

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, D.C. 20549

**AMENDMENT NO. 6
TO
FORM S-1
REGISTRATION STATEMENT**

*Under
The Securities Act of 1933*

TARGACEPT, INC.

(Exact name of registrant as specified in its charter)

Delaware
(State or other jurisdiction
of incorporation or organization)

2834
(Primary Standard Industrial
Classification Code Number)
**200 East First Street, Suite 300
Winston-Salem, North Carolina 27101
(336) 480-2100**

56-2020050
(I.R.S. Employer
Identification Number)

(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)

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

Subject to Completion, Dated February 22, 2005



6,250,000 Shares Common Stock

This is the initial public offering of Targacept, Inc. We are offering 6,250,000 shares of our common stock. We anticipate that the initial public offering price will be between \$11.00 and \$13.00 per share. Our common stock has been approved for listing on the NASDAQ National Market under the symbol "TRGT."

Investing in our common stock involves risk. See "[Risk Factors](#)" beginning on page 8.

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

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

We have granted the underwriters the right to purchase up to 937,500 additional shares of common stock to cover over-allotments.

Deutsche Bank Securities

Pacific Growth Equities, LLC

CIBC World Markets

Lazard

The date of this prospectus is _____, 2005

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 central 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 and limit or potentially eliminate adverse side effects.

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

Cognitive Impairment

- *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 the elderly, including Alzheimer's disease and age associated memory impairment, commonly referred to as AAMI. In 2004, we completed two Phase II clinical trials of ispronicline, one in AAMI and one in mild cognitive impairment, commonly referred to as MCI. We are currently conducting a separate Phase II clinical trial of ispronicline in AAMI. We have two Phase II clinical trials of ispronicline in Alzheimer's disease planned. We expect the first of these trials, which we plan to initiate in mid-2005, to assess ispronicline as a stand-alone treatment for mild Alzheimer's disease. We expect the second of these trials, which we plan to initiate in the first quarter of 2006, to assess ispronicline as a complementary, or add-on, therapy to a currently approved treatment for mild to moderate Alzheimer's disease.
- *TC-1827*. TC-1827 is a novel small molecule that we are developing as an oral treatment for cognitive impairment associated with schizophrenia. TC-1827 is currently a preclinical product candidate. We plan to file an investigational new drug application, or IND, and initiate a Phase I clinical trial of TC-1827 in the first half of 2005.

Pain

- *TC-2696*. TC-2696 is a novel small molecule that we are developing as an oral treatment for acute post-operative pain. Depending on clinical trial results, available resources and other considerations, we may pursue development of TC-2696 for other classes of pain as well. In 2004, we completed a Phase I clinical trial of TC-2696. We plan to initiate a Phase I multiple rising dose clinical trial to further assess the safety and tolerability profile of TC-2696 in the second quarter of 2005.

Depression

- *Inversine and TC-5214.* Inversine, which we believe is the only FDA-approved product designed to target an NNR, is our only product approved by the FDA for marketing. Inversine is approved for the management of moderately severe to severe essential hypertension, a high blood pressure disorder with an unknown origin. However, we believe that Inversine is prescribed predominantly for the treatment of neuropsychiatric disorders, including Tourette's syndrome, autism and bipolar disorder. We are currently conducting a Phase II clinical trial of Inversine as an add-on therapy in patients with major depressive disorder. TC-5214 is one of the molecular components of mecamylamine hydrochloride, the active ingredient in Inversine. TC-5214 is currently a preclinical product candidate. If our ongoing Phase II clinical trial of Inversine is successful, we may accelerate the development of TC-5214 as an add-on therapy for depression.
- *TC-2216.* TC-2216 is a novel small molecule that we are developing as an oral treatment for depression and anxiety disorders. TC-2216 is currently a preclinical product candidate. In 2005, we plan to conduct the additional preclinical toxicology studies necessary to support an IND for clinical trials of TC-2216.

We also have preclinical programs for target indications outside these therapeutic areas in which we believe NNRs can be exploited for medical benefit, including schizophrenia, 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 Alzheimer's disease and other conditions marked by cognitive impairment showed therapeutic improvement when treated with a nicotine patch. We have used this clinical data, together with our deep understanding of the biological characteristics and functions of NNRs that we have built over more than 20 years, to validate NNRs as potential targets for drugs to act upon. We have also developed an expertise in designing compounds of low molecular weight, referred to as small molecules, that can selectively interact with specific NNR subtypes, with the objective of eliciting a desired effect and 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 central 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 used Pentad to design or optimize ispronicline, TC-1827, TC-2696 and TC-2216.

