any discrepancies.

(b) If such accounting firm correctly concludes that additional royalties were owed during such period, the Party shall pay the additional royalties, with interest from the date originally due at the prime rate, as published in *The Wall Street Journal* (Eastern U.S. Edition) on the last business day preceding such date, within thirty (30) days after the date the Party receives such accounting firm's written report so correctly concluding. If the amount of the underpayment is greater than **[********]** of the total amount owed, then the Party shall in addition reimburse the requesting Party for all costs related to such audit.

(c) Each Party shall include in each sublicense granted by it pursuant to this Agreement a provision requiring the Sublicensee to make reports to such Party, to keep and maintain records of sales made pursuant to such sublicense and to grant access to such records by the other Party's independent accountant to the same extent required by this Agreement.

(d) Each Party shall treat all information subject to review under this Section 7.12 in accordance with the confidentiality provisions of Article 9 of this Agreement, and shall cause its accounting firm to enter into an acceptable confidentiality agreement with the other Party obligating such firm to retain all such financial information in confidence pursuant to such confidentiality agreement; ***provided, however,*** that in no event shall such confidentiality agreement prevent the accounting firm from disclosing to its client the information contemplated by Section 7.12(a).

7.13 Taxes. The Party receiving royalties and other payments under this Agreement shall pay any and all taxes levied on account of such payment. If any taxes are required to be withheld by the paying Party, it shall (a) deduct such taxes from the remitting payment, (b) timely pay the taxes to the proper taxing authority, and (c) send proof of payment to the other Party and certify its receipt by the taxing authority within sixty (60) days following such payment.

ARTICLE 8

Inventions and Patents

8.1 Title to Inventions and Documentation.

(a) *Joint Ownership.* Except as otherwise expressly provided in Article 5 and this Section 8.1, the Parties shall jointly own all right, title to and interest in (i) all Joint Research Technology and (ii) all the regulatory and clinical documentation and data for the Territory produced under the Research and Development Plan. Notwithstanding the foregoing, it is the intention of the Parties that neither Party shall gain any advantage as to ownership of inventions as a result of being the first Party to review data provided to either Party on a contract or subcontract basis by a Third Party (other than a Sublicensee) pursuant to the Research and Development Plan. Accordingly, the Parties shall jointly own all inventions conceived solely as a result of the review of screening or development data supplied by Third Parties (other than Sublicensees) pursuant to the Research and Development Plan.

(b) *Sole Ownership.* Except as otherwise expressly provided in Section 2.10, Article 5 and this Section 8.1, Targacept shall own all right, title to and interest in all Research Technology made solely by Targacept and its agents and Dr. Falk shall own all right, title to and interest in all Research Technology made solely by Dr. Falk and its agents.

(c) *Dispute as to Ownership.* In the event that there is a dispute between the Parties as to ownership of any Research Technology or documentation, the EMC shall establish a procedure to resolve such dispute, which may include engaging a Third Party

patent attorney jointly selected by the Parties, who is completely unaffiliated and independent of the Parties, as an expert to resolve such dispute. If the EMC is unable to establish a procedure to resolve such disputes, either Party may seek to resolve such dispute in accordance with Section 14.10 hereof.

8.2 Patent Prosecution. The Parties expect that patent applications will be filed as required to secure suitable Patent Rights covering Collaboration Compounds and inventions that are within the Research Technology or are otherwise applicable to the Field. The Parties agree as follows with respect to the filing and prosecution of such applications:

(a) *Targacept Patents.* Subject to the provisions of this Section 8.2: Targacept shall be responsible for obtaining, prosecuting and maintaining in the United States, Japan and each country in the Territory the Targacept Patents, including Patent Rights covering Research Technology solely owned by Targacept. Targacept shall have the sole and exclusive right (but not the obligation), to obtain, prosecute and maintain Targacept Patents in other countries in the Rest of World as it determines. In this regard, Targacept shall file, prosecute and maintain patent applications in the United States to secure Patents Rights for the Targacept Compounds and any Research Technology solely owned by Targacept and other inventions claimed in the Targacept Patents. Within one year of filing any such United States patent application, Targacept shall file a counterpart International Application under the PCT designating Japan and all member countries included in the Territory and any additional counterpart national patent applications in non-PCT member countries included in the Territory as the Parties shall mutually agree upon (subject to the provisions of Subsection 8.3(e)). Targacept shall bear all costs for filing, prosecuting and maintaining Targacept Patents.

(b) *Dr. Falk Patents.* Dr. Falk shall be responsible for obtaining, prosecuting and maintaining in each country in the Territory the Dr. Falk Patents, including Patent Rights covering Research Technology solely owned by Dr. Falk. Subject to Section 8.3(e), Dr. Falk shall have the sole and exclusive right (but not the obligation) to obtain, prosecute and maintain Dr. Falk Patents in other countries in the Rest of World as it determines. In this regard, Dr. Falk shall file, prosecute and maintain patent applications in Germany to secure Patent Rights for any Research Technology solely owned by Dr. Falk and other inventions claimed in the Dr. Falk Patents. Within one year of filing any such patent application, Dr. Falk shall file a counterpart International Application under the PCT designating all member countries included in the Territory and any additional counterpart national patent applications in non-PCT member countries included in the Territory as the Parties shall mutually agree upon (subject to the provisions of Subsection 8.3(e)). Dr. Falk shall bear all costs for filing, prosecuting and maintaining Dr. Falk Patents throughout the world.

(c) *Joint Patents.* Targacept shall be initially responsible for obtaining, prosecuting and maintaining in each country in the Territory Patent Rights in the name of Targacept and Dr. Falk covering Joint Research Technology. Targacept shall have the sole and exclusive right (but not the obligation) to obtain, prosecute and maintain at its sole expense Joint Patents in other countries in the Rest of World as it determines. Dr. Falk and Targacept shall share equally the costs for filing, prosecuting and maintaining such Joint Patents in each country in the Territory. Notwithstanding the above, either Party may decline to pay its share of the costs for filing, prosecuting and maintaining any Joint Patent(s) in a particular country(ies), in which case the declining Party shall assign to the other Party all its right, title and interest to

any such Joint Patent(s) in the relevant country and upon such assignment such Joint Patent(s) shall become a Dr. Falk Patent(s) or a Targacept Patent(s), as the case may be.

(d) *Cooperation.* Each 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. In addition, such filing Party shall provide the other Party and its patent counsel with an opportunity to consult with the Party and its patent counsel regarding the filing and contents of any such application, amendment, submission or response, and the advice and suggestions of the other Party and its patent counsel shall be taken into reasonable consideration by such Party and its legal counsel in connection with such filing. Each Party shall also provide the other Party with copies of any patentability search reports made by patent counsel with respect to inventions in the Research Technology, including patents located, a copy of each patent application, and each patent that issues thereon.

(e) *Election not to Prosecute.* If a Party elects not to pursue the initial filing of a potential Targacept Patent, Dr. Falk Patent or Joint Patent, as the case may be, that it is obligated to pursue or to support the PCT International filing or the continued prosecution or maintenance of any Targacept Patent, Dr. Falk Patent or Joint Patent, as the case may be, in a particular country for which it has the initial obligation to file pursuant to Section 8.2(a), (b) or (c) or, in the case of Dr. Falk under Section 8.2(b), the right to file (such Party being referred to herein as the "Non-Filing Party"), then it shall notify the other Party promptly in writing and in good time to enable the other Party to meet any applicable deadlines. With respect to Targacept Patents, Dr. Falk Patents or Joint Patents scheduled for international filing with respect to such country, the Non-Filing Party shall notify the other Party in writing at least ninety (90) days before the date required for the convention year filing of such Targacept Patent, Dr. Falk Patent or Joint Patent application or within a reasonable time frame for any other deadline date by which an action must be taken to establish or preserve a Targacept Patent, Dr. Falk Patent or Joint Patent right in such country. The other Party shall then have the right, but not the obligation, to pursue the filing or support the continued prosecution or maintenance of such Targacept Patent, Dr. Falk Patent or Joint Patent, at its expense in such country. If the other Party does so elect to pursue such filing or continue such support, then it shall notify the Non-Filing Party of such election, and the Non-Filing Party shall (i) reasonably cooperate with the other Party in this regard, and (ii) promptly release or assign, as the case may be, to the other Party, without consideration, all right, title and interest in such Targacept Patent, Dr. Falk Patent or Joint Patent in such country. For the avoidance of doubt, in the event that the other Party supports a patent application that the Non-Filing Party is obligated to pursue but declines to support, then such patent applications and patents that may result therefrom shall be considered a Targacept Patent (in the case Dr. Falk is the Non-Filing Party) or an Dr. Falk Patent (in the case Targacept is the Non-Filing Party), as applicable, for purposes of this Agreement. Nothing in this Section 8.3(e) is intended to cause Targacept to be a Non-Filing Party with respect to any Targacept Patent or Joint Patent in any country other than the United States, Japan or those countries included in the Territory.

8.3 Enforcement of Patents.

(a) If either Party considers that any Targacept Patent, Dr. Falk Patent or Joint Patent claiming a Collaboration Compound or Licensed Product, or the manufacture or

use thereof, is being infringed by a Third Party's activities in the Field, it shall notify the other Party and provide it with any evidence of such infringement which is reasonably available. Dr. Falk shall have the first opportunity at its own expense to attempt to remove such infringement in the Territory by commercially appropriate steps, including filing an infringement suit or taking other similar action. Targacept shall have the exclusive right, but not the obligation, to remove or pursue infringers in the Rest of World at its sole cost and expense. In the event that Dr. Falk fails to take commercially appropriate steps with respect to an infringement in the Territory that is likely to have a material adverse effect on the sale of Licensed Products within three (3) months following notice of such infringement, Targacept shall have the right to do so at its expense; provided that if Dr. Falk has commenced negotiations with an alleged infringer of the patent for discontinuance of such infringement within such three-month period, Dr. Falk shall have an additional six (6) months to conclude its negotiations before the other Party may bring suit for such infringement. If required by law for the prosecuting Party to prosecute any suit referred to in this Section 8.3, the other Party shall join such suit as a party, at the prosecuting Party's expense.

(b) The Party not enforcing the applicable Patent Rights shall provide commercially reasonable assistance to the other Party, including joining in infringement suits, providing access to relevant documents and other evidence, making employees available and seeking to obtain necessary Third Party consents, subject to the enforcing Party's reimbursement of any out-of-pocket expenses incurred by the non-enforcing Party.

(c) Any amounts recovered by either Party pursuant to Section 8.3(a) with respect to infringement in the Territory, whether by settlement or judgment, shall be allocated in the following order: (i) to reimburse Dr. Falk and Targacept 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); and (ii) the portion of the award representing lost profits on sales in the Territory shall be **[********]**; (iii) the portion of the award representing lost profits on sales in the United States and Japan shall be **[********]**; and (iv) the portion of the award representing lost profits on sales in any other country in the Rest of World shall be **[********]**, ***provided, however***, that if the infringement activity on which such recovery is based included actions outside the Field, then the Parties shall reasonably agree on an appropriate allocation of such recovery between activities in the Field and activities outside the Field (which will not bear a royalty and which will be retained by the Party owning the relevant Patent Rights).

(d) Except for Third Party infringement activities within the Field covered by the provisions of Section 8.3(a), each Party shall retain the sole and exclusive right to enforce its Patent Rights against all infringers at its sole cost and expense.

8.4 Third Party Patent Rights. If any warning letter or other notice of infringement is received by a Party, or action, suit or proceeding is brought against a Party, alleging infringement of a Patent Right of any Third Party in the manufacture, use or sale of a Licensed Product or in conducting the Research, the Parties shall promptly discuss and decide the best way to respond.

ARTICLE 9

Confidentiality

9.1 Confidentiality Obligations. Each Party agrees that, for the term of this Agreement and for five (5) years thereafter, such Party shall keep, and shall ensure that its officers, directors, employees and agents keep, completely confidential and shall not publish or otherwise disclose and shall not use for any purpose except as expressly permitted hereunder any Confidential Information furnished to it by the other Party pursuant to this Agreement (including, without limitation, Know-How of the disclosing Party) or any Joint Know-How. The foregoing obligations shall not apply to any information to the extent that it can be established by such receiving Party that such information:

(a) was already known to the receiving Party, other than under an obligation of confidentiality, at the time of disclosure;

(b) was generally available to the public or otherwise part of the public domain at the time of its disclosure to the receiving Party;

(c) became generally available to the public or otherwise part of the public domain after its disclosure and other than through any act or omission of the receiving Party in breach of this Agreement;

(d) was subsequently lawfully disclosed to the receiving Party by a Third Party other than in contravention of a confidentiality obligation of such Third Party to the disclosing Party; or

(e) was developed or discovered by employees of the receiving Party or its Affiliates who had no access to the Confidential Information of the disclosing Party.

Each Party shall have, shall obtain or shall have assigned to it written agreements from each of its employees, agents, and consultants who perform substantial work on the research or development of Licensed Products, which agreements shall obligate such persons to similar obligations of confidentiality and, subject to compliance with applicable law related to employee's rights in employee inventions to assign to such Party all inventions made by such persons during the course of performing the Research. Each Party may disclose the other's Confidential Information to the extent such disclosure is reasonably necessary in filing or prosecuting patent applications, prosecuting or defending litigation or as otherwise required by legal process, complying with applicable governmental regulations, making a permitted sublicense of its rights hereunder or conducting clinical trials or otherwise in performing its obligations or exercising its rights hereunder, *provided that* if a Party is required to make any such disclosure of the other Party's Confidential Information, it will give reasonable advance notice to such other Party of such disclosure requirement, will cooperate with such other Party in the efforts of such other Party to secure confidential treatment of such Information prior to its disclosure, and, save to the extent inappropriate in the case of patent applications, will use all reasonable efforts to secure confidential treatment of such information prior to its disclosure (whether through protective orders or confidentiality agreements or otherwise). In addition, each Party shall have the right to disclose to its Affiliates Confidential Information of the other Party,

provided that such Party shall ensure that its Affiliates maintain the confidentiality of such information in accordance with the provisions of this Section 9.1.

9.2 Publications.

(a) Neither Party shall publish nor present the results of the Research or development studies carried out on any Development Compound or Back-Up Compound until after completion of Phase I clinical development with respect thereto and then only with the prior written consent of the other Party. Subject to the foregoing and the restrictions provided below, either Party may publish or present the results of the Research or of development studies carried out by it on such Development Compound, subject to the prior review by the other Party for patentability and protection of such other Party's Confidential Information. Each Party shall provide to the other Party the opportunity to review any proposed abstracts, manuscripts or summaries of presentations that cover the results of the Research or of pre-Phase III clinical development of such Development Compound. Each Party shall designate a person who shall be responsible for approving such publications. Such designated person shall respond in writing promptly and in no event later than sixty (60) days after receipt of the proposed material with either approval of the proposed material or a specific statement of concern, based upon either the need to seek patent protection or concern regarding competitive disadvantage arising from the proposal. In the event of concern, the submitting Party agrees not to submit such publication or to make such presentation that contains such information until the other Party is given a reasonable period of time (not to exceed one hundred twenty (120) days) to seek patent protection for any material in such publication or presentation which it believes is patentable or to resolve any other issues. This Section 9.2(a) shall cease to apply with respect to any Development Compound upon the commercial launch of a Licensed Product containing such Development Compound as an active ingredient. Furthermore, with respect to any proposed abstracts, manuscripts or summaries of presentations by investigators or other Third Parties, such materials shall be subject to review under this Section 9.2(a) to the extent that Dr. Falk or Targacept (as the case may be) has the right to do so.

(b) Each Party also agrees to delete from any such proposed publication any Confidential Information of the other Party upon its reasonable request.

(c) In any publication permitted under this Section 9.2, each Party shall acknowledge its collaboration with the other Party under this Agreement.

9.3 Press Releases. Except to the extent required by law or as otherwise permitted in accordance with this Section 9.3, neither Party shall make any public announcements concerning this Agreement or the subject matter hereof without the prior written consent of the other, which shall not be unreasonably withheld. Notwithstanding the foregoing, the Parties agree that each Party may desire or be required to issue press releases relating to the Agreement or activities thereunder, and the Parties agree to consult with each reasonably and in good faith with respect to the text and timing of such press releases prior to the issuance thereof, provided that a Party may not unreasonably withhold consent to such releases, and that either Party may issue such press releases as it determines, based on advice of counsel, are reasonably necessary to comply with laws or regulations or for appropriate market disclosure. The principles to be observed by Targacept and Dr. Falk in public disclosures with respect to this Agreement shall be: accuracy, compliance with applicable legal requirements, the requirements

of confidentiality under this Article 9 and normal business practice in the pharmaceutical and biotechnology industries for disclosures by companies comparable to Targacept and Dr. Falk. In the event of a public announcement, the Party making such public announcement shall provide the other Party with a reasonable opportunity, judged in the light of the circumstances, and the right to approve the content of such announcement prior to its being made, which approval shall not be delayed or unreasonably withheld.

ARTICLE 10

Indemnification

10.1 Indemnification by Dr. Falk. Dr. Falk shall indemnify, defend and hold Targacept and its Affiliates and each of their respective agents, employees, officers and directors (the "Targacept Indemnitees") harmless from and against any and all liability, damage, loss, cost or expense (including reasonable attorney's fees) in connection with any and all suits, investigations, claims or demands by Third Parties (collectively, the "Losses") arising from or occurring as a result of (a) any breach by Dr. Falk of this Agreement or (b) Dr. Falk's performance of its obligations under this Agreement or (c) the manufacture, use or sale of any Collaboration Compounds or Licensed Products by Dr. Falk and its Affiliates, Sublicensees, distributors and agents in the Territory, except for those Losses for which Targacept has an obligation to indemnify Dr. Falk pursuant to Section 10.2, as to which Losses each party shall indemnify the other to the extent of their respective liability for the Losses. Notwithstanding any provision hereof to the contrary, Dr. Falk shall have no obligation to indemnify any Targacept Indemnitee against any Losses in connection with any product liability claim arising solely out of the manufacture, use or sale of any product by Targacept and its Affiliates, Sublicensees, distributors and agents, regardless of whether such claim sounds in tort, contract, strict liability, products liability or any other legal theory.

10.2 Indemnification by Targacept. Targacept shall indemnify, defend and hold Dr. Falk and its Affiliates and each of their respective agents, employees, officers and directors (the "Dr. Falk Indemnitees") harmless from and against any Losses arising from or occurring as a result of (a) any breach by Targacept of this Agreement, (b) Targacept's performance of its obligations under this Agreement, or (c) the manufacture, use or sale of any Collaboration Compound or any product (including any Licensed Product) containing any Collaboration Compound by Targacept and its Affiliates, Sublicensees, distributors and agents in the Rest of World, except for those Losses for which Dr. Falk has an obligation to indemnify Targacept pursuant to Section 10.1, as to which Losses each Party shall indemnify the other to the extent of their respective liability for the Losses. Notwithstanding any provision hereof to the contrary, Targacept shall have no obligation to indemnify any Dr. Falk Indemnitee against any Losses in connection with any product liability claim arising solely out of the manufacture, use or sale of any Licensed Product by Dr. Falk and its Affiliates, Sublicensees, distributors and agents in the Territory, regardless of whether such claim sounds in tort, contract, strict liability, products liability or any other legal theory.

10.3 Notification of Claims; Conditions to Indemnification Obligations. As a condition to a Party's right to receive indemnification under this Article 10, it shall (a) promptly notify the other Party as soon as it becomes aware of a claim or action for which indemnification may be sought pursuant hereto, (b) cooperate with the indemnifying Party in the

defense of such claim or suit, and (c) permit the indemnifying Party to control the defense of such claim or suit, including without limitation the right to select defense counsel, ***provided***, that the failure to provide prompt notice under clause (a) shall not excuse a Party from its indemnification obligations hereunder except to the extent it can demonstrate actual damages or prejudice arising from such failure. In no event, however, may the indemnifying Party compromise or settle any claim or suit in a manner which admits fault or negligence on the part of the indemnified Party without the prior written consent of the indemnified Party. The indemnifying Party shall have no liability under this Article 10 with respect to claims or suits settled or compromised without its prior written consent.

ARTICLE 11

Termination and Expiration

11.1 Term and Termination. This Agreement shall commence upon the Effective Date and, unless earlier terminated as provided herein, shall expire on the expiration of all royalty and other payment obligations hereunder. The obligation of the Parties to pay royalties to each other shall expire on a country-by-country basis as provided in Section 7.4. Upon expiration of all royalty obligations with respect to a particular Licensed Product, the licenses granted to Dr. Falk under Section 5.1(b) and the licenses granted to Targacept under Section 5.2(d), as the case may be, shall expire, and Dr. Falk or Targacept (as the case may be) shall automatically thereafter be granted a non-exclusive, fully paid up license to make, have made, use, import, sell and offer for sale such Licensed Product in the Territory (in the case of Dr. Falk) or in the Rest of World (in the case of Targacept).

11.2 Termination of the Agreement upon Material Breach.

(a) Failure by a Party to comply with any of its material obligations contained herein shall entitle the Party not in default to give to the Party in default notice specifying the nature of the default, requiring it to make good or otherwise cure such default, and stating its intention to terminate if such default is not cured. If such default is not cured within sixty (60) days after the receipt of such notice (or, if such default cannot be cured within such sixty (60) day period, if the Party in default does not commence and diligently continue actions to cure such default), the Party not in default 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; ***provided, however,*** that such right to terminate shall be stayed in the event that, during such sixty (60) day period, the Party alleged to have been in default shall have initiated dispute resolution in accordance with Section 14.10 with respect to the alleged default, which stay shall last so long as the initiating Party diligently and in good faith cooperates in the prompt resolution of such dispute resolution proceedings.

(b) The right of a Party to terminate this Agreement, as herein above provided, shall not be affected in any way by its waiver or failure to take action with respect to any prior default.

(c) In the event that Dr. Falk is developing or commercializing more than one Development Compound or Licensed Product in the Territory for use in the Field, and Dr. Falk breaches this Agreement in connection with a particular Development Compound or

Licensed Product, then Targacept shall be entitled to terminate this Agreement only with respect to such particular Development Compound or Licensed Product. Furthermore, in the event a breach relating to a particular Development Compound or Licensed Product is limited to a particular Major Country, then Targacept shall be entitled to terminate this Agreement only with respect to such Major Country; ***provided, however***, that Targacept shall be entitled to terminate this Agreement in the event Dr. Falk breaches this Agreement in connection with a particular Development Compound or Licensed Product in two or more Major Countries.

11.3 Termination of the Agreement by Either Party. Either Party may terminate this Agreement in its entirety upon thirty (30) days prior written notice as specified in Sections 2.8 and 3.4 and Targacept may terminate this Agreement upon thirty (30) days written notice to Dr. Falk as set forth in Section 2.9; ***provided, however,*** that neither Party shall be discharged of its liability to the other Party under any previously approved Semi-Annual R&D Plan.

11.4 Termination Upon Insolvency. Either Party may, at its option and without notice, terminate this Agreement effective immediately in the event the other Party (1) admits in writing its inability to pay its debts generally as they become due; (2) institutes proceedings in any jurisdiction to be adjudicated a voluntary bankrupt or insolvent entity, or consents to the filing of a petition of bankruptcy or insolvency against it in any jurisdiction; (3) is adjudicated by a court of competent jurisdiction as being bankrupt or insolvent; (4) seeks reorganization under any bankruptcy or insolvency act or law, or consents to the filing of a petition seeking such reorganization; or (5) has a decree entered against it by a court of competent jurisdiction appointing a receiver, liquidator, trustee, or assignee in bankruptcy or in insolvency covering all or substantially all of such Party's property (which appointment is not vacated within sixty (60) days of the entry of the order of appointment) or providing for the liquidation of such Party's property or business.

11.5 Consequences of Termination.

(a) Upon termination of this Agreement (but not upon expiration of its term under Section 11.1): (i) each Party shall promptly return all relevant records and materials in its possession or control containing or comprising the other Party's Know-How and Confidential Information and to which the former Party does not retain rights hereunder (except one copy of which may be retained in a Party's confidential files for archival purposes); (ii) all licenses granted by each Party to the other under Article 5 shall terminate except as expressly provided otherwise herein; (iii) each Party shall provide the other Party with copies of all reports and data, including preclinical data and reports, obtained by the former Party pursuant to this Agreement that relate to Collaboration Compounds and that have not otherwise been provided to such Party, within sixty (60) days after such termination; ***provided, however,*** that a Party shall not be obligated to provide the foregoing copies in the case where such Party terminates under Sections 11.2 or 11.4 and ***provided further*** that the provision to a Party of the foregoing copies shall not be deemed to create any additional rights or licenses in any such copies or the intellectual property embodied therein, and such Party's rights to use or exploit such information and rights shall be solely as expressly granted elsewhere in this Agreement and, with respect to Joint Know-How or Joint Patents, those rights of such Party as a joint owner); and (iv) any and all claims and payment obligations that accrued prior to the date of such termination shall survive such termination.

(b) In the event either Party terminates the Agreement under Section 11.3, Dr. Falk shall grant Targacept an exclusive, paid-up, worldwide license, with the right to sublicense, under (i) any Patent Rights Controlled by Dr. Falk which claim a Development Compound, Back-Up Compound or Licensed Product (or any method for the preparation, manufacture or use thereof in the Field), (ii) any Know-How Controlled by Dr. Falk which is necessary to research, develop, make, have made, import, use, sell and offer for sale Development Compounds, Back-Up Compounds or Licensed Products in the Field, and (iii) Dr. Falk's rights in Joint Patents, Joint Know-How and Joint Research Technology, solely to research, develop, make, have made, import, use, sell and offer for sale Development Compounds, Back-Up Compounds and Licensed Products for use in the Field.

(c) In the event Targacept terminates the Agreement under Section 11.2 or 11.4, Dr. Falk shall grant Targacept an exclusive, paid-up, worldwide license, with the right to sublicense, under (i) any Patent Rights Controlled by Dr. Falk which claim a Development Compound, Back-Up Compound or Licensed Product (or any method for the preparation, manufacture or use thereof in the Field), (ii) any Know-How Controlled by Dr. Falk which is necessary to research, develop, make, have made, import, use, sell and offer for sale Development Compounds, Back-Up Compounds or Licensed Products in the Field, and (iii) Dr. Falk's rights in Joint Patents, Joint Know-How and Joint Research Technology, solely to research, develop, make, have made, import, use, sell and offer for sale Development Compounds, Back-Up Compounds and Licensed Products for use in the Field. Nothing in this Section 11.5(c) is intended to limit Dr. Falk's right to use Patent Rights and Know-How Controlled by Dr. Falk (i) outside the Field or (ii) inside the Field without involving the use of any Nicotinic Compound.

(d) In connection with the grant of a license pursuant to Section 11.5(b) or 11.5(c), Dr. Falk shall assign to Targacept any and all regulatory filings and Regulatory Approvals (including applications for Regulatory Approval) made by Dr. Falk in the Territory covering Development Compounds, Back-Up Compounds and Licensed Products, and Dr. Falk shall provide appropriate notification of such assignment to applicable regulatory authorities within thirty (30) days after the request of Targacept.

(e) Notwithstanding the provisions of Section 11.5(b) hereof, in the event that Targacept terminates this Agreement pursuant to Sections 11.2 or 11.4, then the restrictions imposed upon it pursuant to, and its obligations under, Sections 2.15 and 5.4 (other than Section 5.4(a)) shall terminate.

(f) Notwithstanding the provisions of Section l1.5(b) hereof, in the event that Dr. Falk terminates this Agreement pursuant to Sections 11.2 or 11.4, then the restrictions imposed upon it pursuant to, and its obligations under, Sections 2.15 and 5.4 (other than Section 5.4(a)) shall terminate.

(g) In the event Dr. Falk terminates the Agreement under Section 11.2 or 11.4, Targacept shall grant Dr. Falk an exclusive, paid-up, license in the Territory, with the right to sublicense, under (i) any Patent Rights Controlled by Targacept which claim a Development Compound, Back-Up Compound or Licensed Product (or any method for the preparation, manufacture or use thereof in the Field), (ii) any Know-How Controlled by Targacept which is necessary to research, develop, make, have made, import, use, sell and offer

for sale Development Compounds, Back-Up Compounds or Licensed Products in the Field, and (iii) Targacept's rights in Joint Patents, Joint Know-How and Joint Research Technology, solely to research, develop, make, have made, import, use, sell and offer for sale Development Compounds, Back-Up Compounds and Licensed Products for use in the Field in the Territory.

11.6 Accrued Rights; Surviving Obligations.

(a) Termination, relinquishment or expiration of this Agreement 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, relinquishment or expiration shall not relieve a Party from obligations that are expressly indicated to survive termination or expiration of this Agreement. Without limiting the foregoing, Sections 2.6(b), 2.6(c), 2.10, 2.11, 2.12, 2.14, 4.1(b), 4.1(c), 5.1(b) (in the event of expiration), 5.2(b), (c) and (d) (unless Dr. Falk terminates this Agreement under Sections 11.2 or 11.4), 5.3, 5.4(a), 5.4(b) (in the event of termination by Dr. Falk under Sections 11.2 or 11.4), 5.4(c) (in the event of expiration of this Agreement or termination of this Agreement by Dr. Falk pursuant to Section 11.3 or by Targacept pursuant to Sections 11.2 or 11.4), 7.11, 7.12, 14.3, 14.9, 14.10, 14.11 and 14.12 and Articles 1, 9, 10, and 11 of this Agreement shall survive the expiration or termination of this Agreement for any reason.

(b) Upon any termination of this Agreement as regards any particular Licensed Product, Dr. Falk shall be entitled, during the six (6) month period following the effective date of such termination, to finish any work-in-progress and to sell any inventory of the Licensed Product which remains on hand as of the date of the termination, so long as Dr. Falk pays to Targacept the royalties applicable to said subsequent sales in accordance with the terms and conditions set forth in this Agreement.

11.7 Rights in Bankruptcy. All rights and licenses granted under or pursuant to this Agreement by Dr. Falk or Targacept are, and shall otherwise be deemed to be, for purposes of Section 365(n) of the U.S. Bankruptcy Code, licenses of right to "intellectual property" as defined under Section 101 of the U.S. 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 U.S. Bankruptcy Code. The Parties further agree that, in the event of the commencement of a bankruptcy proceeding by or against either Party under the U.S. Bankruptcy Code, the Party hereto which 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, and same, if not already in their possession, shall be promptly delivered to them (i) upon any such commencement of a bankruptcy proceeding upon their written request therefor, unless the Party subject to such proceeding elects to continue to perform all of its obligations under this Agreement or (ii) if not delivered under (i) above, following the rejection of this Agreement by or on behalf of the Party subject to such proceeding upon written request therefor by an non-subject Party.

ARTICLE 12

Representations and Warranties

12.1 Representations and Warranties. Each Party represents and warrants to the other Party that, as of the Effective Date:

(a) Such Party is duly organized and validly existing under the laws of the jurisdiction of its incorporation and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof;

(b) Such Party has taken all corporate action necessary to authorize the execution and delivery of this Agreement and the performance of its obligations under this Agreement;

(c) This Agreement is a legal and valid obligation of such Party, binding upon such Party and enforceable against such Party in accordance with the terms of this Agreement. The execution, delivery and performance of this Agreement by such Party does not conflict with any agreement, instrument or understanding, oral or written, to which such Party is a party or by which such Party may be bound, and does not violate any law or regulation of any court, governmental body or administrative or other agency having authority over such Party. All consents, approvals and authorizations from all governmental authorities or other Third Parties required to be obtained by such Party in connection with this Agreement have been obtained;

(d) It has the full and exclusive right, power and authority to enter into this Agreement, to perform its obligations hereunder and to grant the licenses granted under Article 5 hereof;

(e) Subject to compliance with applicable law related to employer's rights in employee inventions, all individuals who perform any research and development activities on behalf of a Party or its Affiliates in connection with this Agreement will have assigned to such Party, directly or indirectly by assignment of another Person, the whole of their rights in any intellectual property conceived or reduced to practice by them as a result of such activities. No Third Party (other than a Sublicensee) will have any rights to any intellectual property which is conceived or developed by any individual who will perform any activities by or on behalf of a Party or its Affiliates in connection with this Agreement; and

(f) With respect to any Materials provided by it to the other Party, it has the full right to provide such Materials and has no reason to believe that the other Party's use of such Materials in accordance with this Agreement will infringe the intellectual property rights of any Third Party.

12.2 Additional Representations and Warranties of Targacept. Targacept represents and warrants to Dr. Falk as of the Effective Date that:

(a) To the best knowledge of Targacept, the Targacept Patents and Targacept Know-How existing as of the Effective Date are not invalid or unenforceable, in whole or in part.

(b) To the best knowledge of Targacept, the inception, development and reduction to practice of the Targacept Patents and Targacept Know-How existing as of the Effective Date has not constituted or involved the misappropriation of trade secrets or other rights or property of any Third Party, Targacept has no knowledge that the Targacept Patents and Targacept Know-How existing as of the Effective Date infringe the intellectual property rights of any Third Party and to the best knowledge of Targacept, Dr. Falk's practice of the Targacept Patents and Targacept Know-How as permitted herein will not infringe any intellectual property rights of any Third Party.

(c) As of the Effective Date, there are no agreements between Targacept and any Third Parties which would preclude or otherwise limit Targacept's ability to conduct its tasks and obligations under the Research and Development Plan or otherwise fulfill its obligations under this Agreement;

(d) As of the Effective Date Targacept has not granted, and during the term of this Agreement Targacept will not grant, any license to any Third Party, either express or implied, or any option to license, to utilize any intellectual property owned or Controlled by Targacept (including under option) to discover, identify, research, develop or market any Development Compound, Back-Up Compound or Licensed Product in the Territory in the Field, except in accordance with this Agreement;

(e) As of the Effective Date, Targacept is the exclusive owner or assignee of the Patent Rights listed on Exhibit D attached hereto. Such Patent Rights constitute all of the Patent Rights that Targacept and its Affiliates own, have under license or have a right to acquire (by option or otherwise) that are useful for the manufacture, use or sale of Targacept Compounds in the Field and Targacept has the right to license such Patent Rights to Dr. Falk under this Agreement. During the term of this Agreement, Targacept will not encumber or diminish the rights granted to Dr. Falk hereunder, including without limitation, by not committing any acts or permitting the occurrence of any omissions which would cause the breach or termination of any Third Party License. As of the Effective Date, no Third Party License is in effect. Targacept will promptly provide Dr. Falk notice of any alleged breach of any Third Party License entered into after the Effective Date.

(f) To the best of Targacept's scientific judgment, the Targacept Compounds include all of the Nicotinic Compounds created or developed at any time solely or jointly by Targacept or any Affiliate thereof, that show significant potential for development as a pharmaceutical product for use in the Field.

ARTICLE 13

Equity Investment by Dr. Falk

On the Effective Date, Dr. Falk shall purchase **[********]** shares of Targacept's common stock, $0.001 par value per share (the "Shares"), for a purchase price of **[********]** per Share (or

U.S. $1,000,000 in the aggregate). The Shares shall be issued and sold pursuant to the subscription agreement in the form of Exhibit E hereto, and shall be subject to all the rights and obligations generally applicable to shares of Targacept's common stock held by non-employee holders, including those arising under Targacept's certificate of incorporation and bylaws, each as amended from time to time, and the Stockholders Agreement dated August 22, 2000 among the holders of Targacept's capital stock and in the form of Exhibit F hereto, which Dr. Falk shall be required to execute on the Effective Date.

ARTICLE 14

Miscellaneous Provisions

14.1 Relationship of the Parties. Nothing in this Agreement is intended or shall be deemed to constitute a partnership, agency or employer-employee relationship between the Parties. Neither Party shall incur any debts or make any commitments for the other.

14.2 Assignments. Except as expressly provided herein, neither this Agreement nor any interest hereunder shall be assignable, nor any other obligation delegable, by a Party without the prior written consent of the other; ***provided, however,*** that a Party may assign this Agreement to any Affiliate or to any successor in interest by way of merger or sale of all or substantially all of its assets in a manner such that the assignor shall remain liable and responsible for the performance and observance of all such Party's duties and obligations hereunder. This Agreement shall be binding upon the successors and permitted assigns of the Parties. Any assignment not in accordance with this Section 14.2 shall be void.

14.3 Disclaimer of Warranties. SUBJECT TO SECTIONS 12.1 AND 12.2, THE PARTIES EXPRESSLY DISCLAIM ALL WARRANTIES, EXPRESS OR IMPLIED, INCLUDING WITHOUT LIMITATION WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, OR NON-INFRINGEMENT OF THIRD PARTY RIGHTS, UNLESS OTHERWISE EXPRESSLY PROVIDED IN THIS AGREEMENT.

14.4 Further Actions. Each Party agrees to execute, acknowledge and deliver such further instruments and to do all such other acts as may be necessary or appropriate in order to carry out the purposes and intent of this Agreement.