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

Risks Associated with Our Business

Our business is subject to numerous risks, as more fully described in the section entitled “Risk Factors” immediately following this prospectus summary. We have a limited operating history and have incurred substantial net losses since our incorporation in 1997. We expect to continue to incur substantial losses for the foreseeable future. Inversine is the only product that we have available for commercial sale, and it generates limited revenues. All of our other product candidates are undergoing clinical trials or are in early stages of development, and failure is common and can occur at any stage of development. In particular, we discontinued development of two of our product candidates, TC-5231 and TC-2403, because they failed to meet defined clinical endpoints in Phase II clinical trials that we completed in 2004. We had been developing TC-5231 as a treatment for attention deficit hyperactivity disorder and TC-2403 as a treatment for ulcerative colitis. 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	6,250,000 shares
Common stock to be outstanding after this offering	20,374,602 shares
Over-allotment option	937,500 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.
NASDAQ National Market symbol	TRGT

The number of shares of our common stock that will be outstanding immediately after this offering is based on 258,542 actual shares outstanding as of January 31, 2005, and also includes:

- 13,760,548 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; and
- 105,512 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 \$12.00 per share.

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

- 986,073 shares of common stock issuable upon the exercise of options outstanding as of January 31, 2005, at a weighted average exercise price of \$4.88 per share, of which options to purchase 588,321 shares were exercisable;
- 40,286 shares of common stock reserved for future grant under our 2000 equity incentive plan as of January 31, 2005; and
- 3,300,000 shares of common stock that will become reserved for future grant under our 2005 stock incentive plan concurrently with the completion of this offering.

Unless otherwise indicated, all information in this prospectus assumes:

- no exercise by the underwriters of their over-allotment option to purchase up to 937,500 shares of our common stock;
- the conversion of all outstanding shares of our convertible preferred stock into 13,760,548 shares of common stock concurrently with the completion of this offering;

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- the issuance of 105,512 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 \$12.00 per share; and
- no exercise of an outstanding warrant exercisable for 215,054 shares of common stock at an exercise price of \$14.63 per share that will expire if not exercised concurrently with the completion of this offering.

In addition, unless otherwise noted, all information in this prospectus gives effect to the one-for-7.5 reverse stock split of our common stock effected on February 3, 2005.

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 into 13,760,548 shares of common stock concurrently with the completion of this offering, as if the conversion had occurred at the date of the original issuance, and to the issuance of 104,167 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 \$12.00 per share, as if the conversion had occurred on the date of the original issuance.

	Year ended December 31,		
	2002	2003	2004
	(in thousands, except share and per share data)		
Statement of Operations Data:			
Net revenue	\$ 2,286	\$ 2,458	\$ 3,738
Operating expenses:			
Research and development	16,244	18,179	22,771
General and administrative	4,135	3,600	5,163
Cost of product sales	244	743	198
Purchased in-process research and development	2,666	—	—
Total operating expenses	23,289	22,522	28,132
Loss from operations	(21,003)	(20,064)	(24,394)
Interest and dividend income	88	791	505
Interest expense	(103)	(122)	(132)
Loss on disposal of fixed assets	(54)	—	(4)
Net loss	(21,072)	(19,395)	(24,025)
Deemed dividend—beneficial conversion feature for series C redeemable convertible preferred stock issued December 2004	—	—	(10,312)
Preferred stock accretion	(4,173)	(8,341)	(8,744)
Net loss attributable to common stockholders	\$ (25,245)	\$ (27,736)	\$ (43,081)
Basic and diluted net loss per share applicable to common stockholders	\$ (339.63)	\$ (254.33)	\$ (196.53)
Shares used to compute basic and diluted net loss per share	74,332	109,053	219,213
Pro forma basic and diluted net loss per share applicable to common stockholders (unaudited)			\$ (3.32)
Shares used to compute pro forma basic and diluted net loss per share (unaudited)			10,334,833

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The pro forma balance sheet information gives effect to the conversion of all outstanding shares of our convertible preferred stock into 13,760,548 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 6,250,000 shares of common stock in this offering at an assumed initial public offering price of \$12.00 per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us; and
- our issuance of 104,623 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 \$12.00 per share.