14.5 Force Majeure. Neither Party shall be liable to the other for failure or delay in the performance of any of its obligations under this Agreement for the time and to the extent such failure or delay is caused by earthquake, riot, civil commotion, war, strike, flood, governmental acts or restrictions or any other reason which is beyond the control of the respective Party. The Party affected by force majeure shall provide the other Party with full particulars thereof as soon as it becomes aware of the same (including its best estimate of the likely extent and duration of the interference with its activities), and will use commercially reasonable efforts to overcome the difficulties created thereby and to resume performance of its obligations as soon as practicable. If the performance of any obligation under this Agreement is delayed owing to a force majeure for any continuous period of more than six (6) months, the parties hereto shall consult with respect to an equitable solution, including the possibility of the mutual termination of this Agreement.

14.6 No Trademark Rights. No right, express or implied, is granted by this Agreement to a Party to use in any manner the name or any other trade name or trademark of a Party in connection with the performance of this Agreement.

14.7 Entire Agreement of the Parties; Amendments. This Agreement and the exhibits hereto constitute and contain the entire understanding and agreement of the Parties respecting the subject matter hereof and cancel and supersede any and all prior negotiations, correspondence, understandings and agreements between the Parties, whether oral or written, regarding such subject matter. No waiver, modification or amendment of any provision of this Agreement shall be valid or effective unless made in writing and signed by a duly authorized officer of each Party.

14.8 Captions. The captions to this Agreement are for convenience only, and are to be of no force or effect in construing or interpreting any of the provisions of this Agreement.

14.9 Applicable Law. This Agreement shall be governed by and interpreted in accordance with the laws of the State of New York, USA, applicable to contracts entered into and to be performed wholly within the State of New York, excluding conflict of laws principles.

14.10 Disputes. In the event of any controversy or claim arising out of, relating to or in connection with any provision of this Agreement, or the rights or obligations of the Parties hereunder, the Parties shall try to settle their differences amicably between themselves. Either Party may initiate such informal dispute resolution by sending written notice of the dispute to the other Party, and within thirty (30) days after such notice appropriate representatives of the Parties shall meet for attempted resolution by good faith negotiations. If such representatives are unable to resolve promptly such disputed matter, it shall be referred to the President of Targacept and the President of Dr. Falk's for discussion and resolution. If such personnel are unable to resolve such dispute within thirty (30) days of initiating such negotiations, either Party may submit any dispute or other claim arising out of or in connection with this Agreement for resolution by binding arbitration in London, England under the Commercial Rules of Arbitration of the International Chamber of Commerce (ICC) before a panel of three independent experts with relevant business, financial, scientific or other experience based on the subject matter of the dispute. Each Party shall select one arbitrator and the arbitrators so selected shall appoint a third arbitrator from a list of qualified persons provided by the ICC. Each Party shall pay its own costs and expenses associated with the arbitration, including the costs of its appointee and one-half the costs of the third arbitrator. Judgment on the award rendered by a majority of the arbitrators shall be binding on the Parties with no right of appeal to any court and such judgement may be entered by either Party in any court having jurisdiction thereof. Nothing in this Section 14.10 shall be construed to limit or preclude a Party from bringing an action in any court of competent jurisdiction for injunctive or other equitable relief including an action for specific performance to compel the other Party to perform its obligations under this Agreement.

14.11 Notices and Deliveries. Any notice, request, delivery, approval or consent required or permitted to be given under this Agreement shall be in writing and shall be deemed to have been sufficiently given if delivered in person, transmitted by telecopier (receipt verified) or by express courier service (signature required) or five (5) days after it was sent by

registered letter, return receipt requested (or its equivalent), to the Party to which it is directed at its address shown below or such other address or facsimile number as such party shall have last given by notice to the other Parties.

If to Dr. Falk, addressed to:

Dr. Falk Pharma GmbH
Leinenweberstrasse 5
79041 Freiburg
Telecopier: 0761-1514-377
Attn: President (*Geschaftsfuhrung)*

If to Targacept, addressed to:

Targacept, Inc.

Postal Mail Address:
P.O. Box 1487
Winston-Salem, NC 27102-1487

Street Address:
950 Reynolds Boulevard
Winston-Salem, NC 27105
Telecopier: (336) 741-1773
Attn: President and Chief Executive Officer

14.12 No Consequential Damages. SUBJECT TO SECTIONS 10.1 AND 10.2, IN NO EVENT SHALL EITHER PARTY OR ANY OF ITS RESPECTIVE AFFILIATES BE LIABLE TO THE OTHER PARTY OR ANY OF ITS AFFILIATES FOR SPECIAL, INDIRECT, INCIDENTAL OR CONSEQUENTIAL DAMAGES, WHETHER IN CONTRACT, WARRANTY, TORT, NEGLIGENCE, STRICT LIABILITY OR OTHERWISE, INCLUDING, BUT NOT LIMITED TO, LOSS OF PROFITS OR REVENUE, OR CLAIMS OF CUSTOMERS OF ANY OF THEM OR OTHER THIRD PARTIES FOR SUCH OR OTHER DAMAGES.

14.13 Waiver. A waiver by either Party of any of the terms and conditions of this Agreement in any instance shall not be deemed or construed to be a waiver of such term or condition for the future, or of any subsequent breach hereof. All rights, remedies, undertakings, obligations and agreements contained in this Agreement shall be cumulative and none of them shall be in limitation of any other remedy, right, undertaking, obligation or agreement of either party.

14.14 Severability. When possible, each provision of this Agreement will be interpreted in such manner as to be effective and valid under applicable law, but if any provision of this Agreement is held to be prohibited by or invalid under applicable law, such provision will be ineffective only to the extent of such prohibition or invalidity, without invalidating the remainder of this Agreement. The parties shall make a good faith effort to replace the invalid or

unenforceable provision with a valid one that in its economic effect is most consistent with the invalid or unenforceable provision.

14.15 Counterparts. This Agreement may be executed simultaneously in any number of counterparts, any one of which need not contain the signature of more than one Party but all such counterparts taken together shall constitute one and the same agreement, each copy of which shall for all purposes be deemed to be an original.

[remainder of page intentionally left blank]

IN WITNESS WHEREOF, the Parties have caused this Agreement to be executed by their respective duly authorized officers as of the day and year first above written.

Targacept, Inc.

By: /s/ J. Donald deBethizy
Name: J. Donald deBethizy
Title: President and CEO

Dr. Falk Pharma GmbH

By: /s/ Ursula Falk
Name: Ursula Falk
Title: Managing Director
Geschaftsfuhrerin

EXHIBIT A

1. Europe

Andorra
Albania
Austria
Belgium
Bulgaria
Bosnia-Herzegovina
Croatia
Cyprus
Czech Republic
Denmark
Estonia
Finland
France
Germany
Gibraltar
Greece
Hungary
Ireland
Iceland
Italy
Republic of Yugoslavia
Latvia
Liechtenstein
Lithuania
Luxembourg
Republic of Macedonia
Malta
Monaco
Netherlands

1. Europe (continued)

North Ireland
Norway
Poland
Portugal
Romania
Russia (including CIS-countries) *Armenia*
Azerbaijan
Georgia
Kazakhstan
Kyrgyzstan
Moldova
Russian Federation Tajikistan
Turkmenistan
Ukraine
Uzbekistan
Belarus
Slovak Republic
Slovenia
Spain
Sweden
Switzerland
Turkey
United Kingdom

2. Middle East

Egypt
Israel

EXHIBIT B

Research and Development Plan

[********]

[Entire 22-page document has been redacted.]

EXHIBIT C

Semi-Annual R&D Plan

[********]

[Entire two-page table has been redacted.]

EXHIBIT D

Targacept Patent Rights

[********]

[Entire four-page document has been redacted.]

EXHIBIT E

SUBSCRIPTION AGREEMENT

Targacept, Inc.
950 Reynolds Boulevard
Winston-Salem, North Carolina 27105

Ladies and Gentlemen:

The undersigned desires, on the terms and conditions set forth herein, to acquire from Targacept, Inc., a Delaware corporation (the "Company"), One Hundred Eleven Thousand, One Hundred Eleven (111,111) shares (the "Shares") of the Company's common stock, $0.001 par value per share ("Common Stock"). The undersigned understands that the Shares have not been registered under the Securities Act of 1933, as amended (the "Securities Act"), or the securities laws of any state (the "State Securities laws").

THE SHARES ARE SUBJECT TO RESTRICTIONS ON TRANSFER AND RESALE AND MAY NOT BE TRANSFERRED OR RESOLD EXCEPT AS PERMITTED UNDER THE SECURITIES ACT OF 1933, AS AMENDED, AND ALL APPLICABLE STATE SECURITIES LAWS, PURSUANT TO REGISTRATION OR EXEMPTION THEREFROM. THE UNDERSIGNED SHOULD BE AWARE THAT IT WILL BE REQUIRED TO BEAR THE FINANCIAL RISKS OF THIS INVESTMENT FOR AN INDEFINITE PERIOD OF TIME.

IN MAKING AN INVESTMENT DECISION THE UNDERSIGNED MUST RELY ON ITS OWN EXAMINATION OF THE COMPANY AND ITS PROPOSED BUSINESS AND PROSPECTS, INCLUDING THE MERITS AND RISKS INVOLVED. THE SHARES HAVE NOT BEEN RECOMMENDED BY ANY FEDERAL OR STATE SHARES COMMISSION OR REGULATORY AUTHORITY.

1. Subscription. Subject to the terms and conditions hereof, the undersigned hereby irrevocably subscribes for the Shares in exchange for the consideration described in Section 3.

2. Acceptance of Subscription and Issuance of Shares. The undersigned understands and agrees that this subscription shall be deemed to be accepted by the Company only when it is signed by a duly authorized officer of the Company (the "Acceptance").

3. Payment and Delivery. In consideration of the issuance of the Shares, the undersigned agrees to pay to the Company $9.00 per Share and to execute and deliver (i) the

Collaborative Research, Development and License Agreement of even date herewith by and between the undersigned and the Company (the "R&D Agreement") and (ii) the Stockholders Agreement dated August 22, 2000 by and among the Company and its stockholders (the "Stockholders Agreement").

4. Representations and Warranties of the Company. As of the date hereof, the Company represents and warrants to the undersigned that:

(a) the Company is a corporation duly organized, validly existing and in good standing under the laws of the State of Delaware and has the requisite corporate power to carry on its business as presently conducted and the requisite corporate power and authority to execute and deliver this Subscription Agreement, the R&D Agreement and the Stockholders Agreement and to perform its obligations hereunder and thereunder;

(b) the Shares, when issued against delivery of the consideration set forth in Section 3, will be legally and validly issued, fully paid and nonassessable and, assuming the accuracy of the representations and warranties made by the undersigned herein, in compliance in all material respects with all applicable federal and state securities laws;

(c) neither the Company nor any person acting on its behalf has offered or sold the Shares to the undersigned by means of any form of general solicitation or general advertising;

(d) no consent, approval, order or authorization of any federal, state or local governmental authority is required to be obtained by the Company in connection with the consummation of the transactions contemplated by this Agreement;

(e) the Company is not in violation or default in any material respect, and the execution and delivery of this Agreement and the consummation of the transactions contemplated hereby will not result in the violation or default in any material respect, of (i) any provision of its Amended and Restated Certificate of Incorporation, as amended, or Amended and Restated Bylaws, (ii) any instrument, judgment, order, writ, decree or contract to which it is a party or by which it is bound or (iii) to its knowledge, any federal or state statute, rule or regulation applicable to the Company, in each case to the extent that such violation or default has or would have a material adverse effect on the business of the Company; and

(f) neither this Agreement, nor any other document or certificate made or delivered to the undersigned in connection herewith, contains any untrue statement of a material fact or omits to state a material fact necessary to make the statements herein or therein not misleading.

5. Representations and Warranties of the Undersigned. The undersigned hereby represents and warrants to the Company and to each officer, director, controlling person, and agent of the Company as follows.

(a) General:

(i) The undersigned has all requisite corporate power and authority to execute and deliver this Subscription Agreement, the R&D Agreement and the Stockholders Agreement and to acquire the Shares and otherwise to perform all the obligations required to be performed by the undersigned hereunder and thereunder, and such execution, delivery and performance does not violate or conflict with the terms of any agreement to which the undersigned is a party or by which the undersigned is bound.

(ii) The undersigned has not received, paid or given, directly or indirectly, any commission or remuneration for or on account of any sale, or the solicitation of any sale, of the Shares.

(iii) The undersigned is not acquiring the Shares as an agent or otherwise for any other person.

(iv) The undersigned has received no representations from the Company or from employees or agents of the Company other than those contained herein or in the R&D Agreement. In making its decision to invest in the Shares, the undersigned has relied solely on the answers to such questions as its duly appointed representatives have raised concerning the transaction.

(v) The purchase of the Shares by the undersigned is consistent with the undersigned's investment objectives.

(b) Information Concerning the Company:

(i) The undersigned is familiar with the business and financial condition, properties, operations and prospects of the Company.

(ii) The undersigned has been given full access to all material information concerning the condition, properties, operations and prospects of the Company, including without limitation books, records and other documents, and

has had an opportunity to ask questions of, and to receive information from, the Company and persons acting on its behalf concerning the terms and conditions of the undersigned's investment in the Shares, and to obtain any additional information necessary to verify the accuracy of the information and data received by the undersigned.

(iii) The undersigned has made such independent investigation of the Company, its management and related matters as the undersigned deemed to be necessary or advisable in connection with this investment; and the undersigned has received all information and data that the undersigned believes to be necessary in order to reach an informed decision as to the advisability of investing in the Shares.

(c) Status of Undersigned:

(i) The undersigned has such knowledge, skill and experience in business, financial and investment matters so as to be capable of evaluating the merits and risks of an investment in the Shares. To the extent necessary, the undersigned has retained at its own expense, and relied upon, appropriate professional advice regarding the investment, tax and legal merits and consequences of this Subscription Agreement and owning the Shares. The undersigned is domiciled in Germany, is not a U.S. Person (as defined in Rule 902(k) promulgated under the Securities Act) and is not acquiring the Shares for the account or benefit of a U.S. Person.

(ii) The undersigned is a corporation, not formed for the specific purpose of acquiring the Shares, with total assets in excess of $5,000,000 and, as such is an "accredited investor" as that term is defined in Rule 501 of Regulation D promulgated under the Securities Act.

(d) Restrictions on Transfer or Sale:

(i) The undersigned is acquiring the Shares solely for the undersigned's own beneficial account, for investment purposes, and not with a view to, or for resale in connection with, any distribution thereof. The undersigned understands that the Shares have not been registered under the Securities Act or any State Securities laws by reason of specific exemptions under the provisions thereof which depend in part upon the investment intent of the undersigned and of the other representations made by the undersigned in this Subscription Agreement. The undersigned understands that the Company is relying upon the representations and agreements contained in this Subscription Agreement (and any supplemental information) for the purpose of determining whether this transaction meets the requirements for such exemptions.

(ii) The undersigned understands that the Shares are "restricted Shares" under applicable federal Securities laws and that the Securities Act and the rules of the Shares and Exchange Commission (the "Commission") provide in substance that the undersigned may dispose of the Shares only pursuant to an effective registration statement under the Securities Act or an exemption therefrom (such as pursuant to Rule 144 under the Securities Act), and understands that the Company has no obligation or intention to register any of the Shares thereunder, or to take action so as to permit sales pursuant to the Securities Act (including Rule 144 thereunder). Accordingly, the undersigned understands that (x) under the Commission's rules, the undersigned may dispose of the Shares principally only in "private placements" that are exempt from registration under the Securities Act, in which event the transferee will acquire "restricted Shares" subject to the same limitations as in the hands of the undersigned and (y) no market will exist for any resale of the Shares and it is impossible to predict whether such a market will ever exist. As a consequence, the undersigned understands that the undersigned must bear the economic risks of the investment in the Shares for an indefinite period of time.

(iii) The undersigned understands that the Shares will become subject to additional restrictions on transfer, including the application of certain rights of first refusal and co-sale rights pursuant to the Stockholders Agreement.

(iv) Independent of any legal or contractual restrictions on the sale of Shares, the undersigned agrees: (A) not to sell, assign, pledge, give, transfer or otherwise dispose of the Shares or any interest therein, or make any offer or attempt to do any of the foregoing, except pursuant to a registration of such Shares under the Securities Act and all applicable State Securities laws or in a transaction which, in the written opinion of counsel for the undersigned or other evidence satisfactory to the Company, is exempt from the registration provisions of the Securities Act and all applicable State Securities laws or is in accordance with the provisions of Regulation S promulgated under the Securities Act; (B) not to engage in any hedging transactions with respect to the Shares, except in compliance with the Securities Act; (C) that the certificate(s) for the Shares will bear a legend making reference to the foregoing restrictions; and (D) that the Company and any transfer agent for the Common Stock shall not give effect to any purported transfer of any of such shares except upon compliance with the foregoing restrictions.

(v) The undersigned has not offered or sold any portion of the Shares and has no present intention of dividing the Shares with others or of reselling or otherwise disposing of any portion of the Shares either currently or after the passage of a fixed or determinable period of time or upon the occurrence or nonoccurrence of any predetermined event or circumstance.

6. Obligations Irrevocable; Further Assurances. Upon the Company's receipt from the undersigned of an executed counterpart of this Subscription Agreement, the obligations

of the undersigned hereunder shall be irrevocable, except with the consent of the Company. Furthermore, the undersigned agrees to furnish any additional information requested to assure compliance with the applicable federal Securities laws (including without limitation the Securities Act and the regulations promulgated thereunder) and all applicable State Securities laws in connection with the purchase and sale of the Shares contemplated hereby.

7. Waiver and Amendment. Neither this Subscription Agreement nor any provisions hereof shall be modified, changed, discharged or terminated, except by an instrument in writing signed by the party against whom any waiver, change, discharge or termination is sought.

8. Assignability. Neither this Subscription Agreement nor any right, remedy, obligation or liability arising hereunder or by reason hereof shall be assignable by either the Company or the undersigned without the prior written consent of the other party.

9. Applicable Law. Subject to the applicability of the federal Securities laws and the State Securities laws, this Subscription Agreement shall be governed by and construed in accordance with the law of the State of North Carolina, regardless of the law that might be applied under principles of conflicts of law.

10. Section and Other Headings. The section and other headings contained in this Subscription Agreement are for reference purposes only and shall not affect the meaning or interpretation of this Subscription Agreement.

11. Counterparts. This Subscription Agreement may be executed in two counterparts, each of which when so executed and delivered shall be deemed to be an original and both of which together shall be deemed to be one and the same agreement.

12. Notices. All notices and other communications provided for herein shall be in writing and shall be deemed to have been duly given when delivered personally, one day after deposited with a internationally-recognized overnight courier service, with charges prepaid, or two days after sent by registered or certified mail, return receipt requested, postage prepaid:

(a) If to the Company, to the following address:

Targacept, Inc.
950 Reynolds Boulevard
Winston-Salem, North Carolina 27105
Attn: Chief Executive Officer

(b) If to the undersigned, to the following address:

Dr. Falk Pharma GmbH

Leinenweberstr 5 79041 Freiburg, Germany
Attn: Chief Executive Officer
(Geschäftsführung)

13. Binding Effect. The provisions of this Subscription Agreement shall be binding upon and accrue to the benefit of the parties hereto and their respective heirs, legal representatives and permitted successors and assigns.

14. Survival. All representations, warranties and covenants contained in this Subscription Agreement shall survive (i) the Acceptance, (ii) changes in the transactions, documents and instruments described herein which are not material, and (iii) the dissolution or liquidation of the Company or the undersigned.

15. Expenses. Each of the Company and the undersigned shall bear its own legal and other expenses with respect to this Agreement.

[remainder of page intentionally left blank]

IN WITNESS WHEREOF, the undersigned has executed this Subscription Agreement as of the date first written above.

DR. FALK PHARMA GmbH

By: /s/ URSULA FALK
Name: Ursula Falk
Title: Managing Director

Accepted as of
January ___, 2001

TARGACEPT, INC.

By: /s/ J. DONALD DEBETHIZY
J. Donald deBethizy
Chief Executive Officer

Exhibit 10.17

[********] 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.

TARGACEPT CONTRACT NO. 03-060-0147

AMENDED AND RESTATED
LICENSE AGREEMENT

This Amended and Restated License Agreement (this "**Agreement**") is made and entered into to be effective the 9th day of March 2004, by and between the UNIVERSITY OF SOUTH FLORIDA RESEARCH FOUNDATION, INC., a corporation not for profit under Chapter 617 of the Florida Statutes and a direct support organization of the University of South Florida ("**University**") pursuant to Section 1004.28 of the Florida Statutes, having its principal office at 4202 East Fowler Avenue, Tampa, Florida 33620, U.S.A. (hereinafter referred to as "**RESEARCH FOUNDATION**"), and Targacept, Inc., a Delaware Corporation, having its principal office at 200 East First Street, Suite 300, Winston-Salem, North Carolina 27101-4165 (hereinafter referred to as "**LICENSEE**") and amends and restates in its entirety the License Agreement dated October 13, 1997, as amended, between RESEARCH FOUNDATION and LICENSEE, as assignee of Layton Bioscience, Inc. (the "**Original Agreement**").

WITNESSETH

WHEREAS, RESEARCH FOUNDATION is the exclusive licensee of certain "Patent Rights" (as later defined herein) relating to the use of mecamylamine to treat neuropsychiatric disorders and has the right to grant licenses under said Patent Rights;

WHEREAS, RESEARCH FOUNDATION desires to have the Patent Rights utilized in the public interest and is willing to grant a license thereunder; and

WHEREAS, LICENSEE intends to develop, produce, manufacture, market and/or sell "Licensed Product(s)" (as later defined herein) and is willing to commit itself to a diligent program of exploiting the Patent Rights so that public utilization shall result therefrom; and

WHEREAS, LICENSEE desires to obtain a license under the Patent Rights upon the terms and conditions hereinafter set forth.

NOW, THEREFORE, in consideration of the premises and the mutual covenants contained herein, the parties hereto agree as follows:

ARTICLE I. DEFINITIONS

For the purposes of this Agreement, the following words and phrases shall have the following meanings:

1.1 "Annual License Fee" shall mean **[********]**, and "Annual Rights Fee" means **[********]**.

1.2 “Competition” shall, with respect to any Licensed Product, be deemed to exist in a particular country for and after the first calendar quarter in which **[********]**.

1.3 “Competitive Product” shall mean, with respect to any Licensed Product, any pharmaceutical product containing an active ingredient that is the same compound as a Named Compound contained in or comprising such Licensed Product, or any analog, salt, solvate, prodrug form, inclusion complex or metabolite thereof, that **[********]**.

1.4 “Confidential Information” shall mean, subject to Paragraph 15.3, information that is confidential, proprietary or otherwise not generally available to the public.

1.5 “Effective Date” shall mean the date so identified above in the preamble to this Agreement.

1.6 “Improvement” shall mean, with respect to any Licensed Product, technology that **[********]**.

1.7 “Licensed Process” shall mean any process that relates to a Named Compound and infringes or would infringe, in whole or in part, a Valid Claim contained in the Patent Rights.

1.8 “Licensed Product” shall mean any product or part thereof containing or comprising a Named Compound that:

(a) infringes or would infringe, in whole or in part, a Valid Claim contained in the Patent Rights in the country in which such product or part thereof is made, used, leased or sold; or

(b) is made by a process that is a Licensed Process in the country in which such product is made, used or sold.

1.9 “LICENSEE” shall include, in addition to Targacept, Inc.: a related company of Targacept, Inc., the voting stock of which is, directly or indirectly, at least fifty percent (50%) owned or controlled by Targacept, Inc.; an organization which directly or indirectly controls more than fifty percent (50%) of the voting stock of Targacept, Inc.; and an organization, the majority ownership of which is, directly or indirectly, common to the ownership of Targacept, Inc.. References in this Paragraph 1.9 to “voting stock” shall mean capital stock entitled to vote in the election of the board of directors or the analogous body of a noncorporate entity.

1.10 “Losses” shall mean all claims and expenses, including reasonable attorneys’ fees, actually incurred.

1.11 “Milestones” shall mean events defined in Appendix B.

1.12 “Named Compounds” shall mean **[********]**.

1.13 “NDA Filing Date” shall mean the date on which LICENSEE (or its sublicensee or collaborative partner) files its first New Drug Application (or its equivalent) with the United States Food and Drug Administration or any comparable foreign regulatory authority for the use of a Licensed Product to treat attention deficit hyperactivity disorder and/or any other neuropsychiatric disease or disorder in any country.

1.14 “Net Sales” shall mean **[********]**.

1.15 “Option Invention” shall mean any discovery, compound, improvement, invention, idea, process or technique, whether or not patentable, that (i) is made, conceived or first reduced to practice by RESEARCH FOUNDATION and (ii) without regard to any rights reserved under Paragraph 2.2, cannot reasonably be practiced without infringing the Patent Rights licensed to LICENSEE hereunder.

1.16 “Patent Rights” shall mean, collectively, (i) the patents and patent applications listed on Appendix A, (ii) all patents that issue from patent applications listed on Appendix A and all reexaminations, reissues, revisions, substitutes, renewals or extensions thereof, and (iii) all other United States and foreign patents that issue from applications that claim priority to patents and patent applications listed on Appendix 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.

1.17 “Special Issue Dispute” shall mean a dispute between the parties as to whether (i) LICENSEE is meeting its diligence obligation hereunder or (ii) a condition that would give rise to a royalty reduction under Paragraph 4.1(b)(i) or 4.1(c) has occurred or been met.

1.18 “Sublicense Fees” shall mean any fees (including the fair market value of any consideration paid other than in cash) received by LICENSEE for a sublicense of Patent Rights, excluding (i) running royalties on the sale or lease of Licensed Products, (ii) payments specifically allocated to research and development for, or to the manufacture or supply of, a Licensed Product or Licensed Process, (iii) amounts received by LICENSEE that it is required to repay (e.g., a loan) and (iv) payments received in exchange for securities of LICENSEE.

1.19 “Substantial LICENSEE IP Rights” shall mean any issued patent or pending patent application owned or licensed by LICENSEE that claims an Improvement, but excluding Improvements for which both LICENSEE and RESEARCH FOUNDATION provided independent inventive contribution.

1.20 “Territory” shall mean the world.

1.21 “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.

ARTICLE II. GRANT

2.1 (a) RESEARCH FOUNDATION hereby grants to LICENSEE the perpetual, exclusive right and license under the Patent Rights to research, develop, make, have made, use, market, distribute, lease, sell, import and export Licensed Products and Licensed Processes for any and all indications in the Territory, with the right to practice all or any portion of the foregoing right and license through subcontractors which, unless specifically sublicensed hereunder, shall not be considered sublicensees hereunder.

(b) In the event that RESEARCH FOUNDATION receives a *bona fide* third party offer whereby such third party would obtain a right or license under any of the Patent Rights for any purpose not exclusively licensed to LICENSEE hereunder (the “**Subject Rights**”), (i) RESEARCH FOUNDATION shall notify LICENSEE of all material terms of such offer in writing (the “**Subject Notice**”) within ten (10) business days after its receipt by RESEARCH FOUNDATION, which notice shall certify as to the receipt of such offer from a *bona fide* third party, and (ii) LICENSEE shall thereupon have a right of refusal to license the Subject Rights on the same terms set forth in the Subject Notice. LICENSEE may exercise its right of first refusal at any time within **[********]** after its receipt of the Subject Notice by written notice to RESEARCH FOUNDATION, and, in such event, the parties shall work diligently towards execution of a definitive license agreement reflecting the terms in the Subject Notice and, to the extent not inconsistent, the terms hereof; provided that, if mutually acceptable, the parties may elect instead to amend and restate this agreement to incorporate the Subject Rights and associated terms. If LICENSEE’s right of refusal expires unexercised, RESEARCH FOUNDATION shall have the right to license the Subject Rights to such third party on the terms set forth in the Subject Notice; provided that, in the event of any substantive change in such terms, RESEARCH FOUNDATION shall again provide the Subject Notice to LICENSEE and LICENSEE shall again have a right of first refusal as provided herein. LICENSEE shall, notwithstanding the periods provided in this Paragraph 2.1(b), use good faith efforts to respond to the Subject Notice (whether the initial Subject Notice or a subsequent Subject Notice following a substantive change in terms) as promptly as reasonably practicable within the applicable period.

(c) RESEARCH FOUNDATION: (i) shall, within thirty (30) days of the identification of each Option Invention, report such Option Invention to LICENSEE, together with any patent disclosures and any supporting technical

data or other information it possesses that may be relevant to understanding the value or commercial significance of such Option Invention; and (ii) hereby grants to LICENSEE a first option to negotiate an exclusive, worldwide, royalty-bearing commercially reasonable license (with the right to sublicense) to RESEARCH FOUNDATION's rights in each Option Invention for any purpose. LICENSEE may exercise any such option by providing written notice to RESEARCH FOUNDATION within sixty (60) days of its receipt of the notice of the applicable Option Invention. Upon exercise of the Option, the parties shall negotiate in good faith the terms of such license based on **[********]**.

2.2 RESEARCH FOUNDATION reserves to the University the right to practice under the Patent Rights solely for the University's internal research and education purposes; provided that the foregoing rights shall be expressly subject to RESEARCH FOUNDATION's obligations pursuant to Paragraph 15.

2.3 Notwithstanding anything herein to the contrary, in no event shall either RESEARCH FOUNDATION or University perform research sponsored by, or for the benefit of, a third party for-profit entity where such research, if performed by such third party for-profit entity, would infringe or would be reasonably likely to infringe the Patent Rights licensed to LICENSEE hereunder.

2.4 The license granted hereunder shall not be construed to confer any rights upon LICENSEE by implication, estoppel or otherwise as to any technology except as specifically set forth herein.

2.5 LICENSEE may grant exclusive or nonexclusive sublicenses to third-party sublicensees with respect to all or any portion of the license granted to LICENSEE hereunder only with the approval of RESEARCH FOUNDATION, which shall: (i) be given unless RESEARCH FOUNDATION reasonably believes in good faith that the proposed sublicense will result in LICENSEE's inability to fulfill its obligations hereunder; (ii) otherwise not be unreasonably withheld or delayed; and (iii) be deemed given unless written notice to the contrary is received by LICENSEE within thirty (30) days after written notice requesting approval is received by RESEARCH FOUNDATION. RESEARCH FOUNDATION shall, notwithstanding the period provided in this Paragraph 2.4, use good faith efforts to respond to LICENSEE'S written notice as promptly as reasonably practicable within such period.

2.6 LICENSEE agrees to forward to RESEARCH FOUNDATION a copy of any and all fully executed sublicense agreements contemplated by Paragraph 2.4. At the request of RESEARCH FOUNDATION, LICENSEE shall also provide copies of all distribution agreements and other such agreements relative to the Licensed Products or involving rights granted to LICENSEE under the agreement.

2.7 Termination of the license granted to LICENSEE in this Agreement shall terminate all sublicenses which may have been granted by LICENSEE; provided that any sublicensee may elect to continue its sublicense by advising RESEARCH

FOUNDATION in writing, within (60) sixty days of the sublicensee's receipt of written notice of such termination from RESEARCH FOUNDATION, of its election and its agreement to assume all of the obligations to RESEARCH FOUNDATION (including obligations for payment) contained in this Agreement. Any sublicense granted by LICENSEE shall contain provisions corresponding to those of this paragraph respecting termination and the conditions of continuance of sublicenses.

2.8 Except as otherwise provided in a research or other written agreement between the parties, each invention, discovery, proprietary development, data and information, in any medium or manifestation, including any method, process, composition of matter, apparatus, device, system, product, article of manufacture or appliance made or developed after the Effective Date, and all intellectual property rights relating thereto, shall be owned exclusively by the party making or developing it, without any accounting, compensation or other obligation hereunder to the other party.

ARTICLE III. DUE DILIGENCE

3.1 LICENSEE shall use commercially reasonable efforts (either alone or through research collaborations or alliances with research organizations, pharmaceutical companies or other third parties) to market and sell, or to develop, one or more Licensed Products or Licensed Processes through a diligent program for exploitation of the Patent Rights, and LICENSEE's failure to use such efforts shall be grounds for RESEARCH FOUNDATION to terminate this Agreement pursuant to Paragraph 13.3. Without limiting the generality of the foregoing, until the NDA Filing Date, LICENSEE shall: (i) spend a minimum of **[********]**to conduct research and development of one or more Licensed Products; provided that, for the avoidance of doubt, any or all of such amount may **[********]**; and (ii) deliver to RESEARCH FOUNDATION, at least annually, a brief report summarizing its research and development activities completed since the last report, research and development activities currently in process, planned future research and development activities and research and development work being performed by third parties. If RESEARCH FOUNDATION believes LICENSEE is failing to comply with its obligations under this Paragraph 3.1, RESEARCH FOUNDATION may send notice to the LICENSEE asserting such belief and the basis therefor. LICENSEE shall have sixty (60) days from its receipt of such notice either to (i) commence compliance with its obligations under this Paragraph 3.1 to RESEARCH FOUNDATION's reasonable satisfaction or (ii) send notice to RESEARCH FOUNDATION requesting that such issue be resolved in accordance with Article XII, in which case the procedures set forth in Article XII shall be followed.

3.2 LICENSEE will use commercially reasonable efforts to effect the NDA Filing Date on or before December 31, 2012; provided that the parties acknowledge that (i) the foregoing target is expressly subject to significant scientific, clinical and

regulatory uncertainties and (ii) failure to meet such target shall not constitute a breach of this Agreement or entitle RESEARCH FOUNDATION to terminate this Agreement if SPONSOR is in compliance with Paragraph 3.1, but shall entitle RESEARCH FOUNDATION, upon sixty (60) days written notice to LICENSEE, to make the license granted in Paragraph 2.1(a) nonexclusive.

3.3 LICENSEE may, but expressly without creating any binding obligation, (i) consider University to conduct or, if applicable, to coordinate particular pre-clinical or early-stage clinical research in furtherance of LICENSEE's diligence obligations hereunder and (ii) communicate with University researchers from time to time regarding the research and development of one or more Licensed Products hereunder.

ARTICLE IV. FEES AND ROYALTIES

4.1 For the rights, privileges and license granted hereunder, LICENSEE shall pay to RESEARCH FOUNDATION:

(a) Milestone payments payable, if at all, at the times and upon achievement of the Milestones set forth on Appendix B.

(b) Running royalties equal to the Applicable Royalty Amount. The "Applicable Royalty Amount" shall be **[********]** of Net Sales of Licensed Products in any country; provided that, with respect to a particular Licensed Product in a particular country:

(i) if (A) **[********]** or (B) there exists Competition for such Licensed Product in such country, the Applicable Royalty Amount shall be reduced to **[********]** of Net Sales of such Licensed Product in such country; and

(ii) if LICENSEE (or a sublicensee) deems it necessary or advisable to secure a third party license in order to practice in such country any portion of the license granted by RESEARCH FOUNDATION hereunder (including, without limitation, the sale of Licensed Products), the Applicable Royalty Amount shall be reduced by **[********]**of the amounts paid to secure such third party license, but in no event to an amount less than **[********]** of Net Sales of Licensed Products in such country.

Notwithstanding the foregoing:

(1) the obligations in this Paragraph 4.1(b) shall expire with respect to Net Sales of a particular Licensed Product in a particular country on the date of expiration of the last-to-expire Valid Claim included in the Patent Rights covering, in whole or in part, such Licensed Product in such country;

(2) if Licensed Products are sold or leased by a sublicensee, LICENSEE shall instead pay to RESEARCH FOUNDATION the lesser of the amount calculated as provided above in this Paragraph 4.1(b) or **[********]** of the running royalties on the sale or lease of Licensed Products actually received by LICENSEE from such sublicensee;

(3) the Company's obligation to pay royalties under this Paragraph 4.1(b) shall be imposed only once with respect to the same unit of a Licensed Product regardless of how many Patent Rights or Valid Claims pertain thereto; and

(4) all Annual License Fees, in the aggregate, paid by LICENSEE hereunder as of the NDA Filing Date shall be creditable against running royalties due under this Paragraph 4.1, after any reduction resulting from application of the various subparagraphs of this Paragraph 4.1; provided that a maximum of **[********]** shall be creditable annually under this subparagraph (4). **[********]**

(c) **[********]** of all Sublicense Fees actually received by LICENSEE from any sublicensee, to be reduced to **[********]** if such sublicense is granted together (whether in the same or in a related agreement) with Substantial LICENSEE IP Rights.

4.2 Royalty payments shall be paid in United States dollars in Tampa, Florida, or at such other place as RESEARCH FOUNDATION may reasonably designate consistent with the laws and regulations controlling in any foreign country. Any withholding taxes that the LICENSEE is required by law to withhold on remittance of the royalty payments will be deducted from the royalty paid. If any currency conversion shall be required in connection with the payment of royalties hereunder, such conversion shall be made by using the exchange rate prevailing at the Chase Manhattan Bank (N.A.) on the last business day of the calendar quarter reporting period to which such royalty payments relate.

4.3 In addition to the foregoing, LICENSEE shall pay to RESEARCH FOUNDATION (i) the Annual License Fee, which obligation shall expire as of the NDA Filing Date, and (ii) for the rights granted to LICENSEE in Paragraph 2.1(b), the Annual Rights Fee, each such payment to be made within thirty (30) days of each anniversary of the Effective Date in United States dollars.

ARTICLE V. REPORTS AND RECORDS

5.1 LICENSEE shall keep full, true and accurate books of account containing all particulars that may be necessary for the purpose of showing the amounts payable to RESEARCH FOUNDATION hereunder for five (5) years following the end of the calendar year to which they pertain. Such books and records shall be made

available, upon reasonable notice and during normal business hours, for the inspection of RESEARCH FOUNDATION or its agents (at the sole expense of RESEARCH FOUNDATION) for the purpose of verifying LICENSEE's royalty statement or compliance in other respects with this Agreement. This obligation to maintain accurate books of account and the right to inspect them shall survive termination of this Agreement for the period described above.

5.2 LICENSEE, within sixty (60) days after March 31, June 30, September 30 and December 31, of each year, shall deliver to RESEARCH FOUNDATION true and accurate reports, giving such particulars of the business conducted by LICENSEE and its sublicensees during the preceding three-month period under this Agreement as shall be pertinent to a royalty accounting hereunder, including an accounting for Licensed Processes used and Licensed Products and the billings, deductions and royalties due with respect thereto. In the event the examination shows an underpayment, LICENSEE shall pay RESEARCH FOUNDATION the amounts underpaid. In addition, in the event the examination shows an underpayment of more than five percent (5%) for any quarter, LICENSEE shall pay the RESEARCH FOUNDATION, in addition to the amounts underpaid, out-of-pocket costs of the audit and interest on the underpayment at the rate of **[********]**.

5.3 With each such report submitted, LICENSEE shall pay to RESEARCH FOUNDATION the royalties due and payable under this Agreement. If no royalties shall be due, LICENSEE shall so report.

5.4 The royalty payments set forth in this Agreement shall, if overdue, bear interest until payment at a rate of **[********]**. The payment of such interest shall not foreclose RESEARCH FOUNDATION from exercising any other rights it may have as a consequence of the lateness of the payment.

ARTICLE VI. PATENT PROSECUTION

6.1 The filing and prosecution of all United States and foreign patent applications and maintenance of all United States and foreign patents within the Patent Rights during the term of this Agreement shall be the responsibility of LICENSEE at its sole expense and acting in good faith. LICENSEE shall (i) provide, or direct its patent counsel to provide, to RESEARCH FOUNDATION copies of all material information specifically relating to the prosecution, issuance and maintenance of the Patent Rights and (ii) give due consideration in good faith to comments timely received from RESEARCH FOUNDATION or its patent counsel. RESEARCH FOUNDATION agrees to promptly provide to LICENSEE such assistance, information, and executed documents needed to facilitate the prosecution, issuance, and maintenance of the Patent Rights as LICENSEE may reasonably request and LICENSEE shall reimburse RESEARCH FOUNDATION for reasonable out-of-pocket expenses incurred to provide such assistance,

information, and documents, subject to received of itemized statements and other appropriate supporting documentation.

6.2 In the event the LICENSEE determines that filing, prosecution or maintenance of any of the U.S. or foreign patent applications or patents within the Patent Rights is not justified and so advises RESEARCH FOUNDATION in writing, RESEARCH FOUNDATION will then have the option to file, prosecute or maintain any such Patent Rights at its own expense. If RESEARCH FOUNDATION does so: (i) RESEARCH FOUNDATION will then have the option to delete such U.S. or foreign patent applications or patents within said Patent Rights from the license granted hereunder for the territory covered thereby; (ii) LICENSEE will have no rights under the license granted hereunder for any such deleted U.S. or foreign patent applications or patent; (iii) RESEARCH FOUNDATION will obtain all rights in and to such deleted U.S. or foreign patent applications or patents and will be free to exploit and to assign or license any such deleted U.S. or foreign patent applications or patents to third parties without effect on the amount of royalties or other payments due to RESEARCH FOUNDATION under Article III.

ARTICLE VII. INFRINGEMENT

7.1 The parties shall inform each other promptly, in writing, of any alleged infringement of the Patent Rights by a third party and any available evidence thereof. Neither party will settle or compromise any claim or action in a manner that imposes any restrictions or obligations on the other party without such other party's written consent, which shall not be unreasonably withheld.

7.2 During the term of this Agreement, LICENSEE shall have the first right, but shall not be obligated, to prosecute at its own expense any such infringements of the Patent Rights and, in furtherance of such right, RESEARCH FOUNDATION hereby agrees that LICENSEE may join RESEARCH FOUNDATION as a party plaintiff in any such suit, without expense to RESEARCH FOUNDATION. Except as provided in Paragraph 7.4, the total cost of any such infringement action commenced solely by LICENSEE shall be borne by LICENSEE, and LICENSEE shall keep any recovery or damages for past infringement derived therefrom. Subject to Paragraph 7.1, LICENSEE shall be entitled to settle any such litigation by agreement, consent, judgment, voluntary dismissal or otherwise.

7.3 If within six (6) months after having been notified of any alleged infringement, LICENSEE shall have been unsuccessful in persuading the alleged infringer to desist and shall not have brought and shall not be diligently prosecuting an infringement action, or if LICENSEE shall notify RESEARCH FOUNDATION at any time prior thereto of its intention not to bring suit against any alleged infringer, then, and in those events only, RESEARCH FOUNDATION shall have the right, but shall not be obligated, to prosecute at its own expense any infringement of the Patent Rights. The total cost of any such infringement action commenced solely by RESEARCH FOUNDATION will be borne by

RESEARCH FOUNDATION, and RESEARCH FOUNDATION will keep any recovery or damages for past infringement derived therefrom. Subject to Paragraph 7.1, RESEARCH FOUNDATION shall be entitled to settle any such litigation by agreement, consent, judgment, voluntary dismissal or otherwise.

7.4 In the event that LICENSEE shall undertake the enforcement and/or defense of the Patent Rights by litigation, LICENSEE may withhold up to fifty percent (50%) of the royalties otherwise thereafter due RESEARCH FOUNDATION hereunder and apply the same toward reimbursement of up to fifty percent (50%) of its expenses, including reasonable attorneys' fees, in connection therewith. Any recovery by LICENSEE of damages for past infringement in any such suit shall be applied first in satisfaction of any unreimbursed expenses and legal fees of LICENSEE relating to the suit and next toward reimbursement of RESEARCH FOUNDATION for any royalties past due or withheld and applied pursuant to this Article VII. LICENSEE shall keep the balance remaining from any such recovery.

7.5 In the event that a declaratory judgment action alleging invalidity or noninfringement of any of the Patent Rights shall be brought against RESEARCH FOUNDATION, LICENSEE at its option, shall have the right, within thirty (30) days after commencement of such action, to intervene and take over the sole defense of the action at its own expense, except as provided in Paragraph 7.4. In such event, LICENSEE shall keep any recovery or damages derived therefrom or from any counterclaims asserted therein.

7.6 In any infringement suit instituted, or declaratory action defended, by either party to enforce or protect the Patent Rights pursuant to this Agreement, the other party hereto shall, at the request and expense of the party initiating or defending such suit, cooperate in all respects and, to the extent possible, have its employees testify when requested and make available relevant records, papers, information, samples, specimens, and the like.

7.7 RESEARCH FOUNDATION warrants and represents that it owns all right, title and interest in and to the Patent Rights, has the lawful right to grant the license provided in this Agreement and that it has not granted rights or licenses in derogation of this Agreement. RESEARCH FOUNDATION agrees that, during the term of this Agreement or any license granted hereunder, RESEARCH FOUNDATION shall not enter into any other agreements that conflict with the rights or obligations provided hereunder, including any rights and obligations that survive termination of this Agreement.

ARTICLE VIII. PRODUCT LIABILITY; INDEMNIFICATION

8.1 LICENSEE shall, at all times during the term of this Agreement and thereafter, indemnify, defend and hold RESEARCH FOUNDATION, the University and their trustees, officers, employees and affiliates, harmless against all Losses

arising directly out of the death of, or injury to, any person or persons or damage to property resulting from the LICENSEE's or any of its sublicensee's production, manufacture, sale, use (both experimental and consumer), lease, consumption or advertisement of the Licensed Product(s), except to the extent such Losses arise, directly or indirectly, out of the negligence or misconduct of RESEARCH FOUNDATION, the University or any of their respective trustees, officers, employees, agents, representatives or affiliates.

8.2 LICENSEE shall procure and maintain liability insurance in amounts customary in the relevant industry in which LICENSEE commercially exploits Licensed Products.

8.3 EXCEPT AS OTHERWISE EXPRESSLY SET FORTH IN THIS AGREEMENT, RESEARCH FOUNDATION MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESSED OR IMPLIED, INCLUDING, BUT NOT LIMITED TO WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, AND VALIDITY OF PATENT RIGHTS CLAIMS, ISSUED OR PENDING. NOTWITHSTANDING ANYTHING IN THIS ARTICLE VIII OR ELSEWHERE HEREIN TO THE CONTRARY, NEITHER PARTY SHALL BE LIABLE FOR LOSS OF PROFITS, LOSS OF USE OR ANY OTHER INCIDENTAL, CONSEQUENTIAL, EXEMPLARY OR SPECIAL DAMAGES WHATSOEVER EVEN IF ADVISED OF THE POSSIBILITY OF SUCH DAMAGES.

ARTICLE IX. EXPORT CONTROLS

9.1 It is understood that RESEARCH FOUNDATION is subject to United States laws and regulations controlling the export of technical data, computer software, laboratory prototypes and other commodities (including the Arms Export Control Act, as amended and the Export Administration Act of 1979), and that its obligations hereunder are contingent on compliance with applicable United States export laws and regulations. The transfer of certain technical data and commodities may require a license from the applicable agency of the United States Government and/or written assurances by LICENSEE that LICENSEE shall not export data or commodities to certain foreign countries without prior approval of such agency. RESEARCH FOUNDATION neither represents that a license will not be required nor that, if required, it will be issued.

ARTICLE X. NON-USE OF NAMES

10.1 LICENSEE shall not use the names of RESEARCH FOUNDATION, the University or of any of its employees, or any adaptation thereof, in any advertising, promotional or sales literature without prior written consent obtained from RESEARCH FOUNDATION in each case, except that (i) LICENSEE may

state that it is licensed by RESEARCH FOUNDATION under one or more of the patents and/or applications comprising the Patent Rights and (ii) to the extent required by law, regulation or court order.

10.2 RESEARCH FOUNDATION shall not use the name of LICENSEE or of any of its employees, or any adaptation thereof, in any advertising, promotional or sales literature without prior written consent obtained from LICENSEE, except RESEARCH FOUNDATION to the extent required by law, regulation or court order.

ARTICLE XI. ASSIGNMENT

11.1 This Agreement is not assignable by either party without the consent of the other party except that (i) LICENSEE may assign this Agreement in connection with any merger, consolidation, sale of all or substantially all of its assets or equity, or sale of a controlling interest in LICENSEE, and (ii) LICENSEE may assign this Agreement to another entity in which LICENSEE maintains at least a majority ownership interest.

ARTICLE XII. DISPUTE RESOLUTION

12.1 No party to this Agreement shall institute a proceeding in any court or administrative agency to resolve a Special Issue Dispute before that party has sought to resolve the Special Issue Dispute through direct negotiation with the other party. If the dispute is not resolved within three weeks after a demand for direct negotiation, the parties shall attempt to resolve such Special Issue Dispute through mediation in Atlanta, Georgia administered by the American Arbitration Association under its commercial mediation rules and procedures then in effect. The mediator shall be mutually acceptable to each of the parties. If the mediator is unable to facilitate a settlement of the Special Issue Dispute within a reasonable period of time, as determined by the mediator, the mediator shall issue a written statement to the parties to that effect and the aggrieved party may then seek relief through final and binding arbitration in Atlanta, Georgia administered by the American Arbitration Association under its commercial arbitration rules and procedures then in effect. All arbitration proceedings shall be before a board of three (3) arbitrators who are knowledgeable about pharmaceutical development, and each party shall select one (1) arbitrator and the selected arbitrators shall select the third arbitrator. The arbitration proceedings shall be conducted in the English language and any award shall be in United States dollars. The cost of the third arbitrator shall be divided equally between the parties and each party shall pay the costs of the arbitrator selected by it. The arbitrators shall have no power to add to, subtract from or modify any of the terms or conditions of this Agreement, shall base any award on applicable laws and judicial precedent and include in such award a statement of the reasons upon which the award is based.

12.2 All applicable statutes of limitation and defenses based upon the passage of time shall be tolled while the procedures specified in this Article XII are pending. The parties shall take such action, if any, required to effectuate such tolling

12.3 Each party is required to continue to perform its obligations under this Agreement pending final resolution of any Special Issue Dispute.

ARTICLE XIII. TERMINATION

13.1 RESEARCH FOUNDATION shall have the right to terminate this Agreement at any time upon notice to LICENSEE in the event either (a) If LICENSEE shall file in any court, pursuant to any statute either of the United States or any state, a petition in bankruptcy or insolvency or for the appointment of a receiver or trustee of all or substantially all of LICENSEE's property, or if LICENSEE shall make an assignment for the benefit of creditors, or if LICENSEE shall commit any other affirmative act of insolvency; or (b) if there shall be filed against LICENSEE in any court, pursuant to any statute either of the United States or any state, an involuntary petition in bankruptcy or insolvency or for reorganization, or if there shall be involuntarily appointed a receiver or trustee of all or substantially all of LICENSEE's property, in either case unless such petition, assignment, affirmative act or appointment is set aside or withdrawn or ceases to be in effect within one hundred twenty (120) days after the date of the filing.

13.2 If LICENSEE fails to pay RESEARCH FOUNDATION royalties due and payable hereunder, RESEARCH FOUNDATION shall have the right to terminate this Agreement on thirty (30) days notice, unless LICENSEE shall pay RESEARCH FOUNDATION within the thirty (30) day period, all such royalties and interest due and payable. Upon the expiration of the thirty (30) day period and unless such termination notice shall have been withdrawn or canceled during the 30-day period, if LICENSEE shall not have paid all such royalties and interest due and payable, the rights, privileges and license granted hereunder shall terminate. For the avoidance of doubt, failure by LICENSEE to pay the Annual Rights Fee to RESEARCH FOUNDATION shall not give rise to a right of termination of this Agreement but, if such failure continues for ten (10) business days following receipt by LICENSEE of written notice thereof from RESEARCH FOUNDATION, the rights granted to LICENSEE under Paragraph 2.1(b), but no other provision of this Agreement, shall terminate.

13.3 Upon any material breach or default of this Agreement by LICENSEE, other than those occurrences set out in Paragraphs 12.1, 13.1 and 13.2 hereinabove, which shall always take precedence in that order over any material breach or default referred to in this Paragraph 13.3, RESEARCH FOUNDATION shall have the right to terminate this Agreement and the rights, privileges and license granted hereunder on thirty (30) days notice to LICENSEE. Such termination shall become effective unless (i) the termination notice shall have been withdrawn or canceled during the 30-day period, (ii) LICENSEE shall have cured such breach

or default prior to the expiration of the thirty (30) day period or (iii) at the expiration of such thirty (30) day period, LICENSEE can demonstrate to RESEARCH FOUNDATION's reasonable satisfaction that it is working diligently and in good faith to cure such breach or default, LICENSEE shall have an additional cure period, not to exceed ninety (90) days.

13.4 LICENSEE shall have the right to terminate this Agreement at any time upon written notice to RESEARCH FOUNDATION and payment of all amounts due RESEARCH FOUNDATION through the effective date of the termination.

13.5 Upon termination of this Agreement for any reason, nothing herein shall be construed to release either party from any obligation that matured prior to the effective date of such termination. LICENSEE may, however, after the effective date of such termination, sell all Licensed Products, and complete Licensed Products in the process of manufacture at the time of such termination and sell the same; provided that LICENSEE shall pay to RESEARCH FOUNDATION the royalties thereon as required by Article IV and shall submit the reports required by Article V.

13.6 If not earlier terminated, this Agreement shall terminate on the date of expiration of the last-to-expire Valid Claim included in the Patent Rights, and LICENSEE shall thereupon have the rights and licenses set forth in Paragraphs 2.1(a) and 2.4 without any further obligation to RESEARCH FOUNDATION hereunder, which rights and licenses shall survive such termination.

ARTICLE XIV. PAYMENTS, NOTICES AND OTHER COMMUNICATIONS

14.1 Any payment, notice or other communication pursuant to this Agreement shall be given in writing and shall be deemed received on the date of personal delivery, one day after deposit with a nationally recognized overnight delivery service with charges prepaid or two days after mailing if sent to such party by Certified First Class Mail, Postage Prepaid, addressed to it at its address below or as it shall designate by written notice given to the other party. In the case of:

RESEARCH FOUNDATION:	LICENSEE:
USF Research Foundation, Inc. Attention: Business Manager USF Box 30445 Tampa, Florida 33620-3044	Targacept, Inc. 200 East First Street, Suite 300 Winston-Salem, NC 27101-4165 Attn: Vice President, Business and Commercial Development

ARTICLE XV. CONFIDENTIALITY

15.1 RESEARCH FOUNDATION and LICENSEE recognize that each party may need to provide certain of its Confidential Information from time to time to the

other party pursuant to this Agreement. The parties expressly agree that Confidential Information does not exist in written form only, but may also include oral, printed, magnetic, electronic, computer-generated or other communications and information learned by inspection of tangible objects. RESEARCH FOUNDATION and LICENSEE agree to hold in confidence, in accordance with this Article XV, any Confidential Information disclosed by one party to the other under this Agreement. For the purpose hereof, “hold in confidence” means that RESEARCH FOUNDATION and LICENSEE will not disclose the Information of the other party to a third party and will protect the Information provided to it by the other party in the same manner in which it protects its own confidential information of similar nature, but will in no event use less than reasonable care. The Confidential Information will remain the property of the party disclosing it.

15.2 The obligations of the receiving party to maintain confidentiality under this Agreement will survive its termination for ten (10) years thereafter.

15.3 Confidential Information does not include information that:

(i) is already known to the receiving party prior to the Effective Date;

(ii) is or becomes publicly known through no fault of receiving party;

(iii) has been or is disclosed to the receiving party by a third party that the receiving party does not know (and is not reckless in not knowing) to be under an obligation of confidence or secrecy to the disclosing party at the time of disclosure;

(iv) is developed by employees or consultants of the receiving party who had no knowledge of the Confidential Information;

(v) is approved for release by written authorization of the disclosing party; or

(vi) is required to be disclosed by law, provided the receiving party promptly notifies the disclosing party in writing prior to such disclosure, considers in good faith any comments or suggested changes to such disclosure from the disclosing party and gives the disclosing party a reasonable opportunity to prevent or limit the disclosure.

15.4 The parties further agree that LICENSEE shall have the right to disclose Confidential Information to: (i) potential sublicensees, assignees or subcontractors for the purpose of allowing any such potential sublicensee, assignee or subcontractor to evaluate whether to enter into a sublicense, assignment or subcontract; (ii) potential sublicensees, assignees or subcontractors, for the purpose of allowing such sublicensee, assignee or subcontractor, as the case may be, to make, have made, use, research, develop, have developed, lease, market, offer to sell, sell, have sold, distribute, improve, import and export Licensed

Products; (iii) a purchaser or potential purchaser of all or substantially all of LICENSEE's assets, or a party with which LICENSEE is then in discussions regarding a potential business combination; and (iv) an investor or lender, or prospective investor or lender, in or to LICENSEE; provided, however, that, except in the case of an actual or prospective investor or lender, LICENSEE shall obtain a confidentiality agreement (substantially similar in content to the provisions of this Paragraph 15) from the party to which such disclosures are to be made prior to any such disclosure.

ARTICLE XVI. MISCELLANEOUS PROVISIONS

16.1 This Agreement shall be construed, governed, interpreted and applied in accordance with the laws of the State of Florida, U.S.A., except that questions affecting the construction and effect of any patent shall be determined by the law of the country in which the patent was granted.

16.2 The parties hereto acknowledge that this Agreement sets forth the entire Agreement and understanding, and supersedes and makes null and void any and all prior understandings and agreements, of the parties hereto as to the subject matter hereof (including without limitation the Original Agreement and the letter between the RESEARCH FOUNDATION and LICENSEE dated April 29, 2003), and shall not be subject to any change or modification except by the execution of a written instrument subscribed to by the parties hereto.

16.3 The provisions of this Agreement are severable, and in the event that any provisions of this Agreement shall be determined to be invalid or unenforceable under any controlling body of the law, such invalidity or unenforceability shall not in any way affect the validity or enforceability of the remaining provisions hereof.

16.4 LICENSEE agrees to mark the Licensed Products sold in the United States (or their respective packagings or packaging inserts) with all applicable United States patent numbers. All Licensed Products shipped to or sold in other countries (or their respective packagings or packaging inserts) shall be marked in such a manner as to conform with the patent laws and practice of the country of manufacture or sale.

16.5 The failure of either party to assert a right hereunder or to insist upon compliance with any term or condition of this Agreement shall not constitute a waiver of that right or excuse a similar subsequent failure to perform any such term or condition by the other party.

16.6 This Agreement will be binding and inure to the benefit of the parties hereto and their respective affiliates and permitted successors and assigns.

16.7 The representations, warranties, covenants, and undertakings contained in this Agreement are for the sole benefit of the parties hereto and their permitted

successors and assigns and such representations, warranties, covenants, and undertakings will not be construed as conferring any rights on any other party, other than the University.

16.8 Nothing contained in this Agreement will be deemed to place the parties hereto in a partnership, joint venture or agency relationship and neither party will have the right or authority to obligate or bind the other party in any manner.

16.9 This Agreement may be executed in two counterparts, each of which will be deemed an original and both of which, taken together, shall constitute one and the same instrument.

[remainder of page intentionally left blank]

IN WITNESS WHEREOF, the parties have hereunto set their hands and seals and fully executed this Agreement the day and year set forth below:

UNIVERSITY OF SOUTH FLORIDA
RESEARCH FOUNDATION, INC.

By /s/ C P Carlucci
Name Carl P. Carlucci
Title President

TARGACEPT, INC.

By /s/ J. Donald deBethizy
Name J. Donald deBethizy
Title President & CEO

Acknowledged and Agreed to:

University of South Florida

By /s/ Priscilla Pope
Name Priscilla Pope
Title Associate Vice President

Patent Applications

No.	Date Filed
60/055,234	11-Aug-1997
08/935,364	22-Sep-1997
US97/20689	07-Nov-1997
US98/16634	11-Aug-1998
09/198,882	23-Nov-1998
09/461,087	14-Dec-1999
09/526,403	15-Mar-2000
09/398,720	20-Sep-1999
60/112,534	16-Dec-1998
US99/30137	16-Dec-1999
US99/30153	16-Dec-1999
09/882,934	15-Jun-2001
09/882,935	15-Jun-2001
10/441,947	19-May-2003

Issued Patents

No.	Date Filed
6,034,079	March 7, 2000

[********]

[Entire page has been redacted.]

Exhibit 10.19

[********] 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.

LICENSE AGREEMENT

between

MEDICAL COLLEGE OF GEORGIA RESEARCH INSTITUTE, INC.

and

TARGACEPT, INC.

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THIS LICENSE AGREEMENT is made and entered into as of this 9th day of July, 2002, by and between the MEDICAL COLLEGE OF GEORGIA RESEARCH INSTITUTE, INC., a nonprofit Georgia corporation with offices located in the Medical College of Georgia, 1120 15th Street, Room CJ-3301, Augusta, Georgia 30912-4810 (hereinafter referred to as "MCGRI") and TARGACEPT, INC., a corporation with corporate headquarters located at 200 East First Street, Suite 300, Winston-Salem, NC 27101-4165 (hereinafter referred to as LICENSEE").

WITNESSETH

WHEREAS, the Medical College of Georgia Research Institute (MCGRI) is the assignee of all right, title, and interest in inventions developed by employees of The Medical College of Georgia (MCG) and is responsible for the protection and commercial development of such inventions; and

WHEREAS, Dr. Mario Marrero, during the course of his employment by the Medical College of Georgia (MCG), developed certain inventions (MCG Case # 016-02 "Methods and Compositions for Treatment of Central Nervous System Disorders") as more fully defined herein; and jointly owned by Targacept through its co-inventor, Dr. Merouane Bencherif;

WHEREAS, MCGRI wants to have the inventions further developed and made available in commerce for use by the public; and

WHEREAS, LICENSEE represents that it has the necessary expertise and resources to fully develop and commercialize the inventions; and

WHEREAS, LICENSEE wishes to obtain certain rights to pursue the development and commercialization of the inventions; and

WHEREAS, MCGRI wishes to grant LICENSEE such rights in accordance with the terms and conditions of this Agreement.

NOW, THEREFORE, for and in consideration of the mutual covenants and the premises herein contained, the parties, intending to be legally bound, hereby agree as follows.

ARTICLE 1. DEFINITIONS

The following terms as used herein shall have the following meaning:

1.1 "Agreement" or "License Agreement" shall mean this Agreement, including all Exhibits attached to this Agreement.

1.2 "Field of Use" means Any and All.

1.3 "Indemnitees" shall mean MCGRI, MCGRI's officers and directors, MCG, MCG's employees, and the Inventors, and their heirs, executors, administrators, and legal representatives.

1.4 “Inventors” shall mean Drs. Mario Marrero and Dr. Merouane Bencherif, each of which will share in intellectual property income according to the policies of their employing institution.

1.5 “License Agreement Year” shall mean the period from July 1 through June 30 of each year during the term of this Agreement.

1.6 “Licensed Patents” shall mean the inventions embodied in the patent applications and patents identified in EXHIBIT A hereof, together with all divisionals, continuations, reissues, and foreign counterparts of such applications or patents.

1.7 “Licensed Product(s)” shall mean any process, service, or product, the manufacture, use, or sale of which is covered by a Valid Claim or incorporates or uses any Licensed Technology.

1.8 “Licensed Technology” shall mean all information and materials proprietary to MCGRI, including designs, technical information, know how, knowledge, data, specifications, test results and other information relating to the Licensed Patents and disclosed by MCGRI to LICENSEE on the date of this Agreement or during the term hereof.

1.9 “Licensed Territory” means the World.

1.10 “LICENSEE’s Development Plan” shall mean EXHIBIT B of this Agreement.

1.11 “Net Selling Price” of Licensed Products shall mean **[********]**.

1.12 “Sale” or “Sold” shall mean the sale, transfer, exchange, or other disposition of Licensed Products whether by gift or otherwise, including but not limited to the use of Licensed Products by LICENSEE or any other person authorized by LICENSEE. Sales of Licensed Products shall be deemed consummated upon the first to occur of: (a) receipt of payment from the purchaser; (b) delivery of Licensed Products to the purchaser or a common carrier; (c) release of Licensed Products from consignment; (d) if deemed Sold by use, when first put to such use; or (e) if otherwise transferred, exchanged, or disposed of whether by gift or otherwise when such transfer, exchange, gift, or other disposition occurs.

1.13 “MCG” shall mean The University of Georgia.

1.14 “Valid Claim” shall mean a claim included among the Licensed Patents so long as such claim shall not have been irrevocably abandoned or held invalid in an unappealable decision of a court or other authority of competent jurisdiction.

ARTICLE 2. GRANT OF LICENSE

2.1 License. MCGRI hereby grants LICENSEE an exclusive right and license to MCGRI’s rights to make, use, and Sell Licensed Products for the Field of Use in the Licensed Territory during the term of this Agreement.

2.2 Retained License. MCGRI retains on behalf of itself, MCG, and any research collaborators, a royalty-free right and license to make and use Licensed Products and to practice Licensed Technology for research and educational purposes only.

2.3 No Implied License. The license and right granted in this Agreement shall not be construed to confer any rights upon LICENSEE by implication, estoppel, or otherwise as to any technology not specifically identified in this Agreement as Licensed Patents or Licensed Technology.

2.4 Government Rights. The Licensed Patents, Licensed Technology, or portions thereof may have been developed with financial or other assistance through grants or contracts funded by the United States government. LICENSEE acknowledges that in accordance with Public Law 96-517 and other statutes, regulations, and Executive Orders as now exist or may be amended or enacted, the United States government has certain rights in the Licensed Patents and Licensed Technology. LICENSEE shall take all action necessary to enable MCGRI to satisfy its obligations under any federal law relating to the Licensed Patents or Licensed Technology. If the United States government should take action which renders it impossible or impractical for MCGRI to grant the rights and license granted herein to LICENSEE under this Agreement or otherwise perform MCGRI's obligations under this Agreement, MCGRI or LICENSEE may terminate this Agreement immediately by notice to the other party. LICENSEE shall not have any right to the return of any payments of any kind made by it to MCGRI prior to the date of termination.

ARTICLE 3. DILIGENCE AND COMMERCIALIZATION

3.1 LICENSEE shall use its best efforts throughout the term of this Agreement to comply with LICENSEE's Development Plan and to bring Licensed Products to market through a thorough, vigorous, and diligent program for exploitation of the right and license granted in this Agreement to LICENSEE and to create, supply, and service in the Licensed Territory as extensive a market as practical. In no instance shall LICENSEE's best efforts be less than efforts customary in LICENSEE's industry.

ARTICLE 4. CONSIDERATION FOR LICENSE

4.1 License Fee. As partial consideration for the license granted to LICENSEE under this Agreement, LICENSEE shall pay MCGRI a license fee of Twenty Five Thousand Dollars ($25,000) at signing, or within ten (10) days of signing, this Agreement.

4.2 Sublicensing Fee. Licensee shall pay MCGRI **[********]** of any fees or payments or non-royalty remuneration, not including Milestone Payments (4.4) paid to LICENSEE by a sublicensee in relation to this License and for rights to all or part of the Licensed Patents

4.3 Royalties. As partial consideration for the license granted to LICENSEE under this Agreement, MCGRI shall earn a royalty equal to **[********]** of the Net Selling Price of all Licensed Products

Sold by LICENSEE or Sublicensee during the term of this Agreement. There shall be an annual minimum royalty of $12,000 effective the first year of product sales.

4.4 Milestone Payments:

- **[********]**
- **[********]**
- **[********]**
- **[********]**

The above payments are due to MCGRI regardless of whether clinical trials and regulatory activities are conducted by LICENSEE or Sublicensee.

4.5 Reimbursement for Patent Expenses. LICENSEE shall assume the responsibility and cost of out-of-pocket fees, costs, and expenses hereafter during the term of this Agreement incurred in filing, prosecuting, and maintaining the Licensed Patents in the Licensed Territory.

ARTICLE 5. REPORTS AND PAYMENTS

5.1 Within thirty (30) days of September 30, December 31, March 31, and June 30 of each year during the term of this Agreement, up to and including September 30, December 31, March 31 and June 30 following the termination or expiration of this Agreement, LICENSEE shall render a written report to MCGRI setting forth for the preceding calendar quarter, the following as may be applicable under the royalty provisions hereof:

(a) the Net Sales Value of all Licensed Products Sold by LICENSEE, Affiliates, and sublicensees under this Agreement; and

(b) the amount of royalty payable; and

(c) any other information reasonably necessary to show the basis on which such royalty has been computed; and

(d) the title of the Licensed Patent(s), the inventor(s), and the five digit MCG code(s) for the Licensed Patent(s).

(e) in case no payment is due for any calendar quarter hereunder, LICENSEE shall so report.

(f) the amount spend on patent prosecution for the licensed intellectual property.

5.2 Each royalty report shall be accompanied by the payment of all royalties due for the quarter calendar year in question.

5.3 All royalties shall be paid in United States funds collectible at one hundred percent (100%) of face value in New York, New York, U.S.A. For purposes of computing the royalty payment on Sales outside the United States, the royalty payment hereunder shall first be determined in the foreign currency of the

country in which Licensed Products are Sold and then converted to United States dollars at the spot rate published by the Wall Street Journal (U.S. edition) on the last day of the quarter for which payment is due.

5.4 In high inflation countries where LICENSEE uses accounting treatment under Statement of Financial Accounting Standards No. 52, Paragraph 11, or the successor equivalent Standard, LICENSEE may for each such country at the end of each quarter convert each month's Sales in that quarter to United States dollars by assuming all Sales in that month occurred on the last day of the month, computing the collection date for that month's Sales to United States dollars at the forecasted exchange rate for that computed collection date; differences between the forecasted exchange rate and the actual exchange rate are to be corrected in the first quarter in which known.

5.5 If Licensed Products are Sold in a country in which conditions or legal restrictions exist which prohibit remittance of United States dollars, LICENSEE shall have the right and option to make the royalty payment for such country by depositing the amount thereof in the currency of the country of Sale at LICENSEE's election, to MCGRI 's account in a bank designated by MCGRI in such country.

5.6 Interest. Payments required under this Agreement shall, if overdue, bear interest until payment at a per annum rate **[********]** above the prime rate in effect at the Trust Company Bank in Atlanta, Georgia, on the due date. The payment of such interest shall not foreclose MCGRI from exercising any other rights it may have because any payment is late.

5.7 All payments and reports due under this Agreement shall be made in person or via the United States mail or private carrier to the following address:

Medical College of Georgia Research Institute, Inc.
Attn: Director, Office of Biomedical Technology Transfer
CJ-3301
Medical College of Georgia
Augusta, Georgia 30912-4810
Facsimile: (706) 721-9517

5.8 All payments should be made payable to: **The Medical College of Georgia Research Institute, and must refer to the technology transfer case # (016-02).**

ARTICLE 6. RECORDS

6.1 Records of Sales. During the term of this Agreement and for a period of three (3) years thereafter, LICENSEE shall keep at its principal place of business true and accurate records of all Sales in accordance with general accepted accounting principles in the respective country where such Sales occur and

in such form and manner so that all royalties owed to MCGRI may be readily and accurately determined. LICENSEE shall furnish MCGRI copies of such records upon MCGRI's request, which shall not be made more often than once per License Agreement Year.

6.2 Audit of Records. MCGRI shall have the right, from time to time at reasonable times during normal business hours through an independent certified public accountant, to examine the records of LICENSEE in order to verify the calculation of any royalties payable under this Agreement. Such examination and verification shall not occur more than once each License Agreement Year and the calendar year immediately following termination of this Agreement. Unless otherwise agreed in writing by LICENSEE, the fees and expenses of performing such examination and verification shall be borne by MCGRI. If such examination reveals an underpayment by LICENSEE of more than **[*********]** for any quarter examined, LICENSEE shall pay MCGRI the amount of such underpayment plus interest and shall reimburse MCGRI for all expenses of the accountant performing the examination.

ARTICLE 7. PATENT PROSECUTION

7.1 Prosecution and Maintenance of Licensed Patents. The prosecution and maintenance of the Licensed Patents shall be the primary responsibility of LICENSEE. LICENSEE shall keep MCGRI informed as to all developments with respect to Licensed Patents. MCGRI shall be afforded reasonable opportunities to advise LICENSEE and cooperate with LICENSEE in such prosecution and maintenance.

LICENSEE, upon ninety (90) days advance written notice to MCGRI, may advise MCGRI that it no longer wishes to pay expenses for filing, prosecuting or maintaining one or more Licensed Patents. MCGRI may, at its option, elect to pay such expenses or permit such Licensed Patents to become abandoned or lapsed. If MCGRI elects to pay such expenses, such patents shall not be subject to any license granted to LICENSEE hereunder.

ARTICLE 8. ABATEMENT OF INFRINGEMENT

8.1 LICENSEE shall promptly inform MCGRI of any suspected infringement of any Licensed Patents. During the term of this Agreement, MCGRI and LICENSEE shall have the right to institute an action for infringement of the Licensed Patents against any such third party in accordance with the following and subject to the rights of any third parties granted licenses to practice the Licensed Patents by MCGRI:

(a) If MCGRI and LICENSEE agree to institute suit jointly, the suit shall be brought in both their names, the out-of-pocket costs thereof shall be borne equally, and any recovery or settlement shall be shared equally. LICENSEE and MCGRI shall agree upon the manner in which they shall exercise control over such action. MCGRI may, if it so desires, also be represented by separate counsel of its own selection. The fees for which counsel shall be paid by MCGRI;

(b) In the absence of agreement to institute a suit jointly, MCGRI may institute suit, and, at its option, name LICENSEE as a plaintiff. MCGRI shall bear the entire cost of such litigation and shall be entitled to retain the entire amount of any recovery or settlement; and

(c) In the absence of agreement to institute a suit jointly and if MCGRI notifies LICENSEE that it has decided not to join in or institute a suit, as provided in (a) or (b) above, LICENSEE may institute suit and, at its option, name MCGRI as a plaintiff. LICENSEE shall bear the entire cost of such litigation, including defending any counterclaims brought against MCGRI and paying any judgments rendered against MCGRI, and shall be entitled to retain the entire amount of any recovery or settlement.

8.2 Should either MCGRI or LICENSEE commence a suit under the provisions of this Article and thereafter elect to abandon such suit, the abandoning party shall give timely notice to the other party who may, if it so desires, continue prosecution of such suit, provided that the sharing of expenses and any recovery in such suit shall be as agreed upon between MCGRI and LICENSEE.