	As of December 31, 2004		
	Actual	Pro Forma (unaudited) (in thousands)	Pro Forma As Adjusted
Balance Sheet Data:			
Cash, cash equivalents and short-term investments	\$ 53,075	\$ 53,075	\$ 122,000
Working capital	50,079	50,079	117,863
Total assets	58,204	58,204	125,983
Long-term debt, net of current portion	3,443	3,443	2,193
Redeemable convertible preferred stock	171,778	—	—
Accumulated deficit	(134,754)	(109,452)	(109,266)
Total stockholders' equity (deficit)	(122,966)	48,812	117,846

RISK FACTORS

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

Risks Related to Our Financial Results and Need for Additional Financing

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

We were incorporated in 1997 and operated as a wholly owned subsidiary of R.J. Reynolds Tobacco Company until August 2000. We have a limited operating history and have incurred substantial net losses since our inception. As of December 31, 2004, we had an accumulated deficit of \$134.8 million. Our net loss was \$24.0 million for the year ended December 31, 2004 and \$19.4 million for the year ended December 31, 2003. 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 \$767,000 for the year ended December 31, 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 origin. However, we believe that the substantial majority of Inversine sales are derived from prescriptions written by a very limited number of physicians for the treatment of neuropsychiatric disorders, including Tourette's syndrome, autism and bipolar disorder, in children and adolescents. If any of these physicians were to change their prescribing habits, Inversine sales would suffer. We do not expect that sales of Inversine will increase substantially in the future.

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

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

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

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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 product candidates through the development process. It is also our objective to continue to invest in our preclinical programs and to file at least one investigational new drug application, or IND, or foreign equivalent each year beginning in 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;

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- 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. We are currently conducting a Phase II clinical trial of Inversine as an add-on therapy in patients with major depressive disorder. Other than Inversine, ispronidine is our only product candidate currently in a Phase II clinical trial, and we have not yet commenced clinical trials of ispronidine for the treatment of Alzheimer's disease. Although we have completed one Phase I clinical trial for TC-2696, our product candidate for the treatment of pain, we plan to conduct an additional Phase I clinical trial for TC-2696. We have not conducted any clinical trials for TC-1827, our product candidate for the treatment of cognitive impairment associated with schizophrenia. Our ability to generate product revenue in the future will depend heavily on the successful development and commercialization of ispronidine, TC-2696 and TC-1827. 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 five 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

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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.

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

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

To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate, through extensive preclinical studies and clinical trials, that the product candidate is safe and effective in humans. The number of clinical trials required to obtain approval varies depending on the particular product candidate, the disease or condition for which it is in development and the regulations applicable to it. Preclinical studies and clinical trials are lengthy and expensive, difficult to design and implement and subject to a historically high rate of failure. The development of each of our product candidates involves significant risks at each stage of testing. A failure of one or more of our clinical trials could occur at any stage of testing. In particular, we completed Phase II clinical trials in 2004 for TC-5231, which we had been developing for attention deficit hyperactivity disorder, and TC-2403, which we had been developing for ulcerative colitis. Because we determined that these product candidates failed to meet defined endpoints of the Phase II clinical trials, we discontinued the development of these product candidates. If we experience similar difficulties or failures in our ongoing or future clinical trials, or if we are not able to design our clinical trials with clear criteria to determine the efficacy of our product candidates, our product candidates may never be approved for sale or become commercially available.

We may not be able to obtain authority 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.

In particular, we are developing ispronicline both as a stand-alone treatment for mild Alzheimer's disease and as an add-on therapy for mild to moderate Alzheimer's disease. To assess ispronicline as an add-on therapy, we plan to conduct a Phase II clinical trial of ispronicline together with a currently approved treatment for mild to moderate Alzheimer's disease that we will select in 2005. We plan to include in the trial of ispronicline as an add-on therapy patients who have been taking the approved treatment for an extended period of time. It is possible that some or all of the patients who participate in this trial will, prior to their participation, have already derived the maximum medical benefit possible for them as a result of their extended use of the currently approved treatment. In that event, ispronicline may appear not to be effective as an add-on therapy because these patients will not be capable of deriving any additional medical benefit from further treatment. As a result, it may be particularly difficult for us to demonstrate in clinical trials that ispronicline is effective as an add-on therapy. If we are unable to demonstrate that ispronicline is effective as an add-on therapy in Alzheimer's

disease patients who are taking other medication, the FDA or foreign regulatory authorities may not grant us approval to market ispronicline as an add-on therapy for mild to moderate Alzheimer's disease.