ARTICLE 9. CONFIDENTIALITY

9.1 LICENSEE shall not, without the express written consent of MCGRI, for any reason or at any time either during or subsequent to the term of this Agreement disclose any information contained in the Licensed Patents or Licensed Technology or any other information pertaining to the Licensed Patents and Licensed Technology (collectively referred to as “Proprietary Information”) to third parties other than Affiliates and LICENSEE’s sublicensees. This obligation of nondisclosure shall not extend to information:

(a) which LICENSEE can demonstrate through documentation to have been within LICENSEE’s legitimate possession prior to the time of disclosure of such information to LICENSEE by MCGRI, MCG, or the Inventors;

(b) which was in the public domain prior to disclosure by MCGRI, MCG, or the Inventors, as evidenced by documents published prior to such disclosure;

(c) which, after disclosure by MCGRI, MCG, or the Inventors, comes into the public domain through no fault of LICENSEE;

(d) which is disclosed to LICENSEE by a third party having legitimate possession of the information and the unrestricted right to make such disclosure.

9.2 Prior Agreements. The provisions of this Agreement supersede and shall be substituted for any terms of any prior confidentiality agreement between LICENSEE and MCGRI which are not consistent with this Agreement.

ARTICLE 10. MERCHANTABILITY AND EXCLUSION OF WARRANTIES

10.1 LICENSEE possesses the necessary expertise and skill in the technical areas in which the Licensed Products and Licensed Technology are involved to make, and has made, its own evaluation of the capabilities, safety, utility, and commercial application of the Licensed Patents and Licensed Technology. ACCORDINGLY, MCGRI MAKES NO REPRESENTATION OR WARRANTY OF ANY KIND WITH RESPECT TO THE LICENSED PATENTS OR LICENSED TECHNOLOGY AND EXPRESSLY DISCLAIMS ANY WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE AND ANY OTHER IMPLIED WARRANTIES WITH RESPECT TO THE CAPABILITIES, SAFETY, UTILITY, OR COMMERCIAL APPLICATION OF LICENSED PATENTS OR LICENSED TECHNOLOGY.

ARTICLE 11. DAMAGES, INDEMNIFICATION, AND INSURANCE

11.1 NO LIABILITY. MCGRI shall not be liable to LICENSEE or LICENSEE's customers for special, incidental, indirect, or consequential damages resulting from defects in the design, testing, labeling, manufacture, or other application of Licensed Products manufactured, tested, designed, or Sold pursuant to this Agreement.

11.2 Indemnification. LICENSEE shall defend, indemnify, and hold harmless the Indemnitees from and against any and all claims, demands, loss, liability, expense, or damage (including investigative costs, court costs and attorneys' fees) Indemnitees may suffer, pay, or incur as a result of claims, demands or actions against any of the Indemnitees arising or alleged to arise by reason of or in connection with any and all personal injury and property damage caused or contributed to in whole or in part by LICENSEE's manufacture, testing, design, use, sale, or labeling of any Licensed Products, or the practice of any Licensed Patents. LICENSEE's obligations under this Article shall survive the expiration or termination of this Agreement for any reason.

11.3 Insurance. Without limiting LICENSEE's indemnity obligations under the preceding paragraph, LICENSEE shall maintain throughout the term of this Agreement and for ten (10) years thereafter a liability insurance policy which:

(a) insures Indemnitees for all claims, damages, and actions mentioned in Article 10.1 of this Agreement;

(b) includes a contractual endorsement providing coverage for all liability which may be incurred by Indemnitees in connection with this Agreement;

(c) requires the insurance carrier to provide MCGRI with no less than thirty (30) days written notice of any change in the terms or coverage of the policy or its cancellation; and

(d) provides Indemnitees product liability coverage in an amount no less than One Million Dollars ($1,000,000) per occurrence for bodily injury and Five Million Dollars ($5,000,000) per occurrence for property damage, subject to a reasonable aggregate amount.

11.4 Notice of Claims. LICENSEE shall promptly notify MCGRI of all claims involving the Indemnitees and will advise MCGRI of the policy amounts that might be needed to defend and pay any such claims.

ARTICLE 12. TERM AND TERMINATION

12.1 Term. Unless sooner terminated as otherwise provided in this Agreement, the term of this Agreement shall commence on the date hereof and shall continue until the earlier of **[********]** from the date hereof or the date of expiration of the last to expire of the Licensed Patents, including any renewals or extensions thereof.

12.2 Termination. MCGRI shall have the right to terminate this Agreement upon the occurrence of any one or more of the following events:

(a) failure of LICENSEE to make any two payments consecutive required pursuant to this Agreement when due; or

(b) failure of LICENSEE to render reports to MCGRI as required by this Agreement; or

(c) failure of LICENSEE to notify MCGRI of intent to file bankruptcy as set forth in Article 12.3 below;

(d) the insolvency of LICENSEE; or

(e) the institution of any proceeding by LICENSEE under any bankruptcy, insolvency, or moratorium law; or

(f) any assignment by LICENSEE of substantially all of its assets for the benefit of creditors; or

(g) placement of LICENSEE's assets in the hands of a trustee or a receiver unless the receivership or trust is dissolved within thirty (30) days thereafter; or

(h) the failure of LICENSEE to comply with LICENSEE's Development Plan; or

(i) the breach of any other material term of this Agreement.

12.3 Notice of Bankruptcy. The LICENSEE must inform MCGRI of its intention to file a voluntary petition in bankruptcy or of another's intention to file an involuntary petition in bankruptcy to be received at least thirty (30) days prior to filing such a petition. A party's filing without conforming to this requirement shall be deemed a material, pre-petition incurable breach.

12.4 Exercise. MCGRI may exercise its right of termination by giving LICENSEE, its trustees or receivers or assigns, thirty (30) days prior written notice of MCGRI's election to terminate. Upon the expiration of such period, this Agreement shall automatically terminate unless the LICENSEE has cured the

breach. Such notice and termination shall not prejudice MCGRI's right to receive royalties or other sums due hereunder and shall not prejudice any cause of action of claim of MCGRI accrued or to accrue on account of any breach or default by LICENSEE.

12.5 Failure to Enforce. The failure of MCGRI at any time, or for any period of time, to enforce any of the provisions of this Agreement shall not be construed as a waiver of such provisions or as a waiver of the right of MCGRI thereafter to enforce each and every such provision.

12.6 Termination by LICENSEE. LICENSEE shall have the right to terminate this Agreement upon the occurrence of either of the following events:

(a) the breach of a material term of this Agreement by MCGRI; or

(b) If the Sale of Licensed Products requires approval by any government agency, and after diligent pursuit of such approval, including but not limited to; performing all alternative tests or analyses as prescribed by such agency regulations, submitting all relevant data to such agency, and pursuing all available administrative procedures and appeal processes permitted by such agency and applicable law, LICENSEE is unable to obtain approval for the Sale of Licensed Products, LICENSEE may notify MCGRI in writing of the final denial of approval to Sell Licensed Products and LICENSEE's desire to terminate this Agreement. MCGRI shall either grant LICENSEE's request for termination of such Agreement or, at MCGRI's sole option, request LICENSEE to provide MCGRI with all files and records pertaining to such applications and permit MCGRI access to all documents and records in the possession of any regulatory authority pertaining to any application by LICENSEE so as to enable MCGRI to verify LICENSEE's efforts to obtain approval for the Sale of Licensed Products. MCGRI shall further be entitled to retain consultants on a confidential basis to assist MCGRI in completing its review. If MCGRI, in its sole discretion, determines that LICENSEE has diligently pursued approval for the Sale of Licensed Products and failed to obtain such approval, MCGRI shall grant LICENSEE's request to terminate the Agreement.

12.7 Exercise. LICENSEE may exercise its right of termination based upon a material breach of this Agreement by MCGRI by giving MCGRI thirty (30) days prior written notice of LICENSEE's election to terminate. Upon the expiration of such period, this Agreement shall automatically terminate unless MCGRI has cured the breach. Such notice and termination shall not prejudice LICENSEE's right to pursue any other remedies available to LICENSEE at law.

Licensee may exercise its right of termination as a result of the failure to obtain approval to Sell Licensed Products by providing MCGRI with a formal written request for such termination. MCGRI shall provide LICENSEE with a formal written response to LICENSEE's request for termination within forty-five (45) days of receiving such request.

12.8 Effect. In the event this Agreement is terminated for any reason whatsoever, LICENSEE shall return, or at MCGRI's direction destroy, all plans, drawings, papers, notes, writings and other documents,

samples, organisms, biological materials and models pertaining to the Licensed Patents and Licensed Technology, retaining no copies, and shall refrain from using or publishing any portion of the Licensed Patents or Licensed Technology as provided in Article 8 of this Agreement. Upon termination of this Agreement, LICENSEE shall cease manufacturing, processing, producing, using, Selling, or distributing Licensed Products; provided, however, that LICENSEE may continue to Sell in the ordinary course of business for a period of one (1) year reasonable quantities of Licensed Products which are fully manufactured and in LICENSEE's normal inventory at the date of termination if (a) all monetary obligations of LICENSEE to MCGRI have been satisfied and (b) royalties on such sales are paid to MCGRI in the amounts and in the manner provided in this Agreement. The provisions of Articles 9, 10, and 11 of this Agreement shall remain in full force and effect notwithstanding the termination of this Agreement.

ARTICLE 13. ASSIGNMENT

13.1 This Agreement is dependent upon the special relationship between the parties and the special knowledge and unique skills of the LICENSEE. Therefore, LICENSEE shall not grant, transfer, convey, or otherwise assign any of its rights or delegate any of its obligations under this Agreement without the prior written consent of MCGRI, except as explicitly permitted under this Agreement. This Agreement shall be assignable by MCGRI to MCG, or any other nonprofit corporation, which promotes the education or research purposes of MCG. The above notwithstanding, LICENSEE is allowed to Sublicense to a third party provided they agree to the provisions of this Agreement.

ARTICLE 14. MISCELLANEOUS

14.1 Export Controls. LICENSEE acknowledges that MCGRI is subject to United States laws and regulations controlling the export of technical data, computer software, laboratory prototypes, and other commodities and that MCGRI's obligations under this Agreement are contingent upon compliance with applicable United States export laws and regulations. The transfer of technical data and commodities may require a license from the cognizant agency of the United States government or written assurances by LICENSEE that LICENSEE shall not export data or commodities to certain foreign countries without the prior approval of certain United States agencies. MCGRI neither represents that an export license shall not be required nor that, if required, such export license shall issue.

14.2 Legal Compliance. LICENSEE shall comply with all laws and regulations relating to its manufacture, processing, producing, use, Selling, or distributing of Licensed Products. LICENSEE shall not take any action which would cause MCGRI or LICENSEE to violate any laws and regulations.

14.3 Independent Contractor. LICENSEE's relationship to MCGRI shall be that of a licensee only. LICENSEE shall not be the agent of MCGRI and shall have no authority to act for or on behalf of MCGRI in

any matter. Persons retained by LICENSEE as employees or agents shall not by reason thereof be deemed to be employees or agents of MCGRI.

14.4 Patent Marking. LICENSEE shall mark Licensed Products Sold in the United States with United States patent numbers. Licensed Products manufactured or Sold in other countries shall be marked in compliance with the intellectual property laws in force in such foreign countries.

14.5 Use of Names. LICENSEE shall obtain the prior written approval of MCGRI, MCG, or the Inventors prior to making use of their names for any commercial purpose.

14.6 Place of Execution. This Agreement and any subsequent modifications or amendments hereto shall be deemed to have been executed in the State of Georgia, U.S.A. This Agreement shall not become effective or binding upon MCGRI until signed on its behalf by its Executive Director in the State of Georgia, U.S.A.

14.7 Governing Law. This Agreement and all amendments, modifications, alterations, or supplements hereto, and the rights of the parties hereunder, shall be construed under and governed by the laws of the State of Georgia and the United States of America. Only courts in the State of Georgia, U.S.A., shall have jurisdiction to hear and decide any controversy or claim between the parties arising under or relating to this Agreement.

14.8 Entire Agreement. This Agreement constitutes the entire agreement between MCGRI and LICENSEE with respect to the subject matter hereof and shall not be modified, amended or terminated except as herein provided or except by another agreement in writing executed by the parties hereto.

14.9 Severability. All rights and restrictions contained herein may be exercised and shall be applicable and binding only to the extent that they do not violate any applicable laws and are intended to be limited to the extent necessary so that they will not render this Agreement illegal, invalid or unenforceable. If any provision or portion of any provision of this Agreement not essential to the commercial purpose of this Agreement shall be held to be illegal, invalid or unenforceable by a court of competent jurisdiction, it is the intention of the parties that the remaining provisions or portions thereof shall constitute their agreement with respect to the subject matter hereof, and all such remaining provisions or portions thereof shall remain in full force and effect. To the extent legally permissible, any illegal, invalid or unenforceable provision of this Agreement shall be replaced by a valid provision which will implement the commercial purpose of the illegal, invalid or unenforceable provision. In the event that any provision essential to the commercial purpose of this Agreement is held to be illegal, invalid or unenforceable and cannot be replaced by a valid provision which will implement the commercial purpose of this Agreement, this Agreement and the rights granted herein shall terminate.

14.10 Force Majeure. Any delays in, or failure of, performance of any party to this Agreement shall not constitute default hereunder, or give rise to any claim for damages, if and to the extent caused by

occurrences beyond the control of the party affected, including, but not limited to, acts of God, strikes or other work stoppages; civil disturbances, fires, floods, explosions, riots, war, rebellion, sabotage, acts of governmental authority or failure of governmental authority to issue licenses or approvals which may be required.

ARTICLE 15. NOTICES

All notices, statements, and reports required or contemplated herein by one party to the other shall be in writing and shall be deemed to have been given upon delivery in person or upon the expiration of five (5) days after deposit in a lawful mail depository in the country of residence of the party giving the notice, registered or certified airmail postage prepaid, and addressed as follows:

If to MCGRI:

Director,
Office of Biomedical Technology Transfer
Medical College of Georgia Research Institute, Inc.
CJ-2211
Medical College of Georgia
Augusta, Georgia 30912-4810
Facsimile: (706) 721-9517

If to LICENSEE:

_____
_____
_____
_____
Facsimile:

Either party hereto may change the address to which notices to such party are to be sent by giving notice to the other party at the address and in the manner provided above. Any notice herein required or permitted to be given may be given, in addition to the manner set forth above, by telex, facsimile or cable, provided that the party giving such notice obtains acknowledgement by telex, facsimile or cable that such notice has been received by the party to be notified. Notice made in this manner shall be deemed to have been given when such acknowledgement has been transmitted.

IN WITNESS WHEREOF, MCGRI and LICENSEE have caused this Agreement to be signed by their duly authorized representatives as of the day and year indicated below.

MEDICAL COLLEGE OF GEORGIA
RESEARCH INSTITUTE, INC.

By: /s/ Betty Aldridge
Name: Betty Aldridge
Title: Executive Director, MCGRI

LICENSEE:

By: /s/ J. Donald deBethizy
Name: J. Donald deBethizy
Title: President & CEO

EXHIBIT A

Licensed Patents

The Medical College of Georgia and its Research Institute ("MCGRI") hold certain title and rights in a joint invention on the alpha 7 nicotinic receptor agonists and the JAK pathway with Targacept, Inc., specifically:

Case #016-02: **"Methods and Compositions for Treatment of Central Nervous System Disorders"**

Inventors: Drs. Mario Marrero and Merouane Bencherif

Patent Status: Provisional U.S. patent application prepared by Targacept, complete with data and claims.

Exhibit 10.20

[********] 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.

LICENSE AGREEMENT

THIS AGREEMENT, made and entered into this 26th day of May, 1999, (the Effective Date) by and between the University of Kentucky Research Foundation, a corporation duly organized and existing under the laws of the Commonwealth of Kentucky and having its principle office at Lexington, Kentucky, U.S.A. (hereinafter referred to as UKRF), and Targacept, Inc., ("TARGACEPT") a subsidiary of R.J.R. Reynolds Tobacco Company ("RJR").

WITNESSETH

WHEREAS, TARGACEPT desires to obtain a license under the Patent Rights upon the terms and conditions hereinafter set forth, and

WHEREAS, UKRF previously has entered into agreements with RJR (and subsequently, TARGACEPT) regarding research and development activities concerning nicotinic compounds for use in therapeutic applications. RJR (and subsequently, TARGACEPT) have funded activities involving collaborative research as well as activities involving a sabbatical program. As a result, UKRF and TARGACEPT jointly own certain technologies (listed in Attachment A, which becomes a part of this agreement), and UKRF has assigned certain technologies to TARGACEPT (listed in Attachment B, which becomes part of this agreement) but which are subject to the terms of that agreement regarding sharing of royalty income, and

WHEREAS, TARGACEPT has entered into an agreement with Rhone-Poulene Rorer, whereby as part of that agreement, certain technologies of TARGACEPT were licensed to Phone-Poulene Rorer; and TARGACEPT is entitled to certain royalty and milestone income, and

WHEREAS, in previous agreements between UKRF and RJR (and subsequently TARGACEPT), it was agreed that UKRF and RJR would negotiate in good faith towards arriving at terms relating to further use of the technology developed during the

collaborative research and sabbatical programs. UKRF and TARGACEPT acknowledge negotiating in good faith towards terms by which that technology can best be developed for commercial application.

NOW, THEREFORE, in consideration of the premises and the mutual covenants contained herein, the parties hereto agree as follows:

ARTICLE 1- Definitions

For the purposes of this agreement, the following words and phrases shall have the following meanings:

1.1 “TARGACEPT” shall mean Targacept and any subsidiary or affiliate of Targacept.

1.2 “Patent Rights” shall mean the United States and Foreign pending patent applications set forth in Attachments “A” and “B” attached hereto and made a part hereof (hereinafter referred to as the “Patent Rights Patent Application(s)”), and the United States patents and Foreign patents issuing from said pending United States and Foreign patent applications or later-filed foreign applications based upon any of said United States patents and applications (hereinafter referred to as the “Patent Rights Patent(s)”) and any continuations, continuations-in-part, divisions reissues or extensions or any of the foregoing.

1.3 “Licensed Product(s)” shall mean any product made or covered by a pending or issued patent included in the Patent Rights.

ARTICLE 2- Grant

2.1 UKRF hereby grants to TARGACEPT the world-wide right and license to the Patent Rights set forth in Attachment A to the full end of the term of each patent included therein unless sooner terminated as hereinafter provided. This grant is expressly subject to the rights of the U.S. Government, if any.

2.2 In order to establish a period of exclusivity for TARGACEPT, UKRF hereby agrees that it shall not grant any other license to make, have made, use, lease and sell the Patent Rights during the period of time commencing with the Effective Date of this Agreement and terminating with the full end of the term of this Agreement, unless sooner terminated as hereinafter provided.

2.3 TARGACEPT shall have the right to sublicense worldwide any of the rights, privileges and license granted hereunder.

2.4 Notwithstanding the foregoing, on behalf of itself and its affiliates, UKRF reserves the right to use the Patent Rights for internal research purposes.

2.5 TARGACEPT agrees that any sublicenses granted by it shall include a contractual provision granting UKRF the right and ability to proceed directly against the sublicensee to require such sublicensee to comply with all terms of the sublicense agreement. TARGACEPT further agrees to include the substance of ARTICLES 4, 5, 8, 9, and 10 of this Agreement in all sublicense agreements.

2.6 TARGACEPT agrees to forward to UKRF a copy of any and all fully executed sublicense agreements, and further agrees to forward to UKRF annually a copy of such reports received by TARGACEPT from its sublicensees during the preceding twelve (12) month period under the sublicenses as shall be pertinent to a royalty accounting under said sublicense agreements.

ARTICLE 3- Due Diligence

TARGACEPT shall use its best efforts to bring the Patent Rights to market through a thorough, vigorous and diligent program for exploitation of the Patent Rights.

ARTICLE 4- Royalties

4.1 For the rights, privileges and license granted hereunder, TARGACEPT shall pay to UKRF in the manner hereinafter provided to the end of the term of the Patent Rights or until this Agreement shall be terminated as hereinafter provided:

(a) A license issue fee of $20,000.00 Dollars, which said license issue fee shall be deemed earned and due immediately upon the execution of this Agreement.

(b) For each of the patents described in Attachment A, a royalty in the amount of **[********]**.

(c) For each of the patents described in Attachment B, a royalty in the amount of **[********]**. Such payments shall only be made if income is based on technology claimed in those patents listed in Attachment B, in countries where those patents are in force. Such payments shall be made for the life of the patents listed in Attachment B.

4.2 As used herein, the phrase “Net Sales Price” shall mean TARGACEPT’s billings for the Licensed Product(s) produced hereunder less the sum of the following:

(a) Discounts allowed in amounts customary in the trade;

(b) Sales, tariff duties and/or use taxes directly imposed and with reference to particular sales;

(c) Outbound transportation prepaid or allowed; and

(d) Amounts allowed or credited on returns.

No deductions shall be made for commissions paid to individuals whether they be with independent sales agencies or regularly employed by TARGACEPT and on its payroll, or for cost of collections. Licensed Product(s) shall be considered “sold” when billed out or invoiced.

4.3 No multiple royalties shall be payable because the Licensed Product(s), its manufacture, lease or sale are or shall be covered by more than one patent application or patent license under this Agreement.

4.4 Royalty payments shall be paid in United States dollars in Lexington, Kentucky, or at such other place as UKRF may reasonably designate consistent with the laws and regulations controlling in any foreign country. Any withholding taxes which TARGACEPT or any sublicensee shall be required by law to withhold on remittance of the royalty payments shall be deducted from royalty paid to UKRF. If any currency conversion shall be required in connection with the payment of royalties hereunder, such conversion shall be made by using the exchange rate prevailing at a first-class foreign exchange bank on the last business day of the calendar quarterly reporting period to which such royalty payments relate.

ARTICLE 5-Reports and Records

5.1 TARGACEPT shall keep full, true and accurate books of account containing all particulars that may be necessary for the purpose of showing the amount payable to UKRF by way of royalty as aforesaid. Said books of account shall be kept at TARGACEPT’s principal place of business or the principal place of business of the

appropriate division of TARGACEPT to which this Agreement relates. Said books and the supporting data shall be open at all reasonable times, for five (5) years following the end of the calendar year to which they pertain, to the inspection of the UKRF Internal Audit Division and/or an independent certified public accountant retained by UKRF and/or an accountant employed by UKRF, for the purpose of verifying TARGACEPT's royalty statement or compliance in other respects with this Agreement.

5.2 TARGACEPT, within thirty (30) days after June 30 and December 31, of each year, shall deliver to UKRF true and accurate reports, giving such particulars of the business conducted by TRAGACEPT during the preceding six-month period under this Agreement as shall be pertinent to a royalty accounting hereunder. These shall include at least the following:

(a) All Licensed Products manufactured and sold;

(b) Total billings for Licensed Product sold;

(c) Deductions applicable as provided in Paragraph 5.2;

(d) Total royalties due;

(e) Names and addresses of all sublicensees of TARGACEPT; and

(f) Annually, the TARGACEPT's certified financial statements for the preceding twelve (12) months including, at a minimum, a Balance Sheet and an Operating Statement.

5.3 With each such report submitted, TARGACEPT shall pay to UKRF the royalties due and payable under this Agreement. If no royalties shall be due, TARGACEPT shall so report.

ARTICLE 6-Patent Prosecution

Patent prosecution shall be in accordance with the applicable collaborative research agreements or sabbatical agreements that gave rise to the patent.

ARTICLE 7- Termination

7.1 If TARGACEPT shall become bankrupt or insolvent, or shall file a petition in bankruptcy, or if the business of TARGACEPT shall be placed in the hands of a receiver, assignee or trustee for the benefit of creditors, whether by the voluntary act of TARGACEPT or otherwise, this Agreement shall automatically terminate.

7.2 Should TARGACEPT fail in its payment to UKRF of royalties due in accordance with the terms of this agreement, UKRF shall have the right to serve notice upon TARGACEPT by certified mail at the address designated herein, of its intention to terminate this Agreement within thirty (30) days after receipt of said notice of termination unless TARGACEPT shall pay to UKRF, within the thirty (30) day period, all such royalties due and payable. Upon the expiration of the thirty (30) day period, if TARGACEPT shall not have paid all such royalties due and payable, the rights, privileges and license granted hereunder shall thereupon immediately terminate.

7.3 Upon any material breach or default of this Agreement by TARGACEPT, other than those occurrences set out in Paragraphs 7.1 and 7.2 hereinabove, which shall always take precedence in that order over any material breach or default referred to in this Paragraph 7.3, UKRF shall have the right to terminate this Agreement and the rights, privileges and license granted hereunder by ninety (90) days' notice by certified mail to TARGACEPT. Such termination shall become effective unless TARGACEPT shall have cured any such breach or default prior to the expiration of the ninety (90) day period from receipt of UKRF's notice of termination.

7.4 TARGACEPT shall have the right to terminate this Agreement at any time on six (6) months' notice by certified mail to UKRF.

7.5 Upon termination of this Agreement for any reason, nothing herein shall be construed to release either party from any obligation that matured prior to the effective date of such termination. TARGACEPT and/or any sublicensee thereof may, however, after the effective date of such termination, sell all licensed product in the process of manufacture at the time of such termination and sell the same, provided that TARGACEPT shall pay to UKRF the royalties theron as required by Article 4 of this Agreement and shall submit the reports required by Article 5 hereof.

ARTICLE 8- Product Liability

8.1 TARGACEPT shall at all times during the term of this Agreement and thereafter, indemnify, defend and hold UKRF, the University of Kentucky, their trustees,

officers, employees and affiliates, harmless against all claims and expenses, including legal expenses and reasonable attorneys' fees, arising out of the death of or injury to any person or persons or out of any damage to property and against any other claim, proceeding, demand, expense and liability of any kind whatsoever resulting from the production, manufacture, sales, use, consumption or advertisement of any Licensed Product(s) or the Patent Rights or arising from any obligation of TARGACEPT hereunder.

8.2 If TARGACEPT produces, manufactures or sells any Licensed Product(s), TARGACEPT will maintain product liability insurance, with an endorsement naming the University of Kentucky Research Foundation, the University of Kentucky, their Board of Trustees, agents officers and employees as additional insureds covering liabilities for the production, manufacture and/or sole of the product. The policy of insurance shall contain a provision of non-cancellation except upon the provision of sixty (60) days notice to the University. Policy limits shall be not less than $5,000,0000 per person per occurrence.

8.3 If TARGACEPT, sublicenses any of the rights, privileges and licenses granted hereunder, TARGACEPT shall require the sublicensee to provide UKRF evidence of such product liability insurance.

ARTICLE 9- Warranties

9.1 TARGACEPT AGREES THAT THE RIGHTS GRANTED ARE MADE AVAILABLE WITHOUT WARRANTY OF ANY KIND EXPRESSED OR IMPLIED INCLUDING, BUT NOT LIMITED TO, THE IMPLIED WARRANTIES OF MERCHANTABILITY AND FITNESS FOR A PARTICULAR PURPOSE, AND FURTHER INCLUDING NO WARRANTY AS TO CONFORMITY WITH WHATEVER USER MANUALS OR OTHER LITERATURE MAY BE ISSUED FROM TIME TO TIME.

9.2 TARGACEPT FURTHER AGREES THAT UKRF HAS NOT CONDUCTED NOR HAD CONDUCTED A PATENTABILITY OR INFRINGEMENT STUDY AND THUS MAKES NO CLAIMS THAT THE LICENSED RIGHTS WILL NOT INFRINGE ANY THIRD PARTIES' VALID PATENT RIGHTS.

ARTICLE 10- Non-Use of Names

TARGACEPT shall not use the names of the University of Kentucky, University of Kentucky Research Foundation nor of Dr. Peter Crooks nor any other employee of the University of Kentucky.

ARTICLE 11- Export Controls

It is understood that UKRF us subject to United States laws and regulations controlling the export of technical data, computer software, laboratory prototypes and other commodities (including the Arms Export Control Act, as amended, and the Export Administration Act of 1979), and that its obligations hereunder are contingent on compliance with applicable United States export laws and regulations. The transfer of certain technical data and commodities may require a license from the cognizant agency of the United States Government and/or written assurances by TARGACEPT that TARGACEPT shall not export data or commodities to certain foreign countries without prior approval of such agency. UKRF neither represents that a license shall not be required nor that, if required, it shall be issued.

ARTICLE 12- Payments, Notices and Other Communications

Any payment, notice or other communication pursuant to this Agreement shall be sufficiently made or given on the date of mailing if sent to such party by certified first class mail, postage prepaid, addressed to it at its address below or as it shall designate by written notice given to the other party:

In the case of UKRF: University of Kentucky Research Foundation
207 Administration Building
Lexington, Kentucky 40506

With a copy to University Legal Counsel
2 Administration Building
Lexington, Kentucky 40506

In the case of TARGACEPT: J.D. deBethizy
Targacept, Inc.
Winston-Salem, NC 27102

ARTICLE 13- Miscellaneous Provisions

13.1 This Agreement shall be construed, governed, interpreted and applied in accordance with the laws of the Commonwealth of Kentucky, U.S.A., except that questions affecting the construction and effect of any patent shall be determined by the law of the country in which patent was granted.

13.2 The partied hereto acknowledge that this Agreement sets forth the entire Agreement and understanding of the partied hereto as to the subject matter hereof, and shall not be subject to any change or modification except by the execution of a written instrument subscribed to by the parties hereto.

13.3 The provisions of this Agreement are severable, and in the event that any provision of this Agreement shall be determined to be invalid or unenforceable under any controlling body of law, such invalidity or unenforceability shall not in any way affect the validity or enforceability of the remaining provisions hereof.

13.4 The failure of either party to assert a right hereunder or to insist upon compliance with any term or condition of this Agreement shall not constitute a waiver of that right or excuse a similar subsequent failure to perform any such term or condition by the other party.

IN WITNESS WHEREOF, the parties hereto have hereunto set their hands and seals and duly executed this License Agreement the day and year first set forth below.

WITNESS:

/s/ Donald G. Keach

UNIVERSITY OF KENTUCKY
RESEARCH FOUNDATION

By: /s/ Jeff L. Fink III

Title: Assistant V.P., RGS

WITNESS:

/s/ A. J. Borschke

TARGACEPT, INC.

By: /s/ J. Donald deBethizy

Title: President

By execution of this Agreement, the undersigned acknowledge receiving a copy of this Agreement, and of having read and reviewed same prior to its execution by the parties.

By: /s/ Peter A. Crooks
Dr. Peter Crooks

5,616,707*

5,726,316

* Also includes Foreign Equivalents

Schedule I

Applications

08/885,397*
08/885,768*
09/098,285*
09/177,231*

Schedule II

Applications

09/053,937*
09/054,179*
09/210,113*

* Also includes Foreign Equivalents

Exhibit 10.21

[********] 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.

LICENSE AGREEMENT

This License Agreement (the "Agreement") effective as of this 12th day of August, 2002, between **Wake Forest University Health Sciences**, an institution organized as a nonprofit corporation under the laws of the state of North Carolina with its principal offices at Medical Center Boulevard, Winston-Salem, North Carolina 27109 ("WFUHS"), and **Targacept, Inc.**, a Delaware corporation with its principal offices at 200 East First Street, Suite 300, Winston-Salem, North Carolina 27101-4165 (the "Company").

WHEREAS, WFUHS is in possession of all right, title, and interest in and to the Patent Rights and the WFUHS Know-How (in each case as defined below) and desires to have the inventions and discoveries included therein or covered thereby utilized in the public interest; and

WHEREAS, WFUHS has the right to grant a license to the Company to said Patent Rights and WFUHS Know-How, and the Company desires to obtain said license, on the terms and conditions set forth herein; and

NOW, THEREFORE, in consideration of the premises and the mutual covenants set forth herein, and for good and valuable consideration, the receipt and sufficiency of which are acknowledged, the parties hereto, intending to be legally bound, agree as follows:

1. Definitions

1.1 "Affiliate" or "Affiliates" means any entity: (i) in which from time to time hereafter the Company owns or controls, directly or indirectly, at least fifty percent (50%) of the capital stock entitled to vote in the election of the board of directors (or the body providing an analogous function for entities other than corporations); (ii) that from time to time hereafter owns or controls, directly or indirectly, at least fifty percent (50%) of the Company's capital stock entitled to vote in the election of directors; and (iii) in which at least fifty percent (50%) of the capital stock entitled to vote in the election of the board of directors (or the body providing an analogous function for entities other than corporations) is from time to time hereafter owned or controlled, directly or indirectly, by an entity that from time to time hereafter owns or controls, directly or indirectly, at least fifty percent (50%) of the Company's capital stock entitled to vote in the election of directors.

1.2 "Development" means invention, discovery, proprietary development, data and information, in any medium or manifestation, including any method, process, composition of matter, apparatus, device, system, product, article of manufacture or appliance.

1.3 "Effective Date" means the date first written above.

1.4 “Field” means worldwide therapeutic use, including without limitation for humans.

1.5 “Invention” means WFUHS#98-14 *Sex Related Deference in Pain Relief from Spinal Compound (RJR 2403)*, discovered and reduced to practice by Dr. James Eisenach, an employee of WFUHS.

1.6 “License” means (i) an exclusive, worldwide right and license under the Patent Rights and (ii) a non-exclusive, worldwide right and license to the WFUHS Know-How to: (a) make, have made, use, research, develop, have developed, lease, market, offer to sell, sell, have sold, distribute, improve, import and export Licensed Products and Licensed Processes in the Field; and (b) otherwise practice the Invention in the Field.

1.7 “Licensed Product” means any product that:

(a) infringes or would infringe, in whole or in part, a Valid Claim included in the Patent Rights in the country in which the product is made, developed, used or sold; or

(b) is manufactured, produced or used using a product or process that infringes or would infringe, in whole or in part, a Valid Claim included in the Patent Rights in the country in which the product or process is used, including without limitation a Licensed Process; or

(c) is manufactured, developed, used or sold using WFUHS Know-How.

1.8 “Licensed Process” means a process for making or using therapeutic agents that infringes or would infringe, in whole or in part, a Valid Claim included in the Patent Rights or is developed using WFUHS Know-How.

1.9 “Major Country” means any of the United States of America, any individual country in the European Union or Japan.

1.10 “Net Sales” means **[********]**

1.11 “Option Agreement” means that certain Option Agreement dated February 16, 2000 between WFUHS and the Company.

1.12 “Patent Rights” means, collectively: (i) United States Patent No. 6,248,744 issued June 9, 2001 (from United States Application No. 09/622,675, the United States National Phase of PCT/US99/03896, which claimed priority to United States Provisional Application No. 60/075,794 filed February 24, 1998) and all other United States and foreign patents that issue from applications that claim priority to United States Provisional Application No. 60/075,794, PCT/US99/03896 or United States Application No. 09/622,675, 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; and (ii) all other patents (U.S. or foreign) now

issued or hereafter issuing on the patent applications described in clause (i) and all reexaminations, reissues, revisions, substitutes, renewals or extensions thereof.

1.13 "Regulatory Approval" means all approvals, licenses, registrations or authorizations of any federal, national, state, provincial or local regulatory agency, department, bureau or other government entity, necessary for the use, storage, import, transport and sale of a Licensed Product in a country.

1.14 "Royalty Expiration Date" means the date of expiration of the last-to-expire Valid Claim included in the Patent Rights covering, in whole or in part, a particular Licensed Product or Licensed Process in the Field in a particular country.

1.15 "Valid Claim" means: (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, unappealable or unappealed within the time allowed for appeal having expired, and that has not 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 abandoned.

1.16 "VCU Covered Product" means any product that:

(a) infringes or would infringe, in whole or in part, a Valid Claim included in the VCU Patents in the country in which the product is made, developed, used or sold; or

(b) is manufactured, produced or used using a product or process that infringes or would infringe, in whole or in part, a Valid Claim included in the VCU Patents in the country in which the product or process is used.

1.17 "VCU Patents" means, collectively: (i) United States Patent No. 5,914,337 issued June 22, 1999 (from United States Application No. 08/908,440 filed August 7, 1997); (ii) United States Patent No. 6,117,891 issued September 12, 2000 (from United States Application No. 09/257,368 filed February 15, 1999 as a continuation of Application No. 08/908,440); (iii) all United States or foreign patents that claim priority to United States Application Nos. 08/908,440 or 09/257,368, including without limitation PCT/US98/1648 (publication number WO 99/07369); and (iv) any continuations, continuations-in-part, divisionals, substitutes, reissues or requests for examination and all reexaminations, reissues, revisions, substitutes, renewals or extensions of any of the patents referred to in clauses (i-iii).

1.18 "WFUHS Know-How" means design criteria, technical data, practices, plans, specifications or formulas owned by WFUHS, or with respect to which WFUHS has use rights and is free to grant the License and sublicenses as provided for in Sections 2.1 and 4.1, respectively, as of the Effective Date and related to the Invention or its use in the Field.

2. Grant of License

2.1 Subject to the terms and conditions hereof, WFUHS hereby grants the License to the Company and its Affiliates.

2.2 WFUHS acknowledges and agrees that all or any portion of the License may be practiced by the Company or its Affiliates through the use of subcontractors and that, unless specifically sublicensed, such subcontractors shall not be considered sublicensees.