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

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

If positive results of our completed clinical trials of ispronicline in AAMI and MCI are not replicated in future clinical trials, we will not obtain the regulatory approvals required to market and sell ispronicline.

Positive findings in preclinical studies of a product candidate may not be predictive of similar results in clinical trials in humans. In addition, positive results in early clinical trials of a product candidate may not be replicated in later clinical trials. In particular, we have completed Phase II clinical trials of ispronicline in AAMI and mild cognitive impairment, commonly referred to as MCI. In these trials, ispronicline demonstrated positive effects on cognition. However, because we designed the size and duration of dosing of our completed Phase II AAMI and MCI trials primarily to evaluate the safety of ispronicline, our findings in those trials on cognition may not be replicated in our ongoing Phase II AAMI trial or in future clinical trials of ispronicline that are designed primarily to evaluate efficacy and involve a large number of subjects and a long duration of dosing.

In addition, like most drugs, the active component of ispronicline must be combined with an inactive component to form a powder, known as a salt, that is suitable for commercialization as a pharmaceutical product. We are developing a salt form of ispronicline that is different from the salt form of ispronicline that we used in our completed trials, that we are currently using in our ongoing Phase II trial in AAMI and that we plan to use in our Phase II trial in mild Alzheimer's disease. We anticipate that we will use the new salt form in our planned Phase II trial of ispronicline as an add-on therapy for Alzheimer's disease and in future clinical trials of ispronicline. The results of our completed clinical trials of ispronicline may not be replicated in our planned Phase II clinical trial of ispronicline as an add-on therapy for Alzheimer's disease or any future clinical trial if we use a different salt form of the product candidate in that Alzheimer's disease trial or any future clinical trial.

In our completed clinical trials of ispronicline in AAMI and MCI, we used a battery of tests developed by CDR Ltd. to assess each subject's cognitive function. We are also using the CDR

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test battery in our ongoing Phase II clinical trial of ispronicline in AAMI and plan to use the CDR test battery in any future clinical trials of ispronicline in AAMI. However, if we change our plans and use an additional or a different test battery for future AAMI trials, there would be a greater risk that the results of our completed Phase I and Phase II clinical trials of ispronicline will not be replicated in those future clinical trials.

If we do not have success in our clinical trials of ispronicline for Alzheimer’s disease, we will not obtain the regulatory approvals required to market ispronicline for Alzheimer’s disease notwithstanding positive results in completed or future clinical trials of ispronicline in other indications.

We are developing ispronicline for conditions marked by various degrees of cognitive impairment in the elderly. Successful results in clinical trials of ispronicline in a condition marked by one degree of cognitive impairment may not be predictive of successful results in clinical trials of ispronicline in a condition marked by more severe cognitive impairment. In particular, we have not yet conducted any clinical trials of ispronicline in Alzheimer’s disease. Our findings in our completed Phase II trials of ispronicline in persons with AAMI or MCI may not be predictive of the effect of ispronicline on cognitive impairment in Alzheimer’s disease patients.

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

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

We are developing ispronicline for conditions marked by cognitive impairment that afflict the elderly, including Alzheimer’s disease and AAMI. Neither the FDA nor, to our knowledge, any foreign regulatory authority has approved a drug indicated for use in the treatment of AAMI. Furthermore, AAMI is not listed in the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, or DSM-IV, the manual published by the American Psychiatric Association to establish diagnostic criteria. We do not know if the FDA or any foreign regulatory authority will be willing to recognize AAMI as a distinct clinical condition, or in the FDA’s terminology, a clinical entity, for which approval of a drug is possible. If neither the FDA nor any foreign regulatory authority recognizes AAMI as a clinical entity, we will not obtain the regulatory approval required to market ispronicline for AAMI even if our clinical trials show that ispronicline is safe and provides a medical benefit for the persons treated.