2.3 The License is subject to the rights of the United States government under guidelines applicable as a result of federal funding to WFUHS to support the development of the Patent Rights and WFUHS Know-How, including, but not limited to, a non-exclusive right and license to the United States government to practice the Patent Rights for governmental purposes. In addition, WFUHS retains the right to use, practice, publish, display, discuss and present the Patent Rights and WFUHS Know-How for noncommercial educational, research, clinical and academic purposes; provided that the foregoing rights shall be expressly subject to WFUHS' obligations pursuant to Section 6.

2.4 The Company shall mark the Licensed Products (i) made, used or sold in the United States with all applicable United States patent numbers and (ii) used, shipped to or sold in other countries in such a manner as to conform with the patent laws and practice of the country of use, shipment or sale.

2.5 Any Development made or developed after the Effective Date, and all intellectual property rights relating thereto, shall be owned exclusively by the party making or developing such Development, without any accounting, compensation or other obligation hereunder to the other party.

3. Royalties and other Financial Consideration

3.1 In partial consideration for the License and the transfer of the WFUHS Know-How, the Company will pay to WFUHS a license fee equal to $25,000. The license fee is due and payable to WFUHS within thirty (30) days of the Effective Date. The license fee is non-refundable and not creditable against any other payments or fees due or payable to WFUHS pursuant to this Agreement.

3.2 In partial consideration for the License and the transfer of the WFUHS Know-How, the Company will pay to WFUHS a royalty equal to **[********]** of Net Sales of any and all Licensed Products that are not also VCU Covered Products (Licensed Products that are also VCU Covered Products being provided for in Section 3.4), such obligation to expire with respect to any particular Licensed Product in a particular country on the Royalty Expiration Date for that country; provided that the Company's obligation to pay royalties under this Section 3.1 shall be imposed only once with respect to the same unit of a Licensed Product regardless of how many Patent Rights or Valid Claims pertain thereto.

3.3 In further consideration for the License and the transfer of the WFUHS Know-How and subject to Section 4.2.2 and Section 4.3.2, the Company will make certain nonrefundable,

noncreditable milestone payments to WFUHS within forty-five (45) days of achievement of the applicable milestone by the Company or, as applicable, its Affiliate with respect to each Licensed Product:

(i) **[********]**;

(ii) **[********]**;

(iii) **[********]**;

(iv) **[********]**;

(v) **[********]**; and

(vi) **[********]**.

3.4 In partial consideration for the License and the transfer of the WFUHS Know-How, the Company will pay to WFUHS a royalty equal to **[********]** of Net Sales of any and all Licensed Products that are also VCU Covered Products (Licensed Products that are not also VCU Covered Products being provided for in Section 3.2), such obligation to expire with respect to any particular Licensed Product in a particular country on the Royalty Expiration Date for that country; provided that the Company's obligation to pay royalties under this Section 3.4 shall be imposed only once with respect to the same unit of a Licensed Product regardless of how many Patent Rights or Valid Claims pertain thereto.

3.5 As of the Effective Date, WFUHS has not incurred any additional unreimbursed fees or other costs for the preparation, filing, prosecution, and maintenance of the Patent Rights. Accordingly, WFUHS acknowledges and agrees that no amounts not previously invoiced to Company shall be due from the Company under Section 3.1 of the Option Agreement.

4. Sublicenses

4.1 WFUHS hereby grants to the Company the exclusive right to grant exclusive or nonexclusive sublicenses to third-party sublicensees with respect to all or any portion of the License granted to the Company hereunder. The Company will provide WFUHS a copy of any and all sublicense agreements within sixty (60) days of execution. Unless WFUHS otherwise expressly consents in writing, no such sublicense shall release the Company from its obligations hereunder.

4.2 For each sublicense granted by the Company hereunder with respect to the sale of Licensed Products that are not also VCU Covered Products (Licensed Products that are also VCU Covered Products being provided for in Section 4.3), the Company will pay to WFUHS the amounts provided below:

4.2.1 Royalties on the sale, lease, license or other transfer of Licensed Products that are not

VCU Covered Products under a sublicense equal to the lesser of: (i) the royalty that WFUHS would have received from the Company under Section 3.2 if such Licensed Products had been sold, licensed, leased or otherwise transferred by the Company instead of the sublicensee or (ii) **[********]** of all royalties received by the Company under such sublicense on sales, leases, licenses or other transfers by such sublicensee; provided that under no circumstances will WFUHS receive less under this Section 4.2.1 than the royalty that WFUHS would have received from the Company under Section 3.2 if (A) such Licensed Product had been sold, licensed, leased or otherwise transferred by the Company instead of the sublicensee and (B) **[********]**.

4.2.2 If a sublicensee first reaches any milestone set forth in Section 3.3 before Company, then, for each milestone so reached by any such sublicensee, the Company shall pay to WFUHS the lesser of:

(1) the amount of the milestone payment set forth in Section 3.3 as if Company had reached such milestone instead of the sublicensee; or

(2) the amount of consideration received by Company from the sublicensee specifically for reaching such milestone; provided that the amount payable in respect of such milestone under this Section 4.2.2 shall in no event be less than **[********]**.

In the event that a payment is required under this Section 4.2.2 with respect to any milestone and such payment is made to WFUHS, no payment with respect to the achievement of the same such milestone by the Company shall be payable at any time under Section 3.3 or otherwise.

4.2.3 If in lieu of, or in addition to, a royalty on sales, licenses, leases, or other transfers of Licensed Products as provided for in Section 4.2.1, a sublicensee **[********]** (all of the foregoing, collectively, "Other Amounts") in consideration of the sublicense, the Company shall pay to WFUHS an amount equal **[********]** of all such Other Amounts (including, without limitation **[********]**); provided that:

(A) if, as of the date payment in respect of such Other Amount is to be made to WFUHS under Section 8.2, any royalties on the actual sale, lease, license or other transfer of Licensed Products have previously been actually paid, or are then payable, to WFUHS under Section 4.2.1, then the maximum amount payable in respect of such Other Amount under this Section 4.2.3 shall be equal to **[********]**; and

(B) any milestone amounts paid by the Company to WFUHS under Section 4.2.2 or Section 4.3.2 shall be creditable against any amounts otherwise payable under this Section 4.2.3, and any amounts paid by the Company to WFUHS under this Section 4.2.3 shall be creditable against any milestone amounts otherwise subsequently due and payable to WFUHS under Section 4.2.2 or Section 4.3.2.

For purposes of clarity:

(Example 1) **[*********]**; and

(Example 2) **[*********]**.

To the extent the Company has fulfilled its obligations to WFUHS pursuant to this Section 4 and is not required to share the same with WFUHS pursuant to this Agreement, the Company shall be entitled to retain all Other Amounts without compensation to WFUHS.

4.3 For each sublicense granted by the Company hereunder with respect to Licensed Products that are also VCU Covered Products (Licensed Products that are not also VCU Covered Products being covered by Section 4.2), the Company will pay to WFUHS the amounts provided below:

4.3.1 Royalties on the sale, lease, license or other transfer of Licensed Products that are also VCU Covered Products under a sublicense equal to the lesser of: (i) the royalty that WFUHS would have received from the Company under Section 3.4 if the VCU Covered Product had been sold, licensed, leased or otherwise transferred by the Company instead of the sublicensee or (ii) **[********]** of all royalties received by the Company under such sublicense on sales, leases, licenses or other transfers by such sublicensee; provided that under no circumstances will WFUHS receive less under this Section 4.3.1 than the royalty that WFUHS would have received from the Company under Section 3.4 if (A) such VCU Covered Product had been sold, licensed, leased or otherwise transferred by the Company instead of the sublicensee and (B) **[********]**.

4.3.2 If a sublicensee first reaches any milestone set forth in Section 3.3 before Company, then, for each milestone so reached by any such sublicensee, Company shall pay to WFUHS the lesser of:

(1) the amount of the milestone payment set forth in Section 3.3 as if Company had reached such milestone instead of the sublicensee; or

(2) the amount of consideration received by Company from the sublicensee specifically for reaching such milestone; provided that the amount payable in respect of such milestone under this Section 4.3.2 shall in no event be less than **[********]**.

In the event that a payment is required under this Section 4.3.2 with respect to any milestone and such payment is made to WFUHS, no payment with respect to the achievement of the same such milestone by the Company shall be payable at any time under Section 3.3 or otherwise.

4.3.3 If in lieu of, or in addition to, a royalty on sales of Licensed Products as provided for in Section 4.3.1, a sublicensee pays or delivers Other Amounts to the Company in

consideration of the sublicense, the Company shall pay to WFUHS an amount equal to **[********]** of all such Other Amounts (including, without limitation, **[********]**); provided that:

(A) if, as of the date payment in respect of such Other Amount is to be made to WFUHS under Section 8.2, any royalties on the actual sale, lease, license or other transfer of Licensed Products have previously been actually paid, or are then payable, to WFUHS under Section 4.3.1, then the maximum amount payable in respect of such Other Amount under this Section 4.3.3 shall be equal to **[********]**; and

(B) any milestone amounts paid by the Company to WFUHS under Section 4.2.2 or Section 4.3.2 shall be creditable against any amounts otherwise payable under this Section 4.3.3, and any amounts paid by the Company to WFUHS under this Section 4.3.3 shall be creditable against any milestone amounts otherwise subsequently due and payable to WFUHS under Section 4.2.2 or Section 4.3.2.

For purposes of clarity:

(Example 1) **[*********]**; and

(Example 2) **[*********]**.

To the extent the Company has fulfilled its obligations to WFUHS pursuant to this Section 4 and is not required to share the same with WFUHS pursuant to this Agreement, the Company shall be entitled to retain all Other Amounts without compensation to WFUHS.

4.4 If a milestone payment or an "Other Amount" (such as an initial license fee) is received by Company and such milestone payment or "Other Amount" cannot be reasonably determined at the date of the applicable payment under Section 8.2 to be with respect to Licensed Products that are not also VCU Covered Products or Licensed Products that are also VCU Covered Products, then such milestone payment or "Other Amount" shall be deemed to be for (i) Licensed Products that are also VCU Covered Products and therefore subject to Section 4.3.3 if both VCU Patents and any Patent Rights are licensed under the sublicense to the sublicensee or (ii) Licensed Products that are not also VCU Covered Products and subject to Section 4.2.3 if any Patent Rights, but no VCU Patents, are licensed under the sublicense to the sublicensee.

4.5 Unless otherwise agreed by WFUHS, termination of the License granted to the Company by WFUHS under this Agreement will terminate all sublicenses that may have been granted by the Company; provided, however, that any sublicensee who desires to continue its sublicense may so advise WFUHS in writing of such sublicensee's desire to continue the sublicense within thirty (30) days of the sublicensee's receipt of written notice of the termination of the Company's License and, subject to the sublicensee's agreement to assume relative to WFUHS all the payment and other obligations contained in this Agreement (or, as applicable, the

sublicense agreement with the Company), WFUHS, in the exercise of reasonable discretion, may elect to continue the sublicense.

4.6 Any sublicense granted by the Company must contain provisions corresponding to those of Section 4.5 relative to termination and the conditions of continuance of any sublicenses.

5. Commercially Reasonable Efforts and Due Diligence

5.1 The Company will use commercially reasonable efforts (either alone or through research collaborations or alliances with research organizations, pharmaceutical companies or other third parties), taking into account all scientific, clinical and regulatory uncertainties, to pursue the development of Licensed Products and to bring Licensed Products to market through a thorough and diligent program for exploitation of the Patent Rights and the marketing and commercialization of the Licensed Products. Upon receipt of Regulatory Approval for the first Licensed Product in a Major Country, the Company will have no further diligence obligations hereunder, other than an obligation to use commercially reasonable efforts to market and sell the Licensed Product in the Major Country in which Regulatory Approval was obtained.

5.2 The Company will prepare and, not later than the **[********]** of the Effective Date, submit to WFUHS a development plan of the Company for bringing the Licensed Products to market. The development plan of Company will be revised and updated from time to time (and not less frequently than once per calendar year) and, upon delivery to WFUHS, each such revision or update will become a part of this Agreement.

5.3 If WFUHS believes the Company is failing to comply with its obligations under Section 5.1, WFUHS may send notice to the Company asserting such belief and the basis therefor. The Company shall have sixty (60) days from its receipt of such notice either to (i) commence compliance with its obligations under Section 5.1 to WFUHS' reasonable satisfaction or (ii) send notice to WFUHS requesting arbitration of such issue in accordance with Section 18.10. In the event that the Company fails to satisfy its obligation set forth in the previous sentence, WFUHS shall have the right, at its option, to convert any portion of the License granted by WFUHS to the Company hereunder to a non-exclusive license, or to cancel the License upon thirty (30) days written notice and to require a reversion back to WFUHS of all rights and all relevant materials, research information and technology, including Patent Rights and WFUHS Know-How, transferred to the Company by WFUHS.

6. Confidentiality

6.1 WFUHS and the Company recognize that each party may need to provide confidential and proprietary information from time to time to the other party pursuant to this Agreement. In recognition of WFUHS as a non-commercial, academic institution, the Company agrees to limit to the extent possible the delivery of confidential information to WFUHS. WFUHS and the Company agree to hold in confidence, in accordance with this Section 6, any information disclosed by one party to the other under this Agreement that is clearly identified as

“confidential” at the time of disclosure (hereinafter “Information”). Information will be provided in written or other tangible form whenever possible marked as “confidential” but, if provided orally or in an other non-tangible form, the Information must be summarized in writing, labeled as “confidential” and be provided to the receiving party with thirty (30) days of first disclosure to be considered confidential under this Agreement. For the purpose hereof, “hold in confidence” means that WFUHS and the Company will not disclose the Information of the other party to a third party and will protect the Information provided to it by the other party in the same manner in which it protects its own confidential information of similar nature, but will in no event use less than reasonable care. The Information will remain the property of the party disclosing such Information.

6.2 The obligations of the receiving party to maintain confidentiality under this Agreement will survive its expiration or termination and will endure for five (5) years from the date of first disclosure of such Information.

6.3 Information does not include information that:

(i) is already known to the receiving party prior to the Effective Date;

(ii) is or becomes publicly known through no fault of receiving party;

(iii) has been or is disclosed to the receiving party by a third party that the receiving party does not know (and is not reckless in not knowing) to be under an obligation of confidence or secrecy to the disclosing party at the time of disclosure;

(iv) is developed by employees or consultants of the receiving party who had no knowledge of the Information, as evidenced by written records;

(v) is approved for release by written authorization of the disclosing party; or

(vi) is required to be disclosed by law, provided the receiving party promptly notifies the disclosing party in writing prior to such disclosure, considers in good faith any comments or suggested changes to such disclosure from the disclosing party and gives the disclosing party a reasonable opportunity to prevent or limit the disclosure.

6.4 The parties further agree that the Company shall have the right to disclose Information and the provisions hereof to: (i) its Affiliates; (ii) potential sublicensees, assignees or subcontractors for the purpose of allowing any such potential sublicensee, assignee or subcontractor to evaluate such technologies and to determine whether to enter into a sublicense, assignment or subcontract; (iii) sublicensees, assignees or subcontractors, for the purpose of allowing such sublicensee, assignee or subcontractor, as the case may be, to make, have made, use, research, develop, have developed, lease, market, offer to sell, sell, have sold, distribute, improve, import and export Licensed Products; (iv) a purchaser or potential purchaser of all or substantially all of the Company’s assets, or a party with which the Company is then in discussions regarding a potential business combination; and (v) an

investor or lender, or prospective investor or lender, in or to the Company; provided, however, that, prior to any such disclosure, the Company shall obtain a confidentiality agreement (substantially similar in content to the provisions of this Section 6) from the party to which such disclosures are to be made.

7. Representations and Disclaimer

7.1 WFUHS represents that, to its actual knowledge, it owns all right, title and interest in and to the Patent Rights existing as of the Effective Date, free of any liens, licenses, encumbrances, restrictions and other legal or equitable claims, other than the rights of the federal government under federal funding guidelines.

7.2 The Company represents that (i) it has the authority and corporate power to enter into this Agreement and (ii) it is the exclusive licensee of the VCU Patents in the Field and such license is in full force and effect as of the Effective Date.

7.3 Information, materials and property, whether tangible or intangible, which may be delivered hereunder to the Company, will be delivered on an "as is, where is" basis without any express or implied warranty except as expressly set forth in Section 7.1. WFUHS HEREBY DISCLAIMS ANY AND ALL REPRESENTATIONS OR WARRANTIES, WHETHER EXPRESS OR IMPLIED, INCLUDING, WITHOUT LIMITATION, ANY IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE, OR ANY IMPLIED WARRANTIES ARISING FROM ANY COURSE OF DEALING, USAGE, OR TRADE PRACTICE. WFUHS MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, AS TO THE VALIDITY OF PATENT RIGHTS, INCLUDING CLAIMS ISSUED OR PENDING, OR THAT THE USE OF ANY TECHNOLOGY UNDER THE PATENT RIGHTS OR WFUHS KNOW-HOW WILL NOT INFRINGE ANY PATENT OR OTHER PROPRIETARY RIGHT OF A THIRD PARTY. WFUHS ASSUMES NO RESPONSIBILITY WITH RESPECT TO THE EXPLOITATION OR COMMERCIALIZATION OF THE PATENT RIGHTS, LICENSED PRODUCTS AND PROCESSES OR WFUHS KNOW-HOW OR THE MANUFACTURE, USE, SALE, LEASE OR DISTRIBUTION OF ANY METHODS, PROCESSES, APPARATUS, DEVICES, SYSTEMS, PRODUCTS, ARTICLES, AND/OR APPLIANCES DERIVED FROM OR USING THE LICENSED PRODUCTS AND PROCESSES, PATENT RIGHTS OR WFUHS KNOW-HOW BY THE COMPANY. NO PARTY WILL BE LIABLE FOR LOSS OF PROFITS, LOSS OF USE OR ANY OTHER INCIDENTAL, CONSEQUENTIAL OR EXEMPLARY DAMAGES.

8. Records, Reports and Payments

8.1 The Company will keep and maintain, and will require any and all of its Affiliates and sublicensees to keep and maintain, complete, accurate, and correct records and books relating to the sale or lease of the Licensed Products for four (4) years following the end of the calendar year to which such records and books pertain.

8.2 The Company will render to WFUHS calendar quarter reports for each calendar quarter during the term hereof. Within thirty (30) days following (i) each such calendar quarter and (ii) expiration of the sixty (60) day period of permissible sales of inventory following termination of this license under Section 10.5, if applicable, the Company will provide to WFUHS a written report setting forth the following information with respect to the immediately preceding calendar quarter or sixty (60) day period, as applicable:

(i) an accounting for all Licensed Products sold, distributed or used;

(ii) gross receipts from the sale of Licensed Products;

(iii) any applicable reductions calculated as provided in the definition of "Net Sales" hereunder;

(iv) total Net Sales;

(v) total of all milestone payments due and payable to WFUHS; and

(vi) total royalties, sublicense revenues, milestone payments and any and all other payments under this Agreement then due.

The Company will remit to WFUHS with each such report the amount of royalty and other payments shown thereby to be due. If no sales of Licensed Products were made during any calendar quarter, the Company will provide to WFUHS a statement to that effect.

8.3 The books and records of account relating to sales of Licensed Products kept by the Company shall be made available upon reasonable notice, during normal business hours for examination by an auditor chosen by WFUHS and reasonably acceptable to the Company, who will be permitted to enter upon the premises of the Company and, at WFUHS's expense, make and retain copies of any and all parts of said books and records of account, including invoices that are relevant to any report required to be rendered by the Company. Any amount determined owed but not paid will be paid promptly to WFUHS with interest accruing from the date finally determined at the rate of **[*********]** per year. In the event any such audit shows that the Company has underpaid its royalty obligation hereunder by **[*********]** or more during any calendar quarter, the Company will reimburse WFUHS for the out-of-pocket expenses actually incurred for such audit. WFUHS may conduct no more than one (1) audit per calendar year.

8.4 Royalty or other payments will be paid in United States dollars to WFUHS in Winston-Salem, North Carolina, or at such other place as WFUHS may reasonably designate consistent with the laws and regulations controlling in any foreign country. Any withholding taxes that the Company is required by law to withhold on remittance of the royalty payments will be deducted from the royalty paid. The Company will cooperate in all reasonable respects with WFUHS, at WFUHS' expense, in WFUHS' filing of documents or in pursuing

other actions deemed appropriate by WFUHS to reclaim any such taxes paid to local, state, or federal governments on a country-by-country basis to which WFUHS may be entitled pursuant to the laws of that locale, state or country. The Company will furnish WFUHS with original copies of all official receipts for such taxes. If any royalties hereunder are based on Net Sales converted from foreign currency, the conversion will be made by using the average exchange rate at a first-class foreign exchange bank for the calendar quarter period to which such royalty payments relate.

9. Patent Prosecution

9.1 The filing and prosecution of all United States and foreign patent applications and maintenance of all United States and foreign patents within the Patent Rights shall be the primary responsibility of WFUHS; provided, however, that WFUHS shall: (i) notify the Company in writing prior to any initial patent application filing in a country and keep the Company informed of, and give the Company a reasonable opportunity to participate in, all major decisions affecting all filing, prosecution and maintenance activities related to the Patent Rights; (ii) provide, or require its patent counsel to provide, to the Company copies of all papers and other materials relating to all patent applications and registrations prior to submission; and (iii) give due consideration to comments of the Company related to patent prosecution. WFUHS will seek patent protection for each invention within the Patent Rights in all countries designated by the Company from time to time so long as the Company assumes full financial responsibility, and actually reimburses WFHUS, for the associated patent preparation, prosecution and maintenance costs in such countries. Upon the failure or refusal of WFUHS to undertake such prosecution efforts, the Company may, upon notice to WFUHS, assume such efforts unless WFUHS commences such efforts to the reasonable satisfaction of the Company within thirty (30) days of such notice. In such event, Company will (i) provide, or require its patent counsel to provide, to WFUHS copies of all papers and other materials relating to all patent applications and registrations prior to submission; and (ii) give due consideration to comments of WFUHS related to patent prosecution.

9.2 Within thirty (30) days following receipt of itemized statements and other proper supporting documentation, the Company will reimburse WFUHS its reasonable fees and costs actually incurred that relate to the preparation, filing, prosecution, and maintenance of the U.S., PCT, and/or foreign patent applications, and any U.S. and foreign patents issuing thereon, within the Patent Rights that are incurred following the Effective Date and that are requested or authorized by the Company.

9.4 In the event the Company determines that filing, prosecution or maintenance of any of the U.S. or foreign patent applications or patents within the Patent Rights is not justified and so advises WFUHS in writing or in the event that Company fails to pay WFUHS within thirty (30) days of receipt of notice of any delinquent payment for any such filing, prosecution, or maintenance, WFUHS will then have the option to file, prosecute or maintain any such Patent Rights at its own expense. If WFUHS does so: (i) WFUHS will then have the option to delete such U.S. or foreign patent applications or patents within said Patent Rights from the License for the territory covered thereby; (ii) the Company will have no rights under the

License for any such deleted U.S. or foreign patent applications or patent; (iii) WFUHS will obtain all rights in and to such deleted U.S. or foreign patent applications or patents and will be free to exploit and to assign or license any such deleted U.S. or foreign patent applications or patents to third parties without effect on the amount of royalties or other payments due to WFUHS under Sections 3 or 4.

9.5 In the event that any claim of any application within the Patent Rights is canceled, abandoned, or otherwise disallowed by a final non-appealable or non-appealed action of a Patent Office having jurisdiction, or in the event that any claim of any patent within the Patent Rights is held invalid or unenforceable by a non-appealable or non-appealed decision by any court of competent jurisdiction, such claim will be deemed to have expired, as of the date of final disallowance or final decision of invalidity or non-enforceability.

10. Termination

10.1 The term of this Agreement and the License shall begin on the Effective Date and, unless sooner canceled or terminated as provided herein, shall expire upon expiration of the last-to-expire patent or patent application included within the Patent Rights.

10.2 If the Company becomes bankrupt or insolvent, or files a petition in bankruptcy, or if the business of the Company is placed in the hands of a receiver, assignee or trustee for the benefit of creditors, whether by the voluntary act of the Company or otherwise, and such proceeding continues unstayed for sixty (60) days, this Agreement will automatically terminate without any notice whatsoever to the Company.

10.3 If the Company at any time defaults in any payment due to WFUHS, including without limitation a royalty, milestone or other payment, or commits a material breach of any material covenant or undertaking set forth herein, WFUHS shall have the right, in addition to all other remedies available to it, to terminate this Agreement and revoke all or any portion of the License herein granted, by giving the Company thirty (30) days prior written notice of such proposed termination; provided that (i) if the Company cures such default or breach within such thirty (30) day period, then this Agreement shall remain in effect and the License herein granted shall be in full force and effect as if no such default or breach had occurred on the part of the Company and (ii) if at the expiration of such 30-day period, the Company can demonstrate to WFUHS' reasonable satisfaction that it is working diligently and in good faith to cure such default or breach, the Company shall have an additional period, not to exceed ninety (90) days, to cure such breach. If at the expiration of such initial 30-day period or such additional 90-day period, if applicable, the Company fails to cure the breach, WFUHS may terminate this Agreement upon notice of termination to the Company. In the event of termination under this Section 10.3, the Company will continue to be obligated to pay to WFUHS any and all license fees, royalties, milestones or other payments payable at the time of termination.

10.4 The Company will have the right to terminate this Agreement with or without cause at any time on sixty (60) days written notice to WFUHS.

10.5 Upon termination hereof for any reason, nothing herein will be construed to release either party from any obligation accrued prior to the effective date of such termination. Any termination hereof will not relieve the Company of any obligations to make any and all payments for any royalties, milestones or other payments that may have accrued prior to the date of such termination. After the effective date of any termination of this Agreement, the Company, for a sixty (60) day period following such termination, may, unless termination is effected under Section 10.3, 10.6, or 13.1 (last sentence), sell all Licensed Products in the inventory of the Company at the usual sales price of the Company for such Licensed Products; provided that the Company shall pay to WFUHS the royalties thereon as required by Section 3 and submit the reports required by Section 8. Any Licensed Products remaining in inventory of the Company following such sixty (60) day period shall be transferred to WFUHS without charge.

10.6 If, at any time during the term hereof, the Company, directly or indirectly, opposes, or assists any third party to oppose, the grant of any letters patent on any patent application within the Patent Rights or disputes, or directly or indirectly assists any third party to dispute, the validity of any patent within the Patent Rights or any of the claims thereof, WFUHS may, at its sole discretion, exercised within sixty (60) days after WFUHS first has notice of such occurrence, terminate all or any portion of the License upon thirty (30) days prior written notice to the Company.

11. Infringement

11.1 Each party will be obligated to promptly inform the other in writing of any alleged infringement by a third party of any of the patents within the Patent Rights, and provide such other parties with any available evidence of infringement. No party will settle or compromise any claim or action in a manner that imposes any restrictions or obligations on the other party or parties without such other party's written consent, which shall not be unreasonably withheld.

11.2 During the term hereof, the Company will have the first right, but not the obligation, to (i) prosecute at its own expense any such infringements of the Patent Rights and, in furtherance of such prosecution, to request that WFUHS join as a party plaintiff in any such suit, without expense to WFUHS, and WFUHS's consent to such request shall not be unreasonably withheld, or (ii) settle the infringement suit, subject to the provisions of Section 11.1, by sublicensing the alleged infringer or by other means.

11.3 In the event that the Company undertakes the enforcement and/or defense of the Patent Rights by litigation, including any declaratory judgment action, the total cost of any such action commenced or defended solely by the Company shall be borne by the Company and the Company shall keep any recovery or damages for past infringement derived therefrom, provided that Company pays to WFUHS any royalties, fees, payment or Other Amounts due and payable to WFUHS pursuant Sections 3 and 4, if any, based on amounts awarded to compensate the Company for lost sales or revenues, including any damages awarded directly

in connection with such lost sales or revenues. Subject to Section 11.1, the Company shall be entitled to settle any such litigation by agreement, consent, judgment, voluntary dismissal or otherwise, provided such settlement does not impose any burden, obligation or responsibility on WFUHS.

11.4 If, within six (6) months after having been notified of any alleged infringement, the Company is unsuccessful in persuading the alleged infringer to desist and has not brought or is not diligently prosecuting an infringement action, or if the Company notifies WFUHS at any time prior thereto of its intention not to bring suit against any alleged infringer, then, and only then, WFUHS will have the right to prosecute at its own expense any infringement of the Patent Rights. The total cost of any such infringement action commenced or defended solely by WFUHS will be borne by WFUHS, and WFUHS will keep any recovery or damages for past infringement derived therefrom. Subject to Section 11.1, WFUHS shall be entitled to settle any such litigation by agreement, consent, judgment, voluntary dismissal or otherwise.

11.5 In the event an infringement action is brought against the Company arising from the use of the Patent Rights, the Company will defend such action and will be solely responsible for all attorneys' fees, costs of defense and liability arising out of that action.

11.6 In the event that a declaratory judgment action alleging invalidity or non-infringement of any of the Patent Rights is brought against the Company, the Company will be responsible, at its sole expense, for the defense of the action and the Company will keep any recovery or damages derived therefrom or from any counterclaims asserted therein unless and until WFUHS elects to intervene and participate in the defense of the action in accordance with the next sentence, and provided further that Company pays to WFUHS any and all amounts due and payable to WFUHS pursuant Sections 3 and 4 of this Agreement due, in whole or in part, to any lost sales or revenues and any damages or awards associated therewith or thereto. WFUHS, at its option, will have the right to intervene and participate in the defense of the action at its own expense whereupon WFUHS and the Company will share in any recovery or damages derived therefrom or from any counterclaims asserted therein in proportion to the total out-of-pocket costs contributed by each party.

11.7 In any infringement suit brought or declaratory judgment action defended by any party to protect any of the Patent Rights, the other party will, at the request and expense of the party initiating such suit, cooperate in all respects and, to the extent possible, make its employees available to testify when requested and make available relevant records, papers, information, samples, specimens and the like.

12. Indemnification and Insurance

12.1 Each of the Company, its Affiliates and their respective sublicensees will, at all times during the term hereof and thereafter, indemnify, hold harmless, and defend WFUHS and Wake Forest University and their respective trustees, officers, directors, employees, agents and affiliates from and against any and all claims, losses, damages, liabilities, costs and expenses,

including legal expenses and reasonable attorneys' fees actually incurred (all of the foregoing, "Losses"), which arise or may arise at any time out of or in connection with its own activities in connection with its use of the Patent Rights, Invention or WFUHS Know-How in the production, manufacture, sale or use of the Licensed Products or Licensed Processes, except to the extent such Losses arise, directly or indirectly, out of the gross negligence or willful misconduct of WFUHS or its officers, agents or employees. The Company will ensure that any sublicense agreement will contain an indemnity provision to this effect in favor of WFUHS.

12.2 The Company and its Affiliates will, and the Company will require its sublicensees to, carry liability insurance at their own expense, adequate to assure its obligations to WFUHS under Section 12.1 and will provide satisfactory evidence of adequate insurance coverage to WFUHS upon its request.

13. Assignment

13.1 The Company may assign or otherwise transfer this Agreement and the License granted hereby only (i) with the approval of WFUHS or (ii) to the assignee or transferee of the Company's entire business or of that part of the Company's business to which the License granted hereby relates (including, without limitation, by operation of law in a merger); provided, however, that such assignee or transferee agrees in writing to be bound by the terms and conditions hereof. If WFUHS raises no reasonable objection in writing to a proposed assignment or transfer within fifteen (15) days after WFUHS receives notice thereof, then WFUHS shall be deemed to have approved such assignment or transfer so long as the assignee or transferee agrees in writing to be bound by the terms and conditions hereof. If the Company sells or otherwise transfers its entire business or that part of its business to which the License granted hereby relates and the assignee or transferee does not agree in writing to be bound by the terms and conditions hereof within fifteen (15) days of any such request by WFUHS, WFUHS will have the right to terminate this Agreement by providing written notice of termination to such transferee or assignee.

14. Non-Use of Names

14.1 The Company will not use the name of WFUHS or any adaptation thereof in any advertising, promotional or sales activities without the prior written consent of WFUHS, except (i) that the Company may state that it is licensed under one or more of the patents or applications within the Patent Rights or (ii) to the extent required by law, regulation or court order.

15. Export Controls

15.1 It is understood that WFUHS is subject to United States laws and regulations controlling the export of technical data, computer software, laboratory prototypes, and other commodities that may require a license from the applicable agency of the United States Government or may require written assurances by the Company that the Company will not export data or commodities to certain foreign countries without prior approval of such agency. WFUHS

does not represent that a license will be required or that, if required, will be issued.

16. Survival

16.1 Sections 1, 2.5, 6, 7, 8.1, 8.3, 10, 12, 16, 17 and 18 shall survive expiration or termination of this Agreement for any reason.

17. Payments, Notices and Other Communications

17.1 Any payment, notice or other communication pursuant to this Agreement shall be given in writing and shall be deemed given upon personal delivery, one day after deposit with a nationally recognized overnight delivery service with charges prepaid or two days after deposit with the United States Post Office, by registered or certified mail, postage prepaid, addressed to the applicable party at its address below (or such other address as it designates by written notice given to the other party):

WFUHS: Director, Office of Technology Asset Management
Wake Forest University Health Sciences
Medical Center Boulevard
Winston-Salem, North Carolina 27157-1023

The Company: Targacept, Inc.
200 East First Street, Suite 300
Winston-Salem, North Carolina 27101-4165
Attention: President

18. Miscellaneous Provisions

18.1 This Agreement will be construed, governed, interpreted, and applied in accordance with the laws of the State of North Carolina, U.S.A. without regard to conflicts-of-law rules. Notwithstanding the foregoing, any questions affecting the construction and effect of any patent will be determined by the law of the country in which the patent was granted.

18.2 The parties hereto acknowledge that this Agreement sets forth the entire agreement and understanding of the parties hereto as to the subject matter hereof and supersedes and cancels any and all prior agreements between the parties relating to the subject matter, including without limitation the Option Agreement. This Agreement will not be subject to any change or modification except by the execution of a written instrument signed by the parties hereto.

18.3 The provisions hereof are severable and, in the event that any provision hereof is determined to be invalid or unenforceable under any controlling body of law, such invalidity or unenforceability will not in any way affect the validity or enforceability of the remaining provisions hereof.

18.4 The failure of either party to assert a right hereunder or to insist upon compliance with any

term or condition hereof will not constitute a waiver of that right or excuse a similar subsequent failure to perform any such term or condition by the other party.

18.5 This Agreement will be binding and inure to the benefit of the parties hereto and their respective affiliates and permitted successors and assigns.

18.6 The representations, warranties, covenants, and undertakings contained in this Agreement are for the sole benefit of the parties hereto and their permitted successors and assigns and such representations, warranties, covenants, and undertakings will not be construed as conferring any rights on any other party.

18.7 Nothing contained in this Agreement will be deemed to place the parties hereto in a partnership, joint venture or agency relationship and neither party will have the right or authority to obligate or bind the other party in any manner.

18.8 This Agreement may be executed in two counterparts, each of which will be deemed an original and both of which, taken together, shall constitute one and the same instrument.

18.9 In the event of any dispute between the parties that arises from this Agreement, the prevailing party in any legal action that is brought to resolve such dispute will be entitled to recover its attorneys' fees and costs from the other party.

18.10 Any controversy or dispute as to whether the Company is satisfying its obligations under Section 5.1 shall be first referred to arbitration in the City of Winston-Salem, North Carolina, USA, under the auspices of, and conducted in accordance with, the rules of the American Arbitration Association. All arbitration proceedings shall be before a board of three (3) arbitrators who are knowledgeable about biotechnology and pharmaceutical development and the legal, tax and other issues affecting institutions of higher learning, and each party shall select one (1) arbitrator and the selected arbitrators shall select the third arbitrator. The arbitration proceedings shall be conducted in the English language and any award shall be in United States dollars. The cost of the third arbitrator shall be divided equally between the parties and each party shall pay the costs of the arbitrator selected by it. Any award of the arbitrators shall be binding on the parties to this Agreement. For the avoidance of doubt, this Section 18.10 is only applicable to disputes, if any, with respect to compliance with the Company's obligations under Section 5.1.

IN WITNESS WHEREOF, the parties hereto have hereunto set their hands and seals and duly executed this License Agreement as of the day and year first set forth above.

Wake Forest University Health Sciences

By: /s/ Spencer Lemons
Spencer Lemons
Director, Technology Asset Management

Targacept, Inc.

By: /s/ J. Donald deBethizy
Dr. J. Donald deBethizy
President and CEO

Exhibit 10.22

[********] 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.

Development and Production Agreement
For
Active Pharmaceutical Ingredients

Between

SIEGFRIED LTD.
Untere Brühlstrasse 4
4800 Zofingen SWITZERLAND

(hereinafter referred to as "SIEGFRIED")

and

TARGACEPT, INC.
200 East First Street, Suite 300
Winston-Salem, NC 27101-4165 USA

(hereinafter referred to as "TARGACEPT")

RECITALS

This DEVELOPMENT AND PRODUCTION Agreement (the "AGREEMENT") is entered into as of the first (1st) day of February 2004 (the "EFFECTIVE DATE") by and between SIEGFRIED and TARGACEPT.

WHEREAS, TARGACEPT presently owns certain patents and patent applications that disclose the composition, preparation or use of certain pharmaceutically active compounds and intermediates and formulations of such compounds (collectively, "COMPOUNDS").

WHEREAS, SIEGFRIED has expertise and is engaged in the development and preparation of pharmaceutically active compounds and intermediates of such compounds, as well as formulations of such compounds and intermediates.

WHEREAS, TARGACEPT is interested in having SIEGFRIED perform DEVELOPMENT on and/or PRODUCTION of certain COMPOUNDS, and SIEGFRIED is willing to carry out such DEVELOPMENT and PRODUCTION on behalf of and for TARGACEPT under the terms and conditions of this AGREEMENT.

NOW, THEREFORE, in consideration of the mutual covenants and promises contained in this AGREEMENT and other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, TARGACEPT and SIEGFRIED agree as follows:

1. DEFINITIONS

For the purpose of this AGREEMENT, the following definitions shall apply:

1.1 "ACT" shall mean the United States Federal Food, Drug and Cosmetics Act and all rules and regulations promulgated thereunder, as the same may be amended from time to time.

1.2 "AFFILIATE" shall mean, with respect to a given party, any business entity controlling, controlled by, or under common control with such party. For the purpose of this definition, the term "control" shall mean the possession of the power to direct or cause the direction of the management and policies of an entity, whether through the ownership of more than fifty percent (50%) of the outstanding voting stock, by contract or otherwise.

1.3 "BATCH" shall mean the material resulting from a single manufacturing order during a specific cycle of PRODUCTION.

1.4 "COMPOUND" shall have the meaning given it in the recitals appearing above.

1.5 "CONFIDENTIAL INFORMATION" shall mean (a) in the case of TARGACEPT,

TARGACEPT IP, NEW IP and any and all information and materials disclosed by TARGACEPT to SIEGFRIED in connection with this AGREEMENT or the activities hereunder and (b) in the case of SIEGFRIED, SIEGFRIED IP and any and all other information and materials, other than NEW IP, disclosed by SIEGFRIED to TARGACEPT in connection with this AGREEMENT or the activities hereunder. In addition, the existence and terms of this AGREEMENT shall be considered CONFIDENTIAL INFORMATION of each party.

1.6 “DEVELOPMENT” shall mean, collectively, the activities pertaining to the development of a synthetic chemical process and/or finished dosage development studies and formulation for a SELECTED COMPOUND to enable PRODUCTION of a PRODUCT (which may include, without limitation, research studies, process optimization, the scale-up of an existing process and delivery of samples of SELECTED COMPOUND) that are described as Phase I – Laboratory under Scope of Work in the mutually agreed upon sub-appendix to Appendix B applicable to that PRODUCT. A separate sequentially numbered sub-appendix (B-1, B-2 and so on) shall be prepared for each SELECTED COMPOUND for which SIEGFRIED undertakes DEVELOPMENT at TARGACEPT’s request hereunder, which sub-appendix shall include the costs chargeable to TARGACEPT for such services (based on the rates specified herein), be dated and signed by an authorized employee of each party, attached hereto and thereupon become a part hereof.

1.7 “EFFECTIVE DATE” shall have the meaning given it in the first sentence of this AGREEMENT.

1.8 “EXCLUSION CONDITIONS” shall mean: (i) with respect to any particular SELECTED COMPOUND or PRODUCT, TARGACEPT (A) licenses or otherwise conveys to a third party the right to manufacture, or to control manufacturing of, such SELECTED COMPOUND or PRODUCT (except where TARGACEPT merely outsources the manufacturing function for such SELECTED COMPOUND OR PRODUCT on a contract basis for its own benefit), (B) enters into a strategic collaboration or partnership, however structured, pursuant to which its collaborator or partner assumes responsibility for, or control of, manufacturing such SELECTED COMPOUND or PRODUCT, or (C) determines, in the exercise of its good faith discretion, that SIEGFRIED’s performance hereunder is sub-standard or otherwise unsatisfactory; or (ii) with respect to any particular task, TARGACEPT determines that SIEGFRIED does not possess the experience, expertise or capability required to perform such task.

1.9 “FDA” shall mean the United States Food and Drug Administration.

1.10 “FULL TIME EQUIVALENT (FTE)” is defined as **[********]** per year of project work as provided by a chemist, pharmaceutical scientist, analytical chemist or regulatory specialist. FTE cost is fully loaded and, without limiting the generality of the foregoing, includes administrative overhead and quality support.

1.11 “GMP” shall mean those practices in the manufacture of pharmaceutical products that are recognized from time to time as the current good manufacturing practices in accordance with FDA regulations, guidelines and other administrative interpretations and rulings in connection therewith, including, but not limited to those regulations cited in 21 C.F.R. §§ 210 and 211 and the International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use, Guidance for Industry Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients, August 2001.

1.12 “KNOW-HOW” shall mean information and materials, including, without limitation, ideas, concepts, discoveries, inventions, developments, improvements, know-how, expertise, trade secrets, designs, devices, equipment, process conditions, specifications, algorithms, notation systems, works of authorship, computer programs, technologies, formulas, techniques, methods, procedures, assay systems, applications, experimental results, data (including, without limitation, analytical, toxicological, pharmacological, clinical, bioequivalence and stability data), documentation, reports, enzymes, reagents, proteins, peptides, organisms, formulations, chemical compounds and products, whether patentable or otherwise.

1.13 “MASTER PRODUCTION RECORD” shall mean, with respect to any particular PRODUCT, the formal set of instructions for PRODUCTION of such PRODUCT.

1.14 “NEW IP” shall mean all NEW KNOW-HOW and all patents, patent applications, copyrights, trade secrets and other intellectual property rights pertaining to NEW KNOW-HOW.

1.15 “NEW KNOW-HOW” shall mean all KNOW-HOW that pertains solely to one or more SELECTED COMPOUNDS, the DEVELOPMENT of one or more SELECTED COMPOUNDS or the PRODUCTION of one or more SELECTED COMPOUNDS into one or more PRODUCTS that is conceived, developed, made and/or reduced to practice by SIEGFRIED during the TERM. NEW KNOW-HOW shall not include or constitute SIEGFRIED KNOW-HOW.

1.16 “PRODUCT” shall mean a SELECTED COMPOUND with particular SPECIFICATIONS.

1.17 “PRODUCTION” shall mean, collectively, the activities pertaining to the pre-commercial production of PRODUCT (which may include, without limitation, the manufacture, storage and supply of quantities of PRODUCT) that are described as Phase II – Kilo Lab or Pilot Production under Scope of Work in the mutually agreed upon sub-appendix to Appendix B applicable to the particular PRODUCT. A separate sequentially numbered sub-appendix (B-1, B-2 and so on) shall be prepared for each PRODUCT for which SIEGFRIED undertakes PRODUCTION at TARGACEPT’s request, which sub-appendix shall include the costs chargeable to TARGACEPT for such services (based on the rates specified herein), be dated and signed by an authorized employee of each party, attached hereto and thereupon become a part hereof.

1.18 “REGULATORY AUTHORITIES” shall mean those agencies or authorities responsible for marketing approval or regulation of any PRODUCT in the United States (including, without limitation, the FDA) or any foreign jurisdiction.

1.19 “SELECTED COMPOUND” shall mean a COMPOUND (or finished dosage form(s) of a COMPOUND) for which TARGACEPT engages SIEGFRIED to perform DEVELOPMENT or PRODUCTION as specified from time to time in a sub-appendix to Appendix A. A separate sequentially numbered sub-appendix (A-1, A-2 and so on) shall be prepared for each SELECTED COMPOUND, which sub-appendix shall be dated and signed by an authorized employee of each party, attached hereto and thereupon become a part hereof.

1.20 “SIEGFRIED IP” shall mean all SIEGFRIED KNOW-HOW and all patents, patent applications, copyrights, trade secrets and other intellectual property rights controlled by SIEGFRIED pertaining to the SIEGFRIED KNOW-HOW.

1.21 “SIEGFRIED KNOW-HOW” shall mean all KNOW-HOW: (a) not in the public domain and in the possession of SIEGFRIED as of the Effective Date; (b) conceived, developed, acquired, made and/or reduced to practice by SIEGFRIED during the TERM that pertains to development or production technologies applicable to the development or preparation of active pharmaceutical compounds and intermediates (but not any SELECTED COMPOUND or PRODUCT) or of formulations of such compounds and intermediates; or (c) conceived, developed, acquired, made and/or reduced to practice by SIEGFRIED during the TERM that pertains to development and production technologies generally applicable to the development or preparation of a variety of active pharmaceutical compounds and intermediates (at least one of which, but not all of which, is a SELECTED COMPOUND or PRODUCT) or of formulations of such compounds and intermediates. SIEGFRIED KNOW-HOW shall not include or constitute NEW KNOW-HOW.

1.22 “SPECIFICATIONS” shall mean the specifications for particular Product set forth in the applicable sub-appendix to Appendix A, as the same may be amended in accordance with the terms of this AGREEMENT.

1.23 “TARGACEPT IP” shall mean all TARGACEPT KNOW-HOW and all patents, patent applications, copyrights, trade secrets and other intellectual property rights controlled by TARGACEPT pertaining to the TARGACEPT KNOW-HOW.

1.24 “TARGACEPT KNOW-HOW” shall mean all KNOW-HOW not in the public domain and in the possession of TARGACEPT as of the Effective Date, or conceived, developed, acquired, made or reduced to practice by TARGACEPT during the TERM, that pertains to one or more SELECTED COMPOUNDS or PRODUCTS or the DEVELOPMENT or PRODUCTION of one or more SELECTED COMPOUNDS or PRODUCTS. TARGACEPT KNOW-HOW shall not include or constitute NEW KNOW-HOW.

1.25 “TERM” shall have the meaning ascribed to it in Section 9.1.

2. DEVELOPMENT and PRODUCTION

2.1 TARGACEPT hereby engages SIEGFRIED to undertake DEVELOPMENT and/or PRODUCTION as set forth in sub-appendices to this AGREEMENT from time to time, upon the terms and conditions set forth in this AGREEMENT, and SIEGFRIED hereby accepts such engagement.

2.2 With respect to each SELECTED COMPOUND for which TARGACEPT engages SIEGFRIED to undertake DEVELOPMENT, SIEGFRIED shall use all commercially reasonable efforts to complete such DEVELOPMENT in accordance with the Scope of Work set forth as Phase I – Laboratory in the applicable sub-appendix to Appendix B so as to meet the timeline and budget for the completion of such DEVELOPMENT set forth in such sub-appendix.

2.3 With respect to each PRODUCT for which TARGACEPT engages SIEGFRIED to undertake PRODUCTION, SIEGFRIED shall use all commercially reasonable efforts to undertake PRODUCTION in accordance with the Scope of Work set forth as Phase II – Pilot Production in the applicable sub-appendix to Appendix B so as to meet the timeline and budget for the completion of PRODUCTION and the delivery of the quantities of PRODUCT set forth in such sub-appendix.

2.4 TARGACEPT shall evaluate the samples of each SELECTED COMPOUND delivered as part of its DEVELOPMENT and shall evaluate the SPECIFICATIONS and MASTER PRODUCTION RECORD prepared by SIEGFRIED for the PRODUCTION of each PRODUCT. In the event that TARGACEPT is not satisfied with the samples of a SELECTED COMPOUND or the SPECIFICATIONS or the MASTER PRODUCTION RECORD for PRODUCTION of a PRODUCT, SIEGFRIED shall continue to consult with TARGACEPT on the process for the PRODUCTION of such PRODUCT. SIEGFRIED shall not initiate PRODUCTION of any PRODUCT unless and until it shall have received written approval from TARGACEPT of the PRODUCT's SPECIFICATIONS (such approved SPECIFICATIONS to be reflected in a duly executed amendment to the sub-appendix to Appendix A applicable to such PRODUCT) and MASTER PRODUCTION RECORD and, once approved by TARGACEPT, shall not change the PRODUCT's SPECIFICATIONS or MASTER PRODUCTION RECORD without TARGACEPT's prior written approval.

2.5 Laboratory studies conducted as part of any DEVELOPMENT may, but need not, be performed in compliance with GMP; provided that all DEVELOPMENT and PRODUCTION associated with the manufacture or storage of any PRODUCT shall be performed in compliance with GMP, SIEGFRIED'S standard operating procedures (SOPs) for the manufacture, storage and delivery of material in compliance with GMP and all applicable laws, regulations, rules and regulatory guidance (including, without limitation, the ACT). Further, each PRODUCT manufactured hereunder shall meet its SPECIFICATIONS, all PRODUCTION of a PRODUCT shall be in accordance with its MASTER PRODUCTION RECORD and SIEGFRIED warrants compliance with the foregoing to TARGACEPT. Without limiting the generality of the foregoing, SIEGFRIED: (i) shall take all steps necessary to ensure that each PRODUCT that it manufactures pursuant to this AGREEMENT is free of cross-contamination from any other manufacturing or similar activities; (ii) shall complete qualified cleaning procedures approved by TARGACEPT after review of SIEGFRIED's applicable SOPs and carry out product changeover according to SIEGFRIED's applicable SOPs prior to manufacturing any PRODUCT for TARGACEPT; (iii) shall not rework any BATCH without TARGACEPT's prior written consent; and (iv) represents and warrants to TARGACEPT that its standard operating procedures for the manufacture, storage and delivery of material in compliance with GMP conform with best industry practices for the manufacture, storage and delivery of such material for use in human clinical trials.

2.6 SIEGFRIED shall perform all DEVELOPMENT and PRODUCTION at its facility located in Zofingen, Switzerland. SIEGFRIED shall commit the personnel, and shall reserve the development and pilot plant capacity, necessary to carry out its obligations pursuant to each sub-appendix to this AGREEMENT. Each project manager or other employee or personnel assigned by SIEGFRIED to the performance of its obligations hereunder shall be appropriately qualified, trained and experienced for the tasks he or she is to perform. SIEGFRIED's project manager and other technical personnel shall make themselves available to meet with TARGACEPT (in person in Zofingen, Switzerland or by telephone) at such times and at such frequency as TARGACEPT shall reasonably request.

2.7 PRODUCT shall be used by TARGACEPT for stability, preclinical, clinical and other pre-commercial purposes.

3. TRANSFER of INFORMATION and MATERIALS

3.1 TARGACEPT shall be responsible for providing SIEGFRIED with such TARGACEPT KNOW-HOW as is reasonably necessary for SIEGFRIED to conduct the DEVELOPMENT of a particular SELECTED COMPOUND or PRODUCTION of a particular PRODUCT called for by any sub-appendix to this AGREEMENT (including, without limitation, any laboratory-scale process or analytical methods).

3.2 SIEGFRIED shall be responsible (subject to the provisions of Section 10.3) for the procurement of all raw materials as are required for SIEGFRIED to conduct the DEVELOPMENT or PRODUCTION called for by any sub-appendix to this AGREEMENT.

3.3 Upon any expiration of the TERM or termination of this AGREEMENT, for whatever reason, SIEGFRIED shall forward to TARGACEPT, upon TARGACEPT's request, all quantities of raw material supplied by TARGACEPT or purchased by SIEGFRIED pursuant to this AGREEMENT, all quantities of each SELECTED COMPOUND or PRODUCT, and all quantities of any other material produced pursuant to this AGREEMENT (including, without limitation, materials constituting works-in-progress) within sixty (60) days. Notwithstanding the foregoing, SIEGFRIED shall be entitled to retain such samples of the foregoing as are required by law or as are required in order for SIEGFRIED to comply with its SOPs.

4. COLLABORATION and REPORTING; REGULATORY SUPPORT

4.1 SIEGFRIED shall perform all DEVELOPMENT and PRODUCTION in collaboration with TARGACEPT and shall keep TARGACEPT regularly informed with respect to the status of all DEVELOPMENT and PRODUCTION. Without limiting the generality of the foregoing, SIEGFRIED shall provide TARGACEPT with monthly written reports summarizing the progress of the work performed or to be performed in accordance with each outstanding sub-appendix to Appendix B.

4.2 At no cost to TARGACEPT, SIEGFRIED shall assign a project manager reasonably acceptable to TARGACEPT to coordinate and monitor all technical aspects of DEVELOPMENT and PRODUCTION of all SELECTED COMPOUNDS.

4.3 Each party shall appoint one representative to be the primary point of contact for the interaction of the parties in connection with this AGREEMENT and all day-to-day communication between the parties under this AGREEMENT shall be addressed to such representatives. Any notice required under this AGREEMENT must be given in writing in accordance with the terms of this Section 4.3. Any report, approval or notice required or permitted to be given under or in connection with this AGREEMENT shall be in writing and sent by (i) certified or registered mail, return receipt requested, postage prepaid, (ii) a nationally-recognized overnight courier service, or (iii) hand delivery to the representative for such party at the address set forth below. A party may change its representative or address by written notice to the other party given in accordance with this Section 4.3. Notice shall be deemed given on the third business day after being sent in the case of delivery by mail, on the first business day after being sent in the case of delivery by overnight courier, and on the date of delivery in the case of delivery by hand or, in each case, upon actual receipt if earlier.

The addresses of the parties and representatives are as follows:

If to TARGACEPT: TARGACEPT, Inc.
200 East First Street, Suite 300
Winston-Salem, NC 27101-4165

Representative: David Moore
E-Mail: david.moore@targacept.com

If to SIEGFRIED: SIEGFRIED Ltd.
Untere Brühlstrasse 4
4800 Zofingen
Switzerland
Representative: Scott M. Powers
E-Mail: scott.powers@siegfried-usa.com

4.4 SIEGFRIED shall, if requested by TARGACEPT: (i) maintain a complete Drug Master File (DMF) containing all information, data and documentation necessary to complete fully the Chemistry, Manufacturing and Controls (CMC) sections of an investigational new drug application (IND) and new drug application (NDA) for submission to the FDA for each SELECTED COMPOUND; (ii) submit each such DMF to the FDA (and those other REGULATORY AUTHORITIES specified by TARGACEPT) in accordance with applicable law and regulations; (iii) provide TARGACEPT with a letter of authorization to enable the FDA and any comparable REGULATORY AUTHORITY in a foreign jurisdiction to access and reference each such DMF; (iv) prepare and provide to TARGACEPT upon request a dossier that includes all validated analytical methods and stability studies for such SELECTED COMPOUND, if applicable, and for the finished dosage form of such PRODUCT, if applicable, sufficient to enable (A) a competent manufacturer of pharmaceutical products to manufacture the SELECTED COMPOUND into PRODUCT or the final dosage form of such PRODUCT, as the case may be, in commercial quantities and (B) TARGACEPT to obtain requisite FDA approval of an NDA and the requisite approval of other REGULATORY AUTHORITIES of the equivalent outside of the United States; (v) provide to TARGACEPT such other documentation and related information as it determines to be necessary, or as TARGACEPT reasonably requests, in connection with the filing of any IND, NDA or other filing or submission to, or correspondence with, the FDA or any comparable foreign REGULATORY AUTHORITY by or on behalf of TARGACEPT; and/or (vi) otherwise cooperate with TARGACEPT in all reasonable respects to assist TARGACEPT in connection with obtaining FDA approval of an IND or NDA (or the approval of the equivalent of any other REGULATORY AUTHORITY); provided that the reasonable costs actually incurred by SIEGFRIED to perform the services requested by TARGACEPT under this Section 4.4, based on actual time spent and the FTE rate set forth in Section 10.2, may be invoiced by SIEGFRIED to TARGACEPT.

5. DOCUMENTATION and RECORD KEEPING; SAMPLES

5.1 SIEGFRIED shall keep complete and accurate accounts, notes, data and records of all work that it performs under this AGREEMENT (including, without limitation, complete and accurate records pertaining to the methods and facilities used for PRODUCTION of PRODUCT). Without limiting the generality of the foregoing, with respect to each BATCH of each PRODUCT, SIEGFRIED shall maintain and submit to TARGACEPT copies of the completed batch record, deviation reports, out-of-specification records, investigation reports, in-process control raw data, analytical data, a certificate of analysis certifying that the BATCH meets the applicable SPECIFICATIONS and the MASTER PRODUCTION RECORD.

5.2 SIEGFRIED shall retain all raw data for three (3) years from the expiration of the TERM or termination of this AGREEMENT for any reason. After this period, SIEGFRIED shall, upon the timely request of TARGACEPT within sixty (60) days after notification from SIEGFRIED, forward such data to TARGACEPT. Otherwise, SIEGFRIED may destroy such raw data.

5.3 SIEGFRIED shall retain samples of PRODUCT for each BATCH for a period of four (4) years after TARGACEPT's acceptance of such BATCH, each such sample size shall be twice the size necessary to conduct quality control testing. In addition, SIEGFRIED shall retain samples of isolated intermediates, if any, for each BATCH in accordance with SIEGFRIED's SOPs. Upon TARGACEPT's written request, SIEGFRIED shall provide TARGACEPT with up to one-half the original amount of any retained sample of PRODUCT or isolated intermediate at no cost to TARGACEPT.

6. QUALITY ASSURANCE AUDITS and INSPECTIONS

6.1 SIEGFRIED's quality assurance group shall closely monitor and report on the DEVELOPMENT of each SELECTED COMPOUND and the PRODUCTION of each PRODUCT, as applicable, in order to verify compliance with GMP and the ACT.

6.2 TARGACEPT shall have the right to request a quality assurance audit of the DEVELOPMENT of any SELECTED COMPOUND or the PRODUCTION of any PRODUCT in order to verify compliance of DEVELOPMENT and PRODUCTION with the terms of this AGREEMENT. All visits shall be during normal business hours, shall not, either individually or when taken together with all other such visits, unreasonably interrupt the operation of SIEGFRIED, and TARGACEPT shall be responsible for all costs that it incurs in connection with any such visit. Further, all visiting employees and consultants of TARGACEPT shall have executed an appropriate non-disclosure agreement or otherwise be under an obligation of confidentiality consistent with Article 8 and shall comply at all times with all security and other personnel and visitor procedures of SIEGFRIED.

6.3 Unless required by law, SIEGFRIED shall have no contact or communication with any REGULATORY AUTHORITY regarding any DEVELOPMENT or PRODUCTION without the prior written consent of TARGACEPT, and TARGACEPT shall be solely responsible for all such contacts and communications. In the event that SIEGFRIED receives any contact or communication from any REGULATORY AUTHORITY pertaining to any DEVELOPMENT or PRODUCTION, SIEGFRIED shall notify TARGACEPT immediately and shall provide TARGACEPT with copies of any tangible manifestations of any such contact or communication within one (1) business day thereafter. TARGACEPT shall be entitled to participate with

SIEGFRIED in the preparation and submission of a response to any such contact or communication. SIEGFRIED shall allow inspections by REGULATORY AUTHORITIES of its facilities or resources involved or to be involved in any DEVELOPMENT and PRODUCTION. In such event, SIEGFRIED shall inform TARGACEPT prior to such inspection if at all possible or, if not possible, immediately following such inspection. TARGACEPT shall be entitled to (i) be present during any such inspection for which SIEGFRIED receives prior notice that (A) is limited to facilities or resources devoted solely to SELECTED COMPOUNDS, DEVELOPMENT or PRODUCTION or (B) could not reasonably be expected to result in TARGACEPT having access to confidential or proprietary information of any third party and (ii) participate with SIEGFRIED, whether or not SIEGFRIED receives prior notice, in the preparation and submission of a response to any contact or communication received from a REGULATORY AUTHORITY following such inspection.

7. RIGHTS, INVENTIONS and PATENTS

7.1 All TARGACEPT IP shall be and remain the exclusive property of TARGACEPT. All SIEGFRIED IP shall be and remain the exclusive property of SIEGFRIED. All NEW IP shall be “works made for hire” and shall be the exclusive property of TARGACEPT. Further, all records of work performed by SIEGFRIED under this AGREEMENT and all reports delivered or required to be delivered by SIEGFRIED to TARGACEPT under this AGREEMENT shall be “works made for hire” and shall be the exclusive property of TARGACEPT. Notwithstanding the foregoing, solely to the extent necessary to comply with applicable laws and regulations, SIEGFRIED shall have the right to keep one (1) copy, or if so required one (1) original, of such records and reports, such records and reports not be used for any commercial purposes whatsoever.

7.2 In the event that TARGACEPT, or its designee, seeks patent protection for any NEW KNOW-HOW, TARGACEPT, or its designee, shall bear the costs, including, but not limited to, attorneys fees, associated with preparing, filing and prosecuting such patent applications and for maintaining such patent protection as may be granted. SIEGFRIED hereby: (i) agrees to promptly disclose, and deliver all information related to, all NEW KNOW-HOW to TARGACEPT; (ii) represents and warrants to TARGACEPT that each of its employees or other personnel that participates in any aspect of DEVELOPMENT or PRODUCTION has taken all necessary steps to irrevocably assign to SIEGFRIED any and all rights that he or she may have in such NEW KNOW HOW or any related NEW IP; (iii) assigns to TARGACEPT any rights it may have or acquire in such NEW KNOW HOW and any related NEW IP; and (iv) agrees to execute such documents and to provide TARGACEPT with such other reasonable assistance at TARGACEPT’s reasonable expense as TARGACEPT may request to assist it in its acquisition and enforcement of NEW IP in any or all countries.

7.3 TARGACEPT hereby grants to SIEGFRIED and its AFFILIATES a non-exclusive, non-sublicensable, royalty-free license under the TARGACEPT IP and NEW IP solely to conduct during the TERM DEVELOPMENT and PRODUCTION requested by TARGACEPT hereunder.

7.4 SIEGFRIED hereby grants to TARGACEPT a non-exclusive, worldwide, perpetual irrevocable, sublicensable, royalty-free license under SIEGFRIED IP conceived, developed, acquired made and/or reduced to practice by SIEGFRIED, in whole or in part, in the performance of DEVELOPMENT or PRODUCTION hereunder to develop, make, have made, use, sell, have sold, offer for sale, import and have imported compounds (and intermediates and formulations of compounds or intermediates) and otherwise to exploit such SIEGFRIED IP in

connection therewith. SIEGFRIED hereby agrees to promptly disclose, and deliver all information related to, such SIEGFRIED IP to TARGACEPT.

7.5 The license granted to TARGACEPT under Section 7.4 is subject to TARGACEPT's payment of all amounts due to SIEGFRIED and not subject to a good faith dispute.

8. CONFIDENTIALITY

8.1 Each party agrees (i) to retain in strict confidence and not to disclose, divulge or otherwise communicate to any other person or entity any CONFIDENTIAL INFORMATION of the other party, whether disclosed prior to or after the Effective Date hereof, and (ii) not to use any such CONFIDENTIAL INFORMATION for any purpose, except pursuant to, and in order to carry out, the terms and objectives of this AGREEMENT, provided that each party (A) may disclose CONFIDENTIAL INFORMATION of the other party to its or any of its AFFILIATE'S officers, directors, employees, agents, consultants, permitted subcontractors or other representatives (the "Representatives"), who, in each case, need to know such CONFIDENTIAL INFORMATION for purposes of its implementation of, and performance of its obligations under, this AGREEMENT, and (B) shall be liable for any breach of this Article 8 caused by any of its Representatives.

8.2 Each party agrees to use at least the same standard of care to safeguard the other party's CONFIDENTIAL INFORMATION as it uses to protect its own proprietary or confidential information of comparable sensitivity (but not less than reasonable care).

8.3 Each party warrants that each of its Representatives to whom any CONFIDENTIAL INFORMATION is revealed shall previously have been informed of the confidential nature of the CONFIDENTIAL INFORMATION and shall be legally obligated to maintain its confidentiality under terms at least as stringent as those contained herein.

8.4 The provisions of Sections 8.1-8.3 shall not apply to any CONFIDENTIAL INFORMATION which:

a) was known by the receiving party prior to its disclosure to the receiving party by the other party, as evidenced by the prior written records of the receiving party (provided that this clause a) shall not apply to NEW IP); or

b) either before or after the date of disclosure to the receiving party by the other party is lawfully disclosed to the receiving party by an independent, unaffiliated third party rightfully in possession of the CONFIDENTIAL INFORMATION; or

c) either before or after the date of disclosure to the receiving party by the other party becomes published or generally known to the public through no fault or omission on the part of the receiving party; or

d) is developed independently by the receiving party without use of CONFIDENTIAL INFORMATION of the other party, as evidenced by the written records of the receiving party; or

e) is required to be disclosed by the receiving party to comply with applicable laws, to defend or prosecute litigation, or to comply with governmental laws or regulations, provided that the receiving party (i) provides prior written notice of such disclosure to the other party, (ii) limits such disclosure to only that necessary to satisfy its legal obligations and (iii) to the extent practicable under the circumstances, provides the other party with a reasonable opportunity to obtain an appropriate protective order or otherwise to contest such disclosure.

8.5 Notwithstanding anything herein to the contrary, the parties agree that neither disclosure or use by TARGACEPT nor use by SIEGFRIED of CONFIDENTIAL INFORMATION of the other party as reasonably necessary in the exercise of the respective licenses granted in Sections 7.3 and 7.4 shall be a violation of any term or condition contained in this Article 8.

8.6 Except as otherwise set forth in this AGREEMENT, nothing herein shall be construed as giving either party any right, title, interest in or ownership of the CONFIDENTIAL INFORMATION of the other party. For the purposes of this AGREEMENT, any specific item disclosed as part of CONFIDENTIAL INFORMATION shall not be deemed to be in the public domain or in the prior possession of the receiving party merely because it is embraced by more general information in the public domain or by more general information in the prior possession of the receiving party.

8.7 The confidentiality obligations of the parties contained in this Article 8 shall remain binding on both parties during the TERM and for a period of seven (7) years after the expiration or termination of this AGREEMENT, regardless of the cause of such expiration or termination. The parties acknowledge that any breach of this Article 8 would cause irreparable harm to the other party and that the non-breaching party shall be entitled to specific performance or injunctive relief to prevent such breach or threatened breach, in addition to whatever remedies such party may otherwise be entitled to at law or in equity.

9. TERM and TERMINATION; SURVIVAL

9.1 The initial term of the AGREEMENT shall commence on the EFFECTIVE DATE and continue for a period of three (3) years (the “Initial Term”), renewable in two (2) year increments thereafter (each a “Renewal Term” and, together with the Initial Term, the “TERM”). Unless either party gives the other notice of its intention not to renew this AGREEMENT by the date twelve (12) months prior to the expiration of the Initial Term or the then-current Renewal Term, as the case may be, this AGREEMENT shall be deemed to be automatically extended for a Renewal Term.

9.2 Either party shall be entitled to terminate the AGREEMENT at any time after twenty-four (24) months upon not less than twelve (12) months written notice; provided that (i) either party shall be entitled to terminate the AGREEMENT immediately in the event of a material breach by the other party that is not cured within thirty (30) days after written notice of such breach and (ii) TARGACEPT shall be entitled to terminate the AGREEMENT upon written notice in the event SIEGFRIED (A) increases its rates applicable in any Renewal Term (or in any portion of any Renewal Term) **[********]** and (B) did not notify TARGACEPT of such increased rates at least **[********]** prior to the date by which TARGACEPT was required pursuant to Section 9.1 to give notice of non-renewal with respect to the Renewal Term in which such increased rates are to take effect. The effective date of any such termination shall be the last day of the TERM.

9.3 Upon termination of the AGREEMENT: (i) all work in process at the time notice of termination is given shall be terminated as soon as practicable thereafter; (ii) SIEGFRIED’s deliverables obligations pursuant to this AGREEMENT (including any and all outstanding sub-appendices to this AGREEMENT) shall survive with respect to all DEVELOPMENT and PRODUCTION completed as of the effective date of such termination; (iii) SIEGFRIED shall

promptly deliver to TARGACEPT any and all PRODUCT in its possession; and (iv) SIEGFRIED may invoice TARGACEPT for its costs, determined as provided herein, (i) for all DEVELOPMENT and PRODUCTION actually performed as of such termination date and (ii) incurred directly to terminate performance hereunder (including, without limitation, any materials necessary to terminate performance, like a reagent) unless TARGACEPT terminates this AGREEMENT for material breach by SIEGFRIED.

9.4 The provisions of Sections 2.5, 3.3, 4.3, 6.3, 7.1 7.2, 7.4, 7.5, 9.3, 9.4, 10.6 (second sentence only), 12.2, 13.2 (second sentence only), 13.3, 13.4, 13.5, 13.6, 13.7, 13.8, 13.9 and Articles 1 (to the extent of definitions specified therein are used in a surviving provision), 5, 8, 14, 15, 16 shall survive any expiration of the TERM or termination of this AGREEMENT for any reason.

10. PURCHASE COMMITMENT, PAYMENT and DELIVERIES

10.1 TARGACEPT shall (i) engage SIEGFRIED to perform a minimum of **[********]** in DEVELOPMENT during 2004 and (ii) not during the TERM engage any party other than SIEGFRIED to develop a synthetic chemical process or finished dosage development studies and formulation for a SELECTED COMPOUND or to effect pre-commercial production of PRODUCT unless an EXCLUSION CONDITION applies. If practicable, TARGACEPT shall use commercially reasonable efforts to communicate its DEVELOPMENT commitments during the TERM to SIEGFRIED on or before December of the year preceding its anticipated expenditures. TARGACEPT agrees to consider in good faith engaging SIEGFRIED for development of COMPOUNDS in the TARGACEPT development pipeline.

10.2 For all DEVELOPMENT requested by TARGACEPT, SIEGFRIED shall charge TARGACEPT an industry discounted Full Time Equivalent (FTE) rate of **[********]** for laboratory work, including all chemicals and services such as analytical method development and dossier preparation.

10.3 For all PRODUCTION requested by TARGACEPT, SIEGFRIED shall charge: (a) a discounted kilo lab rate of **[********]**; (b) a discounted pilot plant rate of **[********]**; and (c) **[********]**.

10.4 If, during the course of DEVELOPMENT, it becomes reasonably apparent to SIEGFRIED that (a) circumstances exist which could not have been foreseen by the parties and (b) such circumstances render the completion of the DEVELOPMENT and PRODUCTION materially more costly than had been foreseen by the parties, SIEGFRIED shall notify TARGACEPT in writing and the parties shall negotiate in good faith in furtherance of mutually acceptable amendment(s) to the appropriate portion(s) of the applicable sub-appendix to Appendix B.

10.5 SIEGFRIED shall invoice TARGACEPT for the DEVELOPMENT and PRODUCTION of each SELECTED COMPOUND at the completion of mutually agreed upon project milestones specified in, or as otherwise specified in, the applicable sub-appendix to Appendix B. Each such invoice will be payable by TARGACEPT thirty (30) days after its receipt.

10.6 Delivery of SELECTED COMPOUND and PRODUCT shall be “FCA ZOFINGEN” as

defined in the current INCOTERMS, except that SIEGFRIED shall be responsible for loading SELECTED COMPOUND and PRODUCT onto the carrier. SIEGFRIED shall monitor shipments, shall notify TARGACEPT of shipments and shipment delays, and shall work diligently with TARGACEPT to resolve any shipment problems of all SELECTED COMPOUNDS and PRODUCTS.

10.7 If the AGREEMENT extends beyond the Initial Term, the rates provided in Sections 10.2 and 10.3 shall be subject to increase by SIEGFRIED at any time and from time to time on thirty (30) days prior written notice to TARGACEPT.

11. COMMERICAL SUPPLY OF PRODUCT

11.1 With respect to any PRODUCT for which TARGACEPT has filed or determines it is likely to file an NDA or its equivalent outside the United States, SIEGFRIED and TARGACEPT shall negotiate in good faith in furtherance of a commercially reasonable Supply Agreement with terms customary for such agreements and that would provide for: (i) SIEGFRIED or one of its affiliates to provide to TARGACEPT such PRODUCT, produced under cGMP conditions in SIEGFRIED's pilot plant or elsewhere as mutually agreed upon (including, without limitation, Siegfried (USA)'s location in Pennsville New Jersey), and in such quantities as TARGACEPT may request from time to time (the PRODUCT and quantity subject to each such request, a "Commercial Supply"), each such deliverable to be in accordance with timelines, specifications and other requirements communicated by TARGACEPT prior to SIEGFRIED commencing production of a particular Commercial Supply; and (ii) TARGACEPT to commit, for a multi-year period, to engage SIEGFRIED to manufacture at least **[********]** of the aggregate amount of such PRODUCT contracted for manufacture by or on behalf of TARGACEPT in each year in such period; provided that TARGACEPT's obligations under this Section 11.1 shall: (i) not apply if an EXCLUSION CONDITION applies; and (ii) be subject to Section 11.2. Should an EXCLUSION CONDITION of the type specified in clause (i) of the definition of EXCLUSION CONDITION (but not any other clause of the definition) apply with respect to a particular PRODUCT, TARGACEPT shall recommend SIEGFRIED as commercial manufacturer to the party with responsibility for or control of commercial manufacture of such PRODUCT.

11.2 If TARGACEPT obtains or receives from a reputable source an offer to supply PRODUCT in like quantity and quality and under similar terms and conditions as required by TARGACEPT from SIEGFRIED at a price **[********]** than the then proposed Supply Agreement price, then TARGACEPT shall so notify SIEGFRIED in writing and provide documentation of the price it has received from the reputable source; provided, however, that TARGACEPT shall be permitted to delete the identity of the source in any documentation provided. Within fifteen (15) days of the date of TARGACEPT'S notice, SIEGFRIED shall notify TARGACEPT in writing of its decision as to match the price offered from the reputable source. If TARGACEPT does not receive such notice from SIEGFRIED prior to the expiration of the fifteen (15) day response period, then TARGACEPT shall be free to discontinue negotiations on such the Supply Agreement for such PRODUCT and pursue other options for supply thereof at its own discretion.

12. WARRANTIES

12.1 Each party represents and warrants that it has the power and authority to enter into the AGREEMENT and to perform its obligations hereunder and that, as of the Effective Date, it is not (and will not hereafter become) a party to any agreement, contract or arrangement with any third party, or under any obligation or restriction (including, without limitation, pursuant to its charter documents or bylaws), which in any way limits or conflicts with its ability to fulfill any of its obligations under this AGREEMENT.

12.2 SIEGFRIED makes no representation or warranty that (i) the processes used in DEVELOPMENT OR PRODUCTION of any SELECTED COMPOUND or PRODUCT or (ii) the production, use or importation of SELECTED COMPOUND or PRODUCT will not infringe any patent or other proprietary right belonging to a third party. Notwithstanding the foregoing, SIEGFRIED represents and warrants to TARGACEPT that, as of the Effective Date, (A) it has not received any notice from any third party that the practice of the SIEGFRIED IP infringes any patent or other proprietary rights of any third party and (B) SIEGFRIED has no knowledge of any third party patent or proprietary rights that might be infringed by the practice of the SIEGFRIED IP. Further, SIEGFRIED covenants with TARGACEPT that it will not knowingly use any infringing or misappropriated SIEGFRIED IP in any DEVELOPMENT or PRODUCTION.

13. PRODUCT QUALITY, INDEMNIFICATION, LIMITATION OF LIABILITY and INSURANCE

13.1 In the case of a material error by SIEGFRIED (or other situation over which SIEGFRIED has control) which results in an inability to meet the parameters, budgets or timelines for DEVELOPMENT or PRODUCTION set forth in a particular sub-appendix to Appendix B, SIEGFRIED shall inform TARGACEPT immediately and shall exercise diligent efforts to remedy the situation so that such parameters, budgets and timelines are achieved as soon as possible thereafter.

13.2 In the event that TARGACEPT believes it is justified in rejecting PRODUCT because it does not meet the requirements of Section 2.5, TARGACEPT shall inform SIEGFRIED accordingly with a written notice delivered within forty-five (45) days from the date of its receipt of the PRODUCT, and SIEGFRIED shall use its best efforts to replace the rejected PRODUCT with compliant PRODUCT as soon as possible thereafter. Without prejudice to the foregoing obligation, if SIEGFRIED does not agree with the basis for TARGACEPT's rejection, the parties shall repeat the sampling and analysis of the rejected PRODUCT. Should TARGACEPT still believe it is justified in rejecting the PRODUCT following such repeated sampling and analysis, TARGACEPT shall have the right to engage an independent third party to perform the sampling and analysis of the rejected PRODUCT. Should the independent third party determine that the PRODUCT does not meet the requirements of Section 2.5, SIEGFRIED shall be responsible for the costs of replacement of the rejected PRODUCT and the sampling and analysis conducted by the independent third party, which replacement and payment of sampling and analysis costs shall, in addition to TARGACEPT's right of termination under Section 9.2, be TARGACEPT's exclusive remedies hereunder in connection therewith.

13.3 Subject to Sections 13.6, 13.7 and 13.8, TARGACEPT shall, at all times during the TERM and for three (3) years thereafter, indemnify, defend and hold harmless SIEGFRIED, and

its directors, officers, employees and AFFILIATES (the "Other SIEGFRIED Indemnified Parties"), from and against any and all third party claims, proceedings, demands and liabilities of any kind whatsoever (all of the foregoing, collectively, "CLAIMS"), including reasonable attorneys' fees and other legal expenses, arising out of the death of or injury to any person or out of any damage to property resulting from the use or consumption of any SELECTED COMPOUND for which SIEGFRIED provided DEVELOPMENT or any PRODUCT for which SIEGFRIED provided PRODUCTION pursuant to this AGREEMENT, unless such CLAIM results from (i) the failure of the PRODUCT (if applicable) to meet the requirements of Section 2.5 or otherwise from the breach of this AGREEMENT by SIEGFRIED or (ii) the negligence or misconduct of SIEGFRIED or any Other SIEGFRIED Indemnified Party.

13.4 Subject to Sections 13.6, 13.7 and 13.8, SIEGFRIED shall, at all times during the TERM and for three (3) years thereafter, indemnify, defend and hold harmless TARGACEPT, and its directors, officers, employees and AFFILIATES, from and against any and all CLAIMS, including reasonable attorneys' fees and legal expenses, arising out of the death of or injury to any person or out of any damage to property resulting from the production, use or consumption of any SELECTED COMPOUND for which SIEGFRIED provided DEVELOPMENT or any PRODUCT for which SIEGFRIED provided PRODUCTION pursuant to this AGREEMENT if such CLAIM results from (i) the failure of the PRODUCT (if applicable) to meet the requirements of Section 2.5 or otherwise from a breach of this AGREEMENT by SIEGFRIED or (ii) the negligence or misconduct of SIEGFRIED or any Other SIEGFRIED Indemnified Party.

13.5 Subject to Sections 13.6, 13.7 and 13.8, TARGACEPT shall, at all times during the TERM and for three (3) years thereafter, indemnify, defend and hold harmless SIEGFRIED and the Other SIEGFRIED Indemnified Parties, from and against any and all CLAIMS, including reasonable attorneys' fees and legal expenses, arising out of any alleged infringement of any patent or other intellectual property right held by a third party in connection with the DEVELOPMENT, use or importation of any SELECTED COMPOUND for which SIEGFRIED provided DEVELOPMENT or the PRODUCTION, use or importation of any PRODUCT for which SIEGFRIED provided PRODUCTION pursuant to this AGREEMENT (but in each case specifically excluding any CLAIM alleging infringement as a result of the exploitation of SIEGFRIED IP or NEW IP).

13.6 Any party seeking to enforce its rights under this Article 13 (an "Indemnified Party") shall notify the party against which enforcement is sought (the "Indemnity Obligor") in writing of the applicable CLAIM promptly (but in any event within ten (10) days after receipt of written notice thereof), specifying in reasonable detail the nature of the CLAIM, and shall provide to the Indemnity Obligor as promptly as practicable thereafter all information and documentation reasonably requested by the Indemnity Obligor to verify the CLAIM asserted. The failure of an Indemnified Party to notify the Indemnity Obligor on a timely basis will not relieve the Indemnity Obligor of any liability that it may have to the Indemnified Party, except to the extent that the Indemnity Obligor's defense of such CLAIM is materially prejudiced by the Indemnified Party's failure to give such notice on a timely basis.

13.7 The Indemnity Obligor may, by giving written notice to the Indemnified Party within fifteen (15) days following its receipt of the notice of the CLAIM, elect to assume the defense or the prosecution thereof, including the engagement of counsel and other advisors at its cost and expense. The Indemnified Party shall have the right to engage counsel separate from counsel engaged by the Indemnity Obligor in any such action and to participate therein, but the fees and

expenses of such counsel shall be at the Indemnified Party's own expense. Whether or not the Indemnity Obligor chooses so to defend or prosecute such claim, all of the parties hereto shall cooperate in the defense or prosecution thereof and shall furnish such records, information and testimony and shall attend such conferences, discovery proceedings and trials as may be reasonably requested in connection therewith. The Indemnity Obligor shall not be liable for settlement of any such Claim effected without its prior written consent, which shall not be unreasonably withheld.

13.8 NO PARTY SHALL BE LIABLE FOR ANY INCIDENTAL, INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES, EVEN IF ADVISED OF THE POSSIBILITY OF SUCH DAMAGES, WHETHER UNDER THEORY OF CONTRACT (INCLUDING, WITHOUT LIMITATION, UNDER THIS ARTICLE 13), TORT (INCLUDING NEGLIGENCE), STRICT LIABILITY OR OTHERWISE.

13.9 At all times during the TERM and for three (3) years thereafter, each of TARGACEPT and SIEGFRIED shall maintain at its own expense a policy or policies of insurance of a type and amount sufficient to satisfy its obligations pursuant to this Article 13. Without limiting the generality of the foregoing, SIEGFRIED represents and warrants to, and covenants with, TARGACEPT that, at all times during the TERM and for three (3) years thereafter, it shall maintain comprehensive general liability insurance (or errors and omissions insurance), in each case with limits of not less than one million dollars ($1,000,000) per occurrence and three million dollars ($3,000,000) in the aggregate, and workers' compensation insurance with such limits as are required by applicable law. Either party shall, upon request, provide the other party with reasonable evidence of such insurance.

14. CHOICE OF LAW

SIEGFRIED subsidiaries and affiliates conduct a portion of their businesses, including particularly production, in the United Sates, principally in New Jersey. Since TARGACEPT is also located in the United States (in North Carolina), the parties believe that it is most convenient and efficient for this AGREEMENT to be governed by United States federal and Delaware state law. Accordingly, this AGREEMENT shall be governed and interpreted in accordance with the laws of the State of Delaware without reference to principles of conflicts of laws, and the parties agree the United Nations Convention On Contracts For The International Sale Of Goods shall not apply to this AGREEMENT.

15. DISPUTE RESOLUTION

Any dispute arising out of or relating to this contract, including the breach, termination or validity thereof, shall first be submitted to mediation and, if not settled during mediation, shall be finally resolved by arbitration in accordance with the CPR Institute for Dispute Resolution Rules for Non-Administered Arbitration by a sole arbitrator experienced in pharmaceutical manufacturing; provided that, notwithstanding the foregoing, a party shall have the right to seek a judicial temporary restraining order, preliminary injunction or similar short-term equitable relief in respect of any alleged breach or threatened breach of Article 8, which relief may be made permanent by the arbitrator(s). The arbitration shall be governed by the Federal Arbitration Act, 9 U.S.C. §§ 1-16, shall be conducted in English and judgment upon the award rendered by the

arbitrator, which shall be binding, shall be in U.S. dollars may be entered by any court having jurisdiction thereof. The place of the arbitration shall be in Washington D.C. The arbitrators shall have no power to add to, subtract from or modify any of the terms or conditions of this AGREEMENT, shall base any award on applicable laws and judicial precedent and include in such award a statement of the reasons upon which the award is based. The parties consent to service of process by registered or certified mail at their respective addresses specified herein or to such other addresses of which notice hereunder shall be given. All applicable statutes of limitation and defenses based upon the passage of time shall be tolled while the procedures specified in this Section 15 are pending, and the parties shall take such action, if any, required to effectuate such tolling. Each party is required to continue to perform its obligations under this AGREEMENT pending final resolution of any dispute arising out of or relating to this AGREEMENT.

16. MISCELLANEOUS

16.1 The working language for DEVELOPMENT and PRODUCTION under this AGREEMENT, the execution of this AGREEMENT, and the interpretation of the terms of this AGREEMENT shall be the English language.

16.2 Neither this AGREEMENT, nor any of the rights or obligations hereunder, may be assigned by either party without the prior written consent of the other party, except that either party may assign this AGREEMENT without such consent, to a third party who acquires all or substantially all of the assets of the assigning party or otherwise acquires all or substantially all of the business of the assigning party to which this AGREEMENT relates.

16.3 Either party shall be excused from performing its obligation under this AGREEMENT if its performance is delayed or prevented by any cause beyond such party's control, including but not limited to, act of God, fire, explosion, weather, disease, war, insurrection, civil strife, riots, government action, or power failure. Performance shall be excused only to the extent of and during the reasonable continuance of such disability. Any deadline or time for performance specified in an appendix to this AGREEMENT that falls due during or subsequent to the occurrence of any of the causes referred to herein shall be automatically extended for a period of time equal to the period of such cause. SIEGFRIED shall immediately notify TARGACEPT if, by reason of any of the causes referred to herein, SIEGFRIED is unable to meet any deadline or time for performance specified in a sub-appendix to this AGREEMENT. The foregoing shall not be construed to alter each party's rights under the first sentence of Section 9.2.

16.4 Nothing herein or in any sub-appendix to this AGREEMENT, shall be deemed or construed to constitute or create between the parties hereto a partnership, joint venture, agency, or other relationship other than as expressly set forth herein. Neither party shall have authority to speak for, represent or obligate the other party in any way without prior written authority from the other party.

16.5 This AGREEMENT and the appendices (and sub-appendices) to this AGREEMENT, which appendices (and sub-appendices) are deemed to be a part of this AGREEMENT for all purposes, contain the complete agreement of the parties with respect to the subject matter hereof and supersede all prior understandings and agreements relating thereto. No waiver, alteration, amendment or modification of any of the provisions hereof shall be binding unless

made in writing and signed by the parties; provided that, notwithstanding the foregoing, each of TARGACEPT AND SIEGFRIED acknowledges and agrees that TARGACEPT may, by written notice to SIEGFRIED, unilaterally modify and amend at any time any sub-appendix hereto applicable to a particular SELECTED COMPOUND or PRODUCT to remove application of this AGREEMENT to such SELECTED COMPOUND or PRODUCT, or to provide for termination of any or all DEVELOPMENT or PRODUCTION activities with respect to such SELECTED COMPOUND, if (i) an EXCLUSION CONDITION applies or (ii) TARGACEPT discontinues or suspends development of such SELECTED COMPOUND or PRODUCT.

16.6 In the event that any term of this AGREEMENT shall violate any applicable statute, ordinance or rule of law in any jurisdiction in which it is used, or otherwise be unenforceable, such provision shall be ineffective to the extent of such violation without invalidating any other provision hereof.

16.7 If during the term of this AGREEMENT, performance of the AGREEMENT should lead to unreasonable hardship for the one or the other Party, taking the interests of both Parties into account, both Parties shall undertake reasonable endeavors to agree amicably to amend this AGREEMENT in the light of the change in circumstances.

16.8 The waiver by the parties of any breach, covenant or condition herein contained shall not be deemed to be a waiver of any subsequent breach of the same or any other term, covenant or condition herein.

16.9 This AGREEMENT may be executed in two counterparts (which may be exchanged by facsimile), each of which shall be deemed an original and both of which together shall constitute but one and the same AGREEMENT.

[The remainder of this page is left blank intentionally.]

In **WITNESS WHEREOF**, the parties have had this AGREEMENT signed by their duly authorized representatives, all as of the effective date.

For and on behalf of

SIEGFRIED LTD.

NAME: /s/ B. Vuenburg

BY: B. Vuenburg

TITLE: SVP Marketing & Development

DATE: 4 Feb. 2004

Witnesseth:

NAME: /s/ Dennis P. Bauer

BY: Dennis P. Bauer

TITLE: VP – Sales & Marketing (USA)

DATE: February 4, 2004

For and on behalf of

TARGACEPT, INC.

NAME: /s/ J. Donald deBethizy

BY: J. Donald deBethizy

TITLE: President and CEO

DATE: 1/29/04

Witnesseth:

NAME: /s/ Peter Zorn

BY: Peter A. Zorn

TITLE: Corporate Counsel

DATE: 1/29/04

APPENDIX A

SELECTED COMPOUNDS

APPENDIX A-1

[insert SELECTED COMPOUND here]

[insert specification detail here]

For and on behalf of

TARGACEPT, INC.

NAME: _____

BY: _____

TITLE: _____

DATE: _____

SIEGFRIED LTD.

NAME: _____

BY: _____

TITLE: _____

DATE: _____

APPENDIX B

SCOPE of WORK for SELECTED COMPOUNDS

APPENDIX B-1

Scope of work - Phase I – Laboratory

[insert detail here]

Scope of work - Phase II – Kilo Lab or Pilot Production

[insert detail here]

For and on behalf of

TARGACEPT, INC.	**SIEGFRIED LTD.**
NAME: _____	NAME: _____
BY: _____	BY: _____
TITLE: _____	TITLE: _____
DATE: _____	DATE: _____

EXHIBIT 10.23

[********] 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.

DEVELOPMENT AGREEMENT

THIS DEVELOPMENT AGREEMENT (this "**Agreement**") is entered into as of December 15, 2004 (the "**Effective Date**") by and between Targacept, Inc., a Delaware corporation with offices at 200 East First Street, Suite 300, Winston-Salem, North Carolina 27101-4165 ("**Targacept**"), and THE STANLEY MEDICAL RESEARCH INSTITUTE, a nonprofit organization with offices at 5430 Grosvenor Lane, Suite 200, Bethesda, Maryland 20814 ("**SMRI**").

RECITALS

WHEREAS, Targacept is a leader in the discovery and development of small molecule drugs that selectively target neuronal nicotinic acetylcholine receptors to treat diseases and disorders of the central nervous system, including schizophrenia;

WHEREAS, SMRI is the world's leading nonprofit organization that supports research on the causes and treatment of schizophrenia and bipolar disorder, through its own laboratory and support of researchers worldwide; and

WHEREAS, SMRI desires to support the further development and commercialization of the Compound (as defined below) in order to accelerate the introduction of a novel therapy for the benefit of schizophrenia patients worldwide.

NOW, THEREFORE, in consideration of the foregoing and the covenants and premises contained in this Agreement, the parties agree as follows:

1. **DEFINITIONS**. As used herein, the following terms shall have the following meanings:

1.1 "**Affiliate**" shall mean, with respect to any Person, any other Person controlling, controlled by or under common control with such Person, either by (i) possession, directly or indirectly through one or more subsidiaries, of the power to direct the management or policies of such Person, whether through the ownership of voting securities, by contract or otherwise, or (ii) the ownership, directly or indirectly through one or more subsidiaries, of more than 50% of the voting securities or other ownership interests of such Person.

1.2 "**Applicable Rate**" shall mean ******** percent (********%) per annum, compounded annually as of each December 31 until paid.

1.3 "**Compound**" shall mean the compound known by Targacept as TC-1827 and its salts.

1.4 "**Confidential Information**" shall mean all information disclosed by one party to the other (or to the DAC) hereunder (including, without limitation, manufacturing, marketing, financial, personnel, scientific and other business information and plans and the material terms of this Agreement) in whatever form, whether oral, written, graphic, electronic or otherwise. For the avoidance of doubt, all Targacept Proprietary Information disclosed to SMRI or to the DAC and all information disclosed by Targacept in furtherance of, or pursuant to, SMRI's quarterly trial reporting system shall constitute Confidential Information of Targacept.

1.5 “**Development Advisory Committee**” or “**DAC**” shall mean the committee formed pursuant to Section 3.1.

1.6 “**Development Plan**” shall mean a plan (including a corresponding budget) for conducting the Development Program that is prepared by Targacept on an annual basis during the Development Term, as may be amended from time to time by Targacept pursuant to Section 2.2.

1.7 “**Development Program**” shall mean a Phase I clinical development program and a single Phase II clinical trial of the Compound and all non-clinical research activities with respect to the Compound necessary to initiate, conduct and complete such clinical development during the Development Term.

1.8 “**Development Program Inventions**” shall mean, collectively, (i) all inventions, improvements and discoveries, whether or not patentable, made, conceived or first reduced to practice in the conduct of work conducted in the Development Program that is actually funded by SMRI hereunder, if any, whether solely by employees of SMRI, solely by employees or contractors of Targacept or jointly by employees of SMRI and employees or contractors of Targacept and (ii) all patents, patent applications and copyrights that claim or cover such inventions, improvements or discoveries. For the avoidance of doubt, Development Program Results shall not constitute Development Program Inventions.

1.9 “**Development Program Results**” shall mean all data and results generated from work conducted in the Development Program that is actually funded by SMRI hereunder.

1.10 “**Development Term**” shall mean the earlier of (i) completion of the Phase II clinical trial of the Compound included in the Development Program or (ii) the fifth anniversary of the Effective Date, as may be extended for additional, consecutive one (1) year periods by written agreement of the parties.

1.11 “**Disclosing Party**” shall mean a party disclosing its Confidential Information to a Receiving Party.

1.12 “**FDA**” shall mean the United States Food and Drug Administration.

1.13 “**First Commercial Sale**” shall mean the first sale for use or consumption of the Targacept Product after Regulatory Approval has been obtained in any jurisdiction, provided that sale to any of Targacept’s Affiliates or Licensees shall not constitute the First Commercial Sale unless the Affiliate or Licensee is the end user of the Targacept Product.

1.14 “**First Maximum**” shall have the meaning provided in Section 4.2(c)(i).

1.15 “**Fourth Maximum**” shall have the meaning set forth in Section 4.2(c)(iv).

1.16 “**Licensee**” shall mean any Third Party that has obtained a license from Targacept to sell the Targacept Product.

1.17 “**License Grant**” shall, as used in Section 6.2, mean an exclusive license (with the right to grant sublicenses) under Targacept Proprietary Information that (i) Targacept owns or licenses (with the right to further sublicense) as of the date of grant, except that such license would

be non-exclusive with respect to Targacept Proprietary Information that are not patent rights, and (ii) is necessary to develop, make, use, sell, offer for sale or import the Compound in the United States, Europe or Japan, as the case may be, to develop, make, use, sell, offer for sale and import the Compound in the United States, Europe or Japan, as the case may be.

1.18 "**Net Sales**" shall mean the excess of (i) the amount invoiced for the sale of the Targacept Product by Targacept or any of its Affiliates or Licensees, as applicable, to Third Parties that are not Affiliates, licensees or sublicensees of the selling party, unless such Affiliates, licensees or sublicensees are the end users of the Targacept Product in which case the amount billed therefor shall be deemed to be the amount that would be invoiced to a Third Party in an arms' length transaction, over (ii) the sum of the following:

(a) cash or quantity discounts allowed;

(b) credits, refunds and allowances for returns, rejections and recalls;

(c) charges for freight, insurance and transportation specifically included in the amount invoiced;

(d) sales and use taxes, duties or other governmental tariffs and other similar taxes incurred; and

(e) accruals for estimated wholesaler chargebacks, contract rebates and bid rebates and Medicaid and other similar government mandated rebates, all of which shall be determined in accordance with Targacept's standard accounting methods.

1.19 "**Note**" shall mean a convertible promissory note in the form attached hereto as Exhibit A.

1.20 "**Person**" shall mean any natural person, corporation, firm, business trust, joint venture, association, organization, company, partnership or other business entity, or any government or agency or political subdivision thereof.

1.21 "**Receiving Party**" shall mean a party receiving from a Disclosing Party its Confidential Information.

1.22 "**Regulatory Approval**" shall mean, collectively, any and all approvals (including price and reimbursement approvals, as applicable), licenses, registrations, or authorizations of the United States or European Union or any country, federal, state or local regulatory agency, department, bureau or other government entity that are necessary for the use, storage, import, transport and sale of the Targacept Product in a particular jurisdiction.

1.23 "**Royalty Term**" shall mean the period commencing with the First Commercial Sale and ending at such time as Targacept's payment obligations under Section 4.2 have terminated pursuant to Section 4.2(c).

1.24 "**Second Maximum**" shall have the meaning provided in Section 4.2(c)(ii).

1.25 "**SMRI Indemnitee**" shall mean any of SMRI, its Affiliates and their respective directors, officers, employees and agents (including, without limitation, the SMRI Development Advisory Committee representative).

1.26 "**Strategic Alliance**" shall mean an agreement entered into by Targacept with a Third Party (i) with respect to the development of the Compound, but excluding an agreement with a Third Party solely with respect to the manufacturing, sale or promotion of the Compound or the Targacept Product, or (ii) for the transfer or sale of all or substantially all of the business of Targacept to which this Agreement relates to a Third Party, whether by merger, sale of stock, sale of assets or otherwise.

1.27 "**Targacept Background Proprietary Information**" means, collectively, the Compound and all: (i) issued patents and pending patent applications as of the Effective Date that are owned or controlled by Targacept or any of its Affiliates that claim or cover the composition of, a pharmaceutical composition of, a method of use of or a manufacturing process for the Compound, and all reexaminations, reissues, revisions, substitutes, renewals or extensions thereof; (ii) patents that issue after the Effective Date from the pending patent applications referenced in clause (i); (iii) other United States and foreign patents that issue after the Effective Date from patent applications that claim priority to the issued patents and pending patent applications referenced in clause (i), 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; and (iv) trade secrets, processes, formulae, specifications, synthesis information, synthesis pathways, data, files, preclinical and clinical research results, derivatives, improvements, inventions and techniques of Targacept or any of its Affiliates in existence as of the Effective Date.

1.28 "**Targacept Foreground Proprietary Information**" means, collectively, all trade secrets, processes, formulae, specifications, synthesis information, synthesis pathways, data, files, preclinical and clinical research results, derivatives, improvements, inventions and techniques, whether or not patentable, made, conceived, learned or first reduced to practice after the Effective Date by, on behalf of or for the benefit of Targacept or any of its Affiliates or Licensees, and all patents, patent applications, trademarks (whether or not registered), copyrights and other intellectual property rights in connection therewith; provided that Development Program Inventions and Development Program Results shall not constitute Targacept Foreground Proprietary Information.

1.29 "**Targacept Product**" shall mean the product, if any, that (i) contains the Compound, (ii) receives Regulatory Approval in any jurisdiction and (iii) is commercialized by Targacept or any of its Affiliates or Licensees, including all formulations and modes of administration thereof.

1.30 "**Targacept Proprietary Information**" means, collectively, Targacept Background Proprietary Information and Targacept Foreground Proprietary Information.

1.31 "**Term**" shall mean the term of this Agreement.

1.32 "**Third Maximum**" shall have the meaning set forth in Section 4.2(c)(iii).

1.33 "**Third Party**" shall mean any Person other than SMRI, Targacept or an Affiliate of SMRI or Targacept.

2. **DEVELOPMENT PROGRAM**.

2.1 **Development Program**. During the Development Term, Targacept shall use commercially reasonable efforts to conduct the Development Program in accordance with the Development Plan and the terms of this Agreement. The initial Development Plan will be completed by Targacept and presented to the DAC within sixty (60) days of the Effective Date.

2.2 **Amendments to the Development Plan**. Targacept may amend the Development Plan from time to time in its sole discretion. If any such amendment to the Development Plan would significantly reduce funding for development of the Compound or significantly extend the timeline for development of the Compound, Targacept shall, prior to finalizing the proposed amendment, provide the proposed amendment to the members of the DAC and to SMRI, and the DAC and SMRI shall have fifteen (15) days to review and provide Targacept comments on such proposed amendment. Targacept shall consider any such input in good faith when finalizing such amendment and shall distribute the finalized amendment to the DAC and SMRI. In the event that SMRI reasonably believes that the finalized amendment will have a material adverse effect on the development of the Compound, SMRI may notify the DAC and Targacept in writing of such belief, which notice shall include the basis for such belief in reasonable detail, provided that such notice is given within five (5) days of receipt of the final amendment. Within five (5) days after such notice from SMRI (or such longer period as agreed by Targacept and SMRI), each member of the DAC shall provide notice in writing to Targacept if he or she rejects the final amendment as proposed. If a majority of the members of the DAC reject the amendment as proposed, SMRI shall have the right to terminate this Agreement pursuant to Section 10.4(a); provided, if SMRI does not terminate this Agreement pursuant to Section 10.4(a), the proposed amendment shall take effect and this Agreement shall continue in full force and effect.

2.3 **Clinical Trials**. Targacept shall register each clinical trial to be conducted pursuant to the Development Program with (i) SMRI's quarterly trial reporting system and (ii) if and to the extent required by law, with the FDA's www.ClinicalTrial.gov website.

3. **GOVERNANCE**.

3.1 **Development Advisory Committee**. Promptly after the Effective Date, the parties will form a Development Advisory Committee comprised of two appointees of Targacept, who shall initially be **** and ****, one appointee of SMRI, who shall initially be ****, and two other individuals with particular experience in the development of schizophrenia therapeutics mutually agreed upon by Targacept and SMRI. The parties contemplate that these two other individuals would be identified within forty-five (45) days after the Effective Date. One (1) member of the DAC shall be selected by Targacept to act as the chairperson of the DAC, and Targacept may replace the chairperson from time to time. The DAC shall review the data and activities of the Development Program and monitor the progress of development in relation to the Development Plan. The DAC shall meet on a semi-annual basis or at such other frequency as it may determine to be appropriate, which meetings may be by conference telephone, videoconference or other similar equipment. The DAC shall agree upon the time and place of DAC meetings. A reasonable number of additional representatives of a party may attend meetings of the DAC. Targacept shall reimburse the member of the DAC appointed by SMRI for all reasonable costs and expenses (including travel and lodging expenses) incurred by him or her to attend DAC meetings, subject to receipt of supporting documentation reasonably acceptable to Targacept.

3.2 **Information and Reports**. Except as otherwise provided in this Agreement, Targacept will make available and disclose to SMRI and each member of the DAC all Development Program Results prior to and in preparation for DAC meetings.

4. **FEES AND PAYMENTS**.

4.1 **Funding**.

(a) Concurrently with the execution of this Agreement, SMRI shall, in support of the Development Program, loan $1,250,000 to Targacept pursuant to the terms set forth in the Note. In connection with the issuance of the Note by Targacept, SMRI hereby makes the representations and warranties set forth on Exhibit B to Targacept.

(b) Subject to the terms and conditions set forth herein, SMRI shall, in support of the Development Program, pay to Targacept each of the following amounts in cash if and promptly at the time the corresponding event occurs:

Event	Amount
****	$ ****
****	$ ****
****	$ ****
****	$ ****

(c) All amounts paid to Targacept by SMRI under this Section 4.1 shall be spent in support of the Development Program.

4.2 **Royalty Payments**.

(a) **Royalty Payments by Targacept**. In consideration for SMRI's license and grant of rights to Targacept under Section 6.1(c) and SMRI's covenants and obligations hereunder, Targacept shall, subject to Sections 4.2(c) and 10, pay to SMRI during the Royalty Term, a royalty equal to the sum of ********.

Aggregate calendar year annual Net Sales	Royalty %
Up to $****	****%
After $**** – and up to $****	****%
After $****	****%

Royalties on Net Sales would be calculated based on the rate applicable to year-to-date sales and paid quarterly.

(b) **Sublicensee Payments**. If, prior to the end of the Term, Targacept sublicenses to a Third Party rights to any Development Program Invention that Targacept licenses from SMRI pursuant to Section 6.1(b), Targacept shall pay to SMRI ********% of any cash fees or other payments actually received by Targacept from such Third Party for such sublicense, excluding (i) royalties on the sale of the Targacept Product, (ii) amounts specifically allocated to research and development for, or to the manufacture or supply of, the Compound or the Targacept Product, (iii) amounts that Targacept is required to repay (e.g., a loan), and (iv) amounts received in exchange for securities of Targacept.

(c) **Maximum Payment Amount**.

(i) In the event that, at any time on or prior to the ******** anniversary of the Effective Date, Targacept makes payments to SMRI under this Section 4.2 at least equal to the total amount SMRI has theretofore paid to Targacept under Section 4.1(b), if any, plus interest on such amount at the Applicable Rate (the "**First Maximum**"), Targacept's obligation to make payments to SMRI pursuant to this Section 4.2 shall terminate. At any time prior to the ******** anniversary of the Effective Date, Targacept may make a lump sum cash payment to SMRI equaling the amount by which the First Maximum exceeds the total amount theretofore paid to SMRI under this Section 4.2 and, upon receipt of such payment by SMRI, Targacept's obligation to make payments to SMRI pursuant to this Section 4.2 shall terminate.

(ii) In the event that, at any time after the ******** anniversary of the Effective Date and on or prior to the ******** anniversary of the Effective Date, Targacept makes total payments to SMRI under this Section 4.2 of ********% of the total amount SMRI has theretofore paid to Targacept under Section 4.1(b) (the "**Second Maximum**"), Targacept's obligation to make payments to SMRI pursuant to this Section 4.2 shall, if not previously terminated, terminate. At any time after the ******** anniversary of the Effective Date and on or prior to the ******** anniversary of the Effective Date, Targacept shall be entitled to make a lump sum cash payment to SMRI equaling the amount by which the Second Maximum exceeds the total amount theretofore paid to SMRI under this Section 4.2 and, upon receipt of such payment by SMRI, Targacept's obligation to make payments to SMRI pursuant to this Section 4.2 shall, if not previously terminated, terminate.

(iii) In the event that, at any time after the ******** anniversary of the Effective Date and on or prior to the ******** anniversary of the Effective Date, Targacept makes total payments to SMRI under this Section 4.2 of ********% of the total amount SMRI has theretofore paid to Targacept under Section 4.1(b) (the "**Third Maximum**"), Targacept's obligation to make payments to SMRI pursuant to this Section 4.2 shall, if not previously terminated, terminate. At any time after the ******** anniversary of the Effective Date and on or prior to the ******** anniversary of the Effective Date, Targacept shall be entitled to make a lump sum cash payment to SMRI equaling the amount by which the Third Maximum exceeds the total amount theretofore paid to SMRI under this Section 4.2 and, upon receipt of such payment by SMRI, Targacept's obligation to make payments to SMRI pursuant to this Section 4.2 shall, if not previously terminated, terminate.

(iv) In the event that, at any time after the ******** anniversary of the Effective Date, Targacept makes total payments to SMRI under this Section 4.2 of ********% of the total amount SMRI has theretofore paid to Targacept under Section 4.1(b) (the "**Fourth Maximum**"),

Targacept's obligation to make payments to SMRI pursuant to this Section 4.2 shall, if not previously terminated, terminate. At any time after the **** anniversary of the Effective Date, Targacept shall be entitled to make a lump sum cash payment to SMRI equaling the amount by which the Fourth Maximum exceeds the total amount theretofore paid to SMRI under this Section 4.2 and, upon receipt of such payment by SMRI, Targacept's obligation to make payments to SMRI pursuant to this Section 4.2 shall, if not previously terminated, terminate.

5. **PAYMENTS; RECORDS; AUDITS**.

5.1 **Payment; Reports**. Payments due under Section 4.2 and reports for the sale of the Targacept Product by Targacept and its Affiliates or Licensees shall be calculated and reported for each calendar quarter. All payments due to SMRI under Section 4.2 shall be paid within sixty (60) days (or, in the event Targacept has a Licensee, ninety (90) days) after the end of each calendar quarter. Each payment shall be accompanied by a report of Net Sales in sufficient detail to permit confirmation of the accuracy of the payment made, including, without limitation, the number of units of the Targacept Product sold by Targacept and its Affiliates or Licensees, the gross sales and Net Sales of the Targacept Product sold by Targacept and its Affiliates or Licensees in U.S. dollars, the exchange rates used, and any other information necessary to determine the amount of royalties and sublicensee payments due under Section 4.2. Targacept will keep complete and accurate records pertaining to such calculation to permit SMRI to confirm the accuracy of payments due hereunder. Targacept shall pay SMRI interest at the Applicable Rate on any past due payments pursuant to Sections 4.2(a) or 4.2(b) that are not paid by Targacept to SMRI within thirty (30) days after receipt of written demand therefor from SMRI.

5.2 **Exchange Rate; Manner and Place of Payment**. All payments hereunder shall be made in U.S. dollars. With respect to amounts payable with respect to Net Sales in any calendar quarter denominated other than in U.S. dollars, if such Net Sales are made by (i) Targacept or any of its Affiliates, conversion shall be made based on the average of the daily rates of exchange for the currency of the country from which payments are payable, as published by *The Wall Street Journal*, Eastern U.S. Edition, during the calendar quarter for which a payment is due, or (ii) a Licensee, conversion shall be made based on the same exchange rate that is used to convert royalty payments by Licensee to Targacept into U.S. dollars or, if none, as provided in clause (i). All payments owed to SMRI under this Agreement shall be made by wire transfer to a bank and account designated in writing by SMRI, unless otherwise specified by SMRI.

5.3 **Records and Audits**. SMRI shall have the right to have an independent certified public accountant inspect the books and records of Targacept and/or its Affiliates (i) no more than once per fiscal year, (ii) upon thirty (30) days prior written notice, (iii) during usual business hours and (iv) only to the limited extent necessary to verify the completeness and accuracy of the records and payments made under this Agreement. Such examination with respect to any calendar quarter shall not take place later than two (2) years following the end of such calendar quarter. The accountant shall inform SMRI only if there has been an underpayment or an overpayment or misappropriation of payments, and if so, the amount thereof. The expense of any such inspection shall be borne by SMRI; provided, however, that if the inspection discloses an underpayment in excess of ten percent (10%) then Targacept shall pay the reasonable out-of-pocket costs to conduct such audit.

5.4 **Withholding of Taxes**. Any withholding of taxes levied by tax authorities outside the United States on payments hereunder shall be borne by the party receiving such payment and

deducted by the party making such payment from the sums otherwise payable by it hereunder for payment to the proper tax authorities. The parties agree to cooperate with each other in the event a party claims exemption from such withholding or seeks deductions under any double taxation or other similar treaty or agreement from time to time in force, such cooperation to consist of providing receipts of payment of such withheld tax or other documents that are available without undue effort or expense.

5.5 **Exchange and Royalty Rate Controls**. If at any time legal restrictions prevent the prompt remittance of part or all royalties on Net Sales in any country where the Targacept Product is sold, payment shall be made through such lawful means or methods as Targacept may determine. When in any country legal restrictions prohibit both the transmittal and deposit of royalties on Net Sales in such country, royalty payments shall be suspended for as long as such prohibition is in effect, and, as soon as such prohibition ceases to be in effect, all royalties that would have been obligated to have been transmitted or deposited, but for the prohibition, shall forthwith be deposited or transmitted promptly, to the extent allowable. If any royalty rate specified in this Agreement shall exceed the maximum lawful rate established in any country, the royalty rate applicable to Net Sales in such country shall automatically be reduced to the maximum lawful rate.

6. **INTELLECTUAL PROPERTY RIGHTS; CLINICAL TRIAL RESULTS**.

6.1 **Intellectual Property; Results**.

(a) SMRI hereby acknowledges and agrees that, as between the parties, Targacept owns all right, title and interest in and to all Targacept Proprietary Information and that, except to the extent expressly provided herein, no right or license in any of the Targacept Proprietary Information is granted to SMRI hereunder.

(b) Targacept agrees to use commercially reasonable efforts to cause any principal investigator or institution with which it contracts to conduct work in the Development Program to assign to Targacept all ownership rights in Development Program Inventions and Development Program Results. Targacept shall notify SMRI promptly in writing of each Development Program Invention that it owns, if any, and any other information reasonably requested pertaining thereto. Subject to Sections 6.1(c) and 10.6, Targacept hereby assigns to SMRI all of its right, title and interest to each Development Program Invention and all Development Program Results that it owns, if any.

(c) SMRI hereby grants to Targacept a perpetual, irrevocable, worldwide exclusive license (with the right to sublicense) to any and all Development Program Inventions (including, without limitation, those assigned to SMRI by Targacept) for all purposes. In addition, SMRI expressly agrees that Targacept may use, disclose and reference any and all such Development Program Results in any manner whatsoever and that such rights are perpetual and irrevocable. Notwithstanding the foregoing, SMRI reserves the right to use such Development Program Inventions and Development Program Results only for its own internal, non-profit, non-commercial, administrative purposes or as expressly permitted by Section 8.5 and for no other purposes whatsoever.

6.2 **Conditional License to SMRI**.

(a) If Targacept has definitively decided to terminate all efforts to commercialize the Compound in any of the United States, Europe or Japan for any reason other than scientific reasons, including termination of (i) its own research, development and commercialization activities in such jurisdiction, (ii) the research, development and commercialization activities of any Affiliate in such jurisdiction, Licensee or transferee or (iii) its efforts, if applicable, to identify any Licensee or transferee of rights to the Compound in such jurisdiction, Targacept shall use commercially reasonable efforts to notify SMRI in writing of such pending termination. If SMRI notifies Targacept in writing within sixty (60) days after the date that such notice is given by Targacept that it is interested in obtaining rights to develop and commercialize the Compound in such jurisdiction and has the resources, either itself or together with a Third Party, to diligently develop and commercialize the Compound in such jurisdiction, then Targacept will use commercially reasonable efforts to negotiate in good faith with SMRI for a period of sixty (60) days (or such longer period as agreed in writing by the parties) for the License Grant in such jurisdiction. For the avoidance of doubt, a deferral, temporary suspension or postponement of development or commercialization efforts by Targacept with respect to the Compound shall not constitute a termination of all efforts under this Section 6.2(a).

(b) If the parties do enter into an agreement providing for the License Grant following good faith negotiation pursuant to Section 6.2(a), then, to the extent the following items are within Targacept's reasonable control and can be provided without breach of any obligation to or agreement with any Third Party, Targacept shall provide SMRI with copies of all preclinical and clinical data and study results, INDs (investigational new drug application(s) filed with the FDA pursuant to Part 312 of Title 21 of the U.S. Code of Federal Regulations, including any amendments thereto) and other regulatory filings, studies, information and materials relating to the development and commercialization of the Compound generated by or on behalf of Targacept (including pharmacology, toxicology, formulation, and stability studies).

(c) If SMRI does not provide notice of its interest to Targacept within the first sixty (60) day period specified under Section 6.2(a), or if SMRI does provide such notice within such period, but the parties do not enter into an agreement providing for the License Grant within the negotiation period specified in Section 6.2(a), then Targacept shall have no further obligations, and SMRI shall have no further rights, under this Section 6.2.

6.3 **Patent Abandonment**. Prior to Targacept abandoning any patent or patent application in the United States that constitutes a Development Program Invention (including abandonment for failure to pay any required fees), other than in the ordinary course of patent prosecution or related strategy, Targacept shall use commercially reasonable efforts to notify SMRI in writing of such pending abandonment, whereupon SMRI shall have the right and opportunity, upon written notice to Targacept provided within thirty (30) days after such notice from Targacept, to take title to the applicable patent or patent application and to maintain the issued patent or continue the prosecution of the patent application at SMRI's own expense; provided, however, that: (i) at such time as SMRI first exercises its rights under this Section 6.3 with respect to any patent or patent application, upon the request of Targacept, SMRI shall be deemed to have granted to Targacept (A) a non-exclusive, irrevocable, royalty-free, non-sublicensable and non-transferable (except as permitted by Section 12.7) right to practice such patent or patent application for Targacept's own internal non-commercial uses and (B) subject to SMRI's right to practice the patent or patent application (and any and all Development Program Inventions claimed in such patent or patent application) for its own

internal research purposes, the first right to negotiate with SMRI, in good faith, the terms of an exclusive license to develop and commercialize any and all Development Program Inventions claimed in such patent or patent application; and (ii) if SMRI and Targacept do not enter into a written exclusive license agreement within ninety (90) days following SMRI's notice to take title to the patent or patent application, SMRI shall be free to negotiate with, and license the rights to develop and commercialize any and all Development Program Inventions claimed in such patent or patent application to, Third Parties.

6.4 **Patent Prosecution**. The filing and prosecution of all United States and foreign patent applications and maintenance of all United States and foreign patents that constitute Development Program Inventions shall be the responsibility of Targacept at its sole expense. SMRI agrees to promptly provide to Targacept such assistance, information and executed documents needed to facilitate the prosecution, issuance and maintenance of Development Program Inventions as Targacept may reasonably request and Targacept shall reimburse SMRI for reasonable out-of-pocket expenses actually incurred to provide such assistance, information and documents, subject to received of itemized statements and other appropriate supporting documentation.

6.5 **Patent Infringements**.

(a) The parties shall inform each other promptly, in writing, of any alleged infringement of a Development Program Invention and any available evidence thereof; provided that no such obligation shall arise in circumstances in which a party learns of an alleged infringement while under a confidentiality obligation to the alleged infringer that was entered into in good faith prior to such party learning of the alleged infringement. Neither party will settle or compromise any claim or action in a manner that imposes any restrictions or obligations on the other party without such other party's written consent, which shall not be unreasonably withheld.

(b) Targacept shall have the first right, but shall not be obligated, to prosecute at its own expense any such infringement of a Development Program Invention and, in furtherance of such right, SMRI hereby agrees that Targacept may join SMRI as a party plaintiff in any such suit, without expense to SMRI. The total cost of any such infringement action commenced solely by Targacept shall be borne by Targacept, and Targacept shall keep any recovery or damages for past infringement derived therefrom. Subject to Section 6.5(a), Targacept shall be entitled to settle any such litigation by agreement, consent, judgment, voluntary dismissal or otherwise.

(c) If within six (6) months after having been notified of any alleged infringement of a Development Program Invention, Targacept shall have been unsuccessful in persuading the alleged infringer to desist and shall not have brought and shall not be diligently prosecuting an infringement action, or if Targacept shall notify SMRI at any time prior thereto of its intention not to bring suit against any alleged infringer, then, and in those events only, SMRI shall have the right, but shall not be obligated, to prosecute at its own expense the infringement of such Development Program Invention. The total cost of any such infringement action commenced solely by SMRI will be borne by SMRI, and SMRI will keep any recovery or damages for past infringement derived therefrom. Subject to Section 6.5(a), SMRI shall be entitled to settle any such litigation by agreement, consent, judgment, voluntary dismissal or otherwise.

(d) In the event that a declaratory judgment action alleging invalidity or noninfringement of a Development Program Invention shall be brought against SMRI, Targacept at its option, shall have the right, within thirty (30) days after commencement of such action, to

intervene and take over the sole defense of the action at its own expense. In such event, Targacept shall keep any recovery or damages derived therefrom or from any counterclaims asserted therein.

(e) In any infringement suit instituted, or declaratory action defended, by either party to enforce or protect a Development Program Invention, the other party hereto shall, at the request and expense of the party initiating or defending such suit, cooperate in all respects and, to the extent practicable, allow its employees testify when requested and make available relevant records, papers, information, samples, specimens and the like.

7. **REPRESENTATIONS AND WARRANTIES**.

7.1 **Representations and Warranties**. Each party represents to the other that, as of the Effective Date:

(a) it is duly organized and validly existing under the laws of its state of incorporation or formation and has full corporate power and authority to enter into this Agreement and to carry out the provisions hereof;

(b) it is duly authorized to execute and deliver this Agreement and to perform its obligations hereunder, and the person or persons executing this Agreement on its behalf is duly authorized to do so;

(c) this Agreement is legally binding upon it and enforceable in accordance with its terms, except that: (i) enforceability may be limited by bankruptcy, insolvency or other similar laws affecting creditors' rights generally and (ii) the availability of equitable remedies may be limited by equitable principles of general applicability; and

(d) its execution, delivery and performance of this Agreement does not conflict with any agreement, instrument or understanding, oral or written, to which it is a party or by which it is bound or violate any material law or regulation of any court, governmental body or administrative or other agency having jurisdiction over it.

7.2 **Disclaimers**.

(a) Except as specifically set forth in this Agreement, NEITHER PARTY MAKES ANY REPRESENTATIONS AND WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED.

(b) Without limiting the generality of Section 7.2(a), TARGACEPT EXPRESSLY DISCLAIMS ANY WARRANTY, EXPRESS OR IMPLIED, WITH RESPECT TO (i) THE SUCCESS OF THE DEVELOPMENT PROGRAM AND (ii) THE SAFETY, EFFICACY, USEFULNESS OR SUCCESSFUL COMMERCIALIZATION OF THE COMPOUND OR THE TARGACEPT PRODUCT.

8. **CONFIDENTIALITY; PUBLICATION**.

8.1 **Confidentiality**. Except to the extent expressly authorized by this Agreement or otherwise agreed in writing by the parties, the parties agree that, during the Term and for ten (10) years thereafter, the Receiving Party shall keep confidential and shall not publish or otherwise

disclose and shall not use for any purpose (other than as expressly provided for in this Agreement) any Confidential Information of the other party. Each Receiving Party may use Confidential Information of the Disclosing Party only to accomplish the purposes of this Agreement. Each Receiving Party will use at least the same standard of care (but not less than reasonable care) to protect the Confidential Information of the Disclosing Party as it uses to protect its own proprietary or confidential information and to ensure that its employees, agents, consultants and other representatives do not disclose or make any unauthorized use of its proprietary or confidential information. Each Receiving Party will promptly notify the Disclosing Party upon discovery of any unauthorized use or disclosure of the Disclosing Party's Confidential Information. For purposes of this Section 8 (except Section 8.5), Development Program Inventions and Development Program Results shall be deemed Confidential Information of Targacept disclosed to SMRI.

8.2 **Exceptions**. The obligations of confidentiality and non-use contained in Section 8.1 shall not apply to Confidential Information that:

(a) is now, or hereafter becomes, through no act or failure to act on the part of the Receiving Party, generally known or available;

(b) is known by the Receiving Party at the time of receiving such information, other than under an obligation of confidentiality, as evidenced by its written records;

(c) is hereafter furnished to the Receiving Party by a Third Party without restriction on disclosure known to the Receiving Party;

(d) is independently developed by the Receiving Party without the aid, application or use of Confidential Information of the Disclosing Party, as evidenced by the Receiving Party's written records; or

(e) is the subject of a written permission to disclose provided by the Disclosing Party.

8.3 **Terms of Agreement**. The parties agree that this Agreement and the terms hereof shall be considered Confidential Information of both parties. Notwithstanding the foregoing, either party may disclose such terms (i) to investors, lenders, potential investors or lenders, (ii) as required by applicable law or regulation and (iii) with respect to Targacept only, to bona fide potential Licensees.

8.4 **Authorized Disclosure**. Each Receiving Party may disclose the Disclosing Party's Confidential Information to the extent such disclosure is reasonably necessary in connection with:

(a) regulatory filings;

(b) prosecuting or defending litigation;

(c) complying with applicable court orders or governmental regulations; or

(d) due diligence or similar investigations by Affiliates, licensees, employees, consultants, agents or other Third Parties who agree to be bound by similar terms of confidentiality and non-use at least equivalent in scope to those set forth in this Section 8.

Notwithstanding the foregoing, in the event a Receiving Party is required to make a disclosure of the Disclosing Party's Confidential Information pursuant to this Section 8.4, it will seek to secure confidential treatment of such information at least as diligently as such party would use to protect its own Confidential Information. The parties will use commercially reasonable efforts to consult with each other on the provisions of this Agreement to be redacted in any filings made by the parties with the Securities and Exchange Commission or as otherwise required by law.

8.5 **Publications**. SMRI may publish a summary of work conducted in the Development Program in SMRI's annual reports and on SMRI's website; provided that in no event shall SMRI publish such summary prior to the earliest of (i) such time as Targacept or its designee publishes the results of such work; (ii) ******** (********) months after completion of such work; or (iii) receipt by SMRI of Targacept's written consent to such publication. In no event shall SMRI disclose or use any Confidential Information of Targacept in such publication without Targacept's prior written consent, which may not be unreasonably withheld; provided, however, that Targacept acknowledges that, in order to preserve its tax-exempt status, SMRI must be able to publish a summary of work performed under the Development Program and Targacept will work in good faith with SMRI to reach agreement upon the summary of such work to be published by SMRI and will not unreasonably withhold its consent to the inclusion of Confidential Information of Targacept contained in such summary. Targacept shall be free to publish papers regarding the Development Program without the prior written consent of SMRI and shall use commercially reasonable efforts to publicize SMRI's monetary contribution to the Development Program in any such papers.

9. **INDEMNIFICATION**.

9.1 Indemnification. Targacept shall indemnify, defend and hold harmless each SMRI Indemnitee from and against any and all Third Party claims, actions, suits, proceedings, demands, liabilities, damages, losses, costs, penalties, fines and expenses (including court costs and the reasonable fees of attorneys and other professionals) to the extent resulting directly from:

(a) Targacept's breach of any of its representations, warranties, covenants or obligations under this Agreement;

(b) the gross negligence or willful misconduct of Targacept or any of its Affiliates in connection with Targacept's performance of its obligations under this Agreement (including, without limitation, the conduct of the Development Program by Targacept); or

(c) personal injury (including death) suffered by any subject in a clinical trial conducted in the Development Program that is actually funded by SMRI hereunder if such injury is caused by the administration of the Compound;

provided that, notwithstanding the foregoing, Targacept shall have no obligations under this Section 9.1 with respect to any Third Party claim, action, suit, proceeding, demand, liability, damage, loss, cost, penalty, fine and expense that results, directly or indirectly, from the gross negligence or willful misconduct of any SMRI Indemnitee or the breach by SMRI of any of its representations, warranties, covenants or obligations under this Agreement.

9.2 **Procedures for Indemnification**. Promptly after receipt by an SMRI Indemnitee of notice of any Third Party claim, action, suit, proceeding or demand, such SMRI Indemnitee shall, if a

claim under Section 9.1 in respect thereof is to be made against Targacept, deliver to Targacept written notice thereof, and Targacept shall have the right to assume and manage the defense thereof (and to pursue all claims available against Third Parties), including the right to select counsel and the right to settle, compromise or litigate with respect to any such Third Party claim, action, suit, proceeding or demand (but, in the case of settlement or compromise, only after obtaining SMRI's prior written consent); provided, however, that Targacept shall not be required to obtain SMRI's prior written consent to any proposed settlement or compromise that (i) includes a release of SMRI from any liability (monetary or otherwise) and (ii) does not include a waiver by SMRI of any of its rights or an admission by SMRI of any wrongdoing or guilt. Each SMRI Indemnitee shall have the right to employ counsel separate from counsel employed by Targacept, but the fees and expenses of such counsel shall be at the SMRI Indemnitee's own expense.

9.3 **Advance Payment of Expenses; Complete Indemnification**. Subject to Section 9.2, the expenses of an SMRI Indemnitee incurred in defending a Third Party claim, action, suit or proceeding shall be paid by Targacept as they are incurred and in advance of the final disposition of such Third Party claim, action, suit or proceeding, upon receipt of an undertaking by or on behalf of the SMRI Indemnitee to repay the amount if it is ultimately determined by a court of competent jurisdiction that such SMRI Indemnitee is not entitled to be indemnified by Targacept. All costs and expenses incurred by an SMRI Indemnitee directly in connection with enforcement of Section 9.1 also shall be reimbursed by Targacept if it is ultimately determined by a court of competent jurisdiction that Targacept has an obligation under Section 9.1 that it has not met.

9.4 **Insurance**. Targacept will maintain at its own expense, with a reputable insurance carrier, product liability insurance and comprehensive general liability insurance in an amount consistent with industry standards during the term of this Agreement. Targacept will, upon request, provide SMRI with a certificate of insurance evidencing such coverage.

10. **TERM AND TERMINATION**.

10.1 **Term of the Agreement**. The Term shall commence on the Effective Date and continue until such time as Targacept's payment obligations under Section 4.2 have terminated pursuant to Section 4.2(c), unless earlier terminated pursuant to Section 10.2, 10.3, 10.4 or 10.5 or extended by mutual written agreement of the parties.

10.2 **Termination by Mutual Agreement**. The parties may at any time terminate this Agreement by mutual written agreement. The effective date of any such termination shall be the last day of the Term.

10.3 **Termination by Targacept**. Targacept may terminate this Agreement upon thirty (30) days prior written notice to SMRI in the event that Targacept enters into a Strategic Alliance. The effective date of any such termination shall be the last day of the Term.

10.4 **Termination by SMRI**.

(a) SMRI may terminate this Agreement upon thirty (30) days prior written notice to Targacept in the event that SMRI (i) disagrees with an amendment to the Development Plan proposed by Targacept that is rejected by a majority of the members of the DAC as contemplated by Section 2.2 or (ii) believes, in good faith and based on information provided by the DAC, that reasonable progress on the Development Program is not occurring in accordance with the

Development Plan. The effective date of any such termination shall be the last day of the Term. Prior to any termination under this Section 10.4(a), SMRI agrees to meet with the DAC and Targacept to discuss and implement improvements or refinements to the Development Program or Development Plan to provide comfort to SMRI, acting reasonably and in good faith, that reasonable progress will be made, in which case this Agreement shall not be so terminated.

(b) SMRI may terminate this Agreement with thirty (30) days prior written notice in the event that Targacept abandons the Development Program; provided that (i) SMRI shall have the right to apply future payments due under Section 4.1 to other schizophrenia-related research being conducted by Targacept if and as mutually agreed to by the parties in lieu of terminating this Agreement under this Section 10.4(b) and (ii) for the avoidance of doubt, a deferral, temporary suspension or postponement of activities under the Development Program shall not constitute abandonment under this Section 10.4(b).

10.5 **Termination for Cause**. Each party shall have the right to terminate this Agreement upon sixty (60) days prior written notice to the other upon the occurrence of either of the following:

(a) upon or after the bankruptcy, insolvency, dissolution or winding up of the other party (other than a dissolution or winding up for the purpose of reconstruction or amalgamation); or

(b) upon or after the breach of any material provision of this Agreement by the other party if the breaching party has not cured such breach within the sixty (60) day period following written notice of termination by the non-breaching party.

The effective date of any such termination shall be the last day of the Term.

10.6 **Effect of Termination or Expiration; Surviving Obligations**. Expiration or termination of this Agreement shall not affect any rights or obligations of either party accruing prior to such expiration or termination. Upon expiration or termination of this Agreement, all rights and obligations of the parties under this Agreement shall terminate, except that: (i) the terms of Sections 1, 5.3, 6.1, 6.4, 6.5, 7.2, 8, 9.1, 9.2, 9.3, 10.6, 11 and 12 shall survive any expiration or termination of this Agreement (provided that, except for the last sentence of Section 8.5, the survival of Section 8.5 shall apply only to a clinical trial conducted in the Development Program for which the first subject was enrolled and randomized prior to the effective date of such termination and no publication right of SMRI or obligation of Targacept shall attach to any clinical trial conducted in the Development Program for which the first subject was not enrolled and randomized prior to the effective date of such termination); and (ii) in addition, if this Agreement is terminated by Targacept under Section 10.3 or by SMRI under Section 10.4 or 10.5, the terms of Section 4.2, 5, 6.2, 6.3 and 9.4 shall also survive such termination until the last day of the Royalty Term. Upon expiration or termination of this Agreement or, if clause (ii) above is applicable, upon expiration of the Royalty Term, all right, title and interest in and to any and all Development Program Inventions and Development Program Results shall thereupon be assigned and conveyed to Targacept and SMRI shall promptly take all actions and execute all documents reasonably requested by Targacept in furtherance of the foregoing. Except as otherwise provided in this Section 10.6, each party shall, promptly after expiration or termination of this Agreement, return or dispose of any Confidential Information of the other party in accordance with the instructions of such other party.

11. **GOVERNING LAW; DISPUTE RESOLUTION**.

11.1 **Governing Law**. This Agreement shall be governed by the laws of the State of Delaware as such laws are applied to contracts entered into or to be performed entirely within such state.

11.2 **Dispute Resolution**. Except with respect to matters for which injunctive relief is sought, in the event of any dispute, the parties shall refer such dispute to the Chief Executive Officer of Targacept and the Executive Director of SMRI for attempted resolution by good faith negotiations within sixty (60) days after such referral is made. During such period of good faith negotiations, any applicable time periods under this Agreement shall be tolled. In the event such executives are unable to resolve such dispute within such sixty (60) day period, the parties shall submit their dispute to binding arbitration to be held in Washington D.C., such arbitration to be conducted pursuant to the American Arbitration Association's procedure rules applicable to commercial disputes then in effect. The award of the arbitrator shall include an award of reasonable attorneys' fees and costs to the prevailing party.

11.3 **Jurisdiction and Venue**. Except as provided in Section 11.2, any claim or controversy arising out of or related to this Agreement or any breach hereof (including claims for injunctive relief) shall be adjudicated in the state and federal courts in Montgomery County having jurisdiction over disputes arising in the State of Maryland, and the parties hereby consent to the jurisdiction and venue of such courts.

12. **General Provisions**.

12.1 Notices. All notices required or permitted to be given under this Agreement shall be in writing and shall be mailed by registered or certified mail, Federal Express or other nationally recognized overnight delivery service, addressed to the signatory to whom such notice is required or permitted to be given and transmitted by facsimile to the number indicated below. All notices shall be deemed to have been given when mailed, as evidenced by the postmark at the point of mailing, or faxed.

All notices to SMRI shall be addressed as follows:	Stanley Medical Research Institute 5430 Grosvenor Lane, Suite 200 Bethesda, MD 20814 Attn: Dr. Michael Knable, DO Fax: (301) 571-0769
with a copy to:	Stanley Medical Research Institute 5430 Grosvenor Lane, Suite 200 Bethesda, MD 20814 Attn: Lori Keenan Fax: (301) 571-0769
All notices to Targacept shall be addressed as follows:	Targacept, Inc. 200 East First Street, Suite 300 Winston-Salem, NC 27101 Attn: Vice President, Business and Commercial Development Attn: Corporate Counsel Fax: (336) 480-2103

Any party may, by written notice to the other, designate a new address or fax number to which notices to the party giving the notice shall thereafter be mailed or faxed.

12.2 **Force Majeure**. No party shall be liable for any delay or failure of performance (other than payment obligations) to the extent such delay or failure is caused by circumstances beyond its reasonable control and that it is unable to prevent, provided that the party claiming excuse uses its commercially reasonable efforts to overcome the same.

12.3 **Entirety of Agreement**. This Agreement (and the exhibits attached hereto) embodies the entire, final and complete agreement and understanding between the parties and replaces and supersedes all prior discussions and agreements between them with respect to its subject matter. No modification or waiver of any terms or conditions hereof shall be effective unless made in writing and signed by a duly authorized officer of each party.

12.4 **Non-Waiver**. The failure of a party in any one or more instances to insist upon strict performance of any of the terms and conditions of this Agreement shall not constitute a waiver or relinquishment, to any extent, of the right to assert or rely upon any such terms or conditions on any future occasion.

12.5 **Disclaimer of Agency or Partnership**. Neither party is, or will be deemed to be, the legal representative or agent of the other, nor shall either party have the right or authority to assume, create, or incur any third party liability or obligation of any kind, express or implied, against or in the name of or on behalf of another except as expressly set forth in this Agreement. In addition, neither party shall be deemed to be a member of a partnership with the other party, nor shall SMRI be deemed to be a “Sponsor” (as defined by the FDA) of any clinical trial for the Targacept Product.

12.6 **Severability**. If a court of competent jurisdiction declares any provision of this Agreement invalid or unenforceable, or if any government or other agency having jurisdiction over either Targacept or SMRI deems any provision to be contrary to any laws, then that provision shall be severed and the remainder of the Agreement shall continue in full force and effect. To the extent possible, the parties shall give effect to such severed provision in a manner that will render such provision valid without impairing the parties’ original intent.

12.7 **Assignment**. Except as expressly provided hereunder, neither this Agreement nor any rights or obligations hereunder may be assigned or otherwise transferred by either party without the prior written consent of the other party (which consent shall not be unreasonably withheld); provided, however, that (i) Targacept may assign this Agreement and its rights and obligations hereunder without SMRI’s consent to any of its Affiliates or in connection with the transfer or sale of all or substantially all of the business of such party to which this Agreement relates, whether by merger, sale of stock, sale of assets or otherwise and (ii) SMRI may assign without Targacept’s consent only its right to receive payments under this Agreement to a taxable wholly owned subsidiary of SMRI. The rights and obligations of the parties under this Agreement shall be binding

upon and inure to the benefit of the successors and permitted assigns of the parties. Any purported assignment that is not in accordance with this Section 12.7 shall be void and of no force or effect.

12.8 **Headings**. The headings contained in this Agreement are inserted for reference only and shall not be deemed a part of the text hereof.

12.9 **Limitation of Liability**. EXCEPT FOR LIABILITY FOR BREACH OF CONFIDENTIALITY, NEITHER PARTY SHALL BE LIABLE TO THE OTHER FOR INDIRECT, INCIDENTAL, CONSEQUENTIAL, SPECIAL OR EXEMPLARY DAMAGES, INCLUDING BUT NOT LIMITED TO LOST PROFITS, ARISING FROM OR RELATING TO ANY BREACH OF THIS AGREEMENT, REGARDLESS OF ANY NOTICE OF THE POSSIBILITY OF SUCH DAMAGES.

12.10 **Counterparts**. This Agreement may be executed in two counterparts (which may be exchanged by facsimile with full force and effect), each of which shall be an original and all of which shall constitute together the same document.

12.11 **Public Disclosure**. Except for such disclosure as is deemed necessary, in the reasonable judgment of a party, to comply with applicable laws or regulations, no public announcement, news release, public statement or publication relating to the existence of this Agreement, or the terms hereof, will be made without the other party's prior written approval, which approval shall not be unreasonably withheld. The parties agree that they will use reasonable efforts to coordinate the initial announcement or press release relating to the existence of this Agreement so that such initial announcement or press release is made within forty-five (45) days of the Effective Date.

12.12 **Expenses**. Each party shall pay all costs and expenses that it incurs with respect to the negotiation, execution, delivery and performance of this Agreement, except that Targacept shall reimburse the reasonable fees of and expenses of counsel for SMRI in connection with the negotiation, execution and delivery of this Agreement (not to exceed $**** in the aggregate without the prior written consent of Targacept).

[remainder of page intentionally left blank]

IN WITNESS WHEREOF, the parties hereto have duly executed this DEVELOPMENT AGREEMENT.

Targacept, Inc.

By: /s/ J. Donald deBethizy

Name: J. Donald deBethizy

Title: President and Chief Executive Officer

The Stanley Medical Research Institute

By: /s/ Michael Knable, D.O.

Name: Michael Knable, D.O.

Title: Executive Director

[SIGNATURE PAGE TO DEVELOPMENT AGREEMENT]

EXHIBIT A

THIS CONVERTIBLE PROMISSORY NOTE HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED. NO SALE OR DISPOSITION MAY BE EFFECTED EXCEPT IN COMPLIANCE WITH RULE 144 UNDER SAID ACT OR AN EFFECTIVE REGISTRATION STATEMENT RELATED THERETO OR AN OPINION OF COUNSEL FOR HOLDER REASONABLY SATISFACTORY TO PAYOR THAT SUCH REGISTRATION IS NOT REQUIRED UNDER THE ACT OR RECEIPT OF A NO-ACTION LETTER FROM THE SECURITIES AND EXCHANGE COMMISSION.

CONVERTIBLE PROMISSORY NOTE

$1,250,000 **December 15, 2004**

For value received TARGACEPT, INC., a Delaware corporation ("**Payor**"), promises to pay to the order of THE STANLEY MEDICAL RESEARCH INSTITUTE or its assigns ("**Holder**") the principal sum of $1,250,000, together with interest on the outstanding balance hereof at the rate of ten percent (10%) per annum, compounded annually as of each December 31 (beginning December 31, 2005) until paid. Interest shall commence with the date hereof and shall continue on the outstanding principal until paid in full or converted. Interest shall be computed on the basis of a year of 365 days for the actual number of days elapsed.

1. This note (this "**Note**") is issued pursuant to the terms of that certain Development Agreement between Holder and Payor (the "**Agreement**") of even date herewith (the "**Agreement Date**").

2. All payments of interest and principal shall be in lawful money of the United States of America and shall be made to Holder. All payments shall be applied first to accrued interest, and thereafter to principal.

3. In the event that Payor issues and sells shares of its common stock, $0.001 par value per share (the "**Common Stock**"), before January 1, 2007 (the "**Maturity Date**") in a firm commitment underwritten public offering registered pursuant to the Securities Act of 1933, as amended (the "**Initial Public Offering**"), and, as of the date such Initial Public Offering is closed this Note has not been paid in full, the outstanding principal balance of this Note, together with interest hereon through the date such Initial Public Offering is closed, shall automatically convert in whole without any further action by Holder into shares of Payor's Common Stock effective upon the closing of the Initial Public Offering at a conversion price equal to the price per share to the public of a share of Payor's Common Stock in the Initial Public Offering (rounded to the nearest whole share). For the avoidance of doubt, no fractional share would be issued.

4. Unless this Note has been converted in accordance with the terms of Section 3 above, the entire outstanding principal balance and all unpaid accrued interest shall become fully due and payable in cash on the Maturity Date.

5. Payor may prepay this Note, in whole or in part and at any time, or from time to time, prior to the Maturity Date without the consent of Holder.

6. If there is an Event of Default (as defined below), Payor shall pay all reasonable attorneys' fees and court costs incurred by Holder in enforcing and collecting this Note.

7. If there shall be any Event of Default hereunder, upon the declaration of Holder, this Note shall accelerate and all principal and unpaid accrued interest shall become due and payable. From and after the occurrence of an Event of Default, this Note shall bear interest at the rate of fifteen percent (15%) per annum, compounded annually. The occurrence of any one or more of the following shall constitute an Event of Default:

(a) Payor fails to pay any amount when due hereunder;

(b) Payor files any petition or action for relief under any bankruptcy, reorganization, insolvency or moratorium law or any other law for the relief of, or relating to, debtors, now or hereafter in effect, or makes any assignment for the benefit of creditors; or

(c) An involuntary petition is filed against Payor (unless such petition is dismissed or discharged within sixty (60) days, under any bankruptcy statute now or hereafter in effect, or a custodian, receiver, trustee, assignee for the benefit of creditors (or other similar official) is appointed to take possession, custody or control of any property of Payor.

8. Payor hereby waives demand, notice, presentment, protest and notice of dishonor.

9. This Note shall be governed by construed and under the laws of the State of Delaware, as applied to agreements among Delaware residents, made and to be performed entirely within the State of Delaware, without giving effect to conflicts of laws principles.

10. The indebtedness evidenced by this Note is subordinated in right of payment to the prior payment in full of any Senior Indebtedness in existence on the date of this Note. "**Senior Indebtedness**" shall mean, unless expressly subordinated to or made on a parity with the amounts due under this Note, all amounts due in connection with (a) indebtedness of Payor to banks, equipment lessors or other financial institutions and (b) any such indebtedness or any debentures, notes or other evidence of indebtedness issued in exchange for such Senior Indebtedness, or any indebtedness arising from the satisfaction of such Senior Indebtedness by a guarantor.

11. Any term of this Note may be amended or waived with the written consent of Payor and Holder.

Targacept, Inc.

By: _____

Name: _____

Title: _____

EXHIBIT B

SMRI REPRESENTATIONS AND WARRANTIES

1. **Purchase for Own Account**. SMRI is acquiring the Note and any securities issuable upon conversion of the Note (collectively, the "**Securities**") (i) solely for its own account and beneficial interest for investment and not for resale or with a view to distribution of the Securities or any part thereof, (ii) has no present intention of selling (in connection with a distribution or otherwise), granting any participation in, or otherwise distributing the same, and (iii) does not presently have reason to anticipate a change in such intention.

2. **Investment Experience and Qualified Institutional Buyer/Accredited Investor Status**. SMRI is a qualified institutional buyer as defined in Rule 144A promulgated under the Securities Act of 1933, as amended (the "**Securities Act**"). Without limiting the generality of the foregoing, SMRI has at least $100,000,000 invested in entities that it does not control, is not controlled by or is not under common control with. SMRI is an investor in securities of companies in the development stage and acknowledges that it is able to protect its own interests and bear the economic risk of its investment and has such knowledge and experience in financial or business matters that it is capable of evaluating the merits and risks of the investment in the Securities hereunder. SMRI believes it has received all the information it considers necessary or appropriate for deciding whether to purchase the Securities.

3. **Restricted Securities**. SMRI understands that the Securities are, or when issued, will be, restricted securities under the federal securities laws inasmuch as they are being acquired from Targacept in a transaction not involving a public offering and that under such laws and applicable regulations such securities may be resold without registration under the Securities Act only in certain limited circumstances. In this connection, SMRI is familiar with Rule 144 promulgated under the Securities Act, as presently in effect, and understands the resale limitations imposed thereby and by the Securities Act.

4. **Further Limitations on Disposition**. Without in any way limiting the representations set forth above, SMRI further represents, warrants and agrees that it will not make any disposition of all or any portion of the Securities unless:

(a) there is then in effect a registration statement under the Securities Act (a "**Registration Statement**"), covering such proposed disposition and such disposition is made in accordance with such Registration Statement;

(b) the disposition is made pursuant to Rule 144 or similar provisions of federal securities laws as in effect from time to time; or

(c) it shall have (i) notified Targacept of the proposed disposition and (ii) if requested by Targacept, furnished Targacept with an opinion of counsel, reasonably satisfactory to Targacept, that such disposition will not require registration of such Securities under the Securities Act.

5. **Restrictive Legend**. SMRI understands and agrees that all certificates evidencing the Securities may bear the following legend:

THE SECURITIES REPRESENTED HEREBY HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), AND MAY NOT BE OFFERED, SOLD OR OTHERWISE TRANSFERRED, ASSIGNED, PLEDGED OR HYPOTHECATED UNLESS (A) PURSUANT TO RULE 144 OR RULE 144A UNDER THE ACT OR (B) THERE IS AN EFFECTIVE REGISTRATION STATEMENT UNDER THE ACT COVERING SUCH SECURITIES OR (C) THE COMPANY RECEIVES AN OPINION OF COUNSEL FOR THE HOLDER OF THESE SECURITIES REASONABLY SATISFACTORY TO THE COMPANY AND ITS COUNSEL STATING THAT SUCH SALE, TRANSFER, ASSIGNMENT, PLEDGE OR HYPOTHECATION IS EXEMPT FROM THE REGISTRATION AND PROSPECTUS DELIVERY REQUIREMENTS OF THE ACT.

6. **"Stand-Off" Agreement**. SMRI, if requested by Targacept or the managing underwriter of an offering by Targacept of Common Stock or other securities of Targacept pursuant to a Registration Statement, shall agree not to sell publicly or otherwise transfer or dispose of the Securities or any securities of Targacept held by SMRI for a specified period of time (not to exceed 180 days, except under circumstances in which all other current stockholders of Targacept are similarly restricted) following the effective date of such Registration Statement.

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 January 22, 2004 (except Note 18 as to which the date is , 2004), in Amendment No. 3 to the Registration Statement (Form S-1 No. 333-115538) and related Prospectus of Targacept, Inc. dated December 15, 2004.

Ernst & Young LLP

Greensboro, North Carolina
, 2004

The forgoing consent is in the form that will be signed upon the completion of the restatement of capital accounts described in Note 18 to the financial statements.

/s/ Ernst & Young LLP

Greensboro, North Carolina
December 15, 2004