When the FDA assesses whether a proposed clinical entity justifies labeling, it generally requires that the existence of the clinical entity be broadly accepted by medical experts in the relevant clinical discipline and that the clinical entity can be defined in practice. This means that the clinical entity must be able to be diagnosed using valid and reliable criteria that are widely

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accepted by those medical experts. The FDA imposes these requirements to assure that both the population for whom a drug is intended and the effects of the drug in that population can be adequately described in labeling for the drug. The FDA has informed us that it believes it is questionable whether AAMI satisfies these criteria. In a recent letter that we received from the FDA in response to our submission of the protocol for our ongoing Phase II trial of ispronidine for the treatment of AAMI, the FDA advised us that, in its view, because varying methodologies and criteria have historically been used by medical experts to define AAMI, the requisite consensus in the medical community has not been established. As a result, the FDA has informed us that it is unclear whether our Phase II clinical trial design and efficacy endpoints will measure the clinical effects appropriate for a treatment for AAMI. If we are unable to establish to the satisfaction of the FDA or foreign regulatory authorities that AAMI can be identified using criteria that are accepted in the medical community, that both the deficit in cognitive performance associated with the condition and its subsequent improvement can be measured and that the improvement is clinically meaningful, we will not obtain the regulatory approval required to market ispronidine for AAMI.

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 ispronidine in persons with MCI. In that trial, we limited the eligible

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patient population to persons whose condition was sufficiently severe to qualify for a diagnosis of MCI, but not severe enough to qualify for a diagnosis of dementia. Similarly, in our planned Phase II clinical trial of ispronicline as a stand-alone treatment for mild Alzheimer's disease and our planned Phase II clinical trial of ispronicline as an add-on therapy to a currently approved treatment for mild to moderate Alzheimer's disease, we plan to limit the eligible patient population. In our trial of ispronicline as a stand-alone treatment, we plan to limit the eligible patient population to persons diagnosed with Alzheimer's disease, but whose condition has not yet progressed from the mild stage of Alzheimer's disease to the moderate stage. In our trial of ispronicline as an add-on therapy, we plan to limit the eligible patient population to persons diagnosed with Alzheimer's disease who have been taking a stable dose of the approved treatment for between six and 18 months. As a result of these inclusion limits, we could experience delays in recruitment for one or both of these trials similar to those that we experienced in our MCI trial. In addition, our planned design of the trial of ispronicline as a stand-alone treatment would require some of the Alzheimer's disease patients to be assigned randomly into a dosing group that would receive placebo instead of ispronicline. Those patients would not receive any medication for the duration of the trial. As a result, Alzheimer's disease patients or their caregivers may be unwilling or unable to give informed consent to participate in the trial, which would result in delays in patient enrollment. Our failure to enroll patients in a clinical trial could delay the completion of the clinical trial beyond our current expectations. In addition, the FDA could require us 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.

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.

In particular, although we have conducted four Phase I clinical trials of ispronicline, we have not conducted, and do not plan to conduct, a Phase I clinical trial to evaluate the safety and tolerability of ispronicline when taken together with any other drug. The FDA may require that, before we initiate our planned Phase II clinical trial of ispronicline as an add-on therapy to a currently approved treatment for mild to moderate Alzheimer's disease, we conduct a Phase I clinical trial to evaluate the safety and tolerability of ispronicline when taken together with the approved treatment for Alzheimer's disease, which would delay and increase the cost of our clinical development of ispronicline as an add-on therapy for Alzheimer's disease.

In addition, we plan to file an IND and initiate a Phase I clinical trial of TC-1827, our product candidate for cognitive impairment associated with schizophrenia, in the first half of 2005. In one preclinical study of TC-1827 conducted with monkeys, two of ten monkeys that were given high doses of TC-1827 were found at the end of the study to have low levels of platelets in their blood, a condition known as thrombocytopenia. We plan to repeat the study in which thrombocytopenia was observed at the same time as we conduct our initial Phase I clinical trial of TC-1827. It is possible that the FDA will require that we complete the study in monkeys before commencing the Phase I trial. If the FDA were to require that we conduct the study in monkeys before we conduct Phase I clinical development of TC-1827, our development of TC-1827 for cognitive impairment associated with schizophrenia would be delayed.

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. Through 2004, we spent managerial and financial resources on clinical trials for two product candidates that we have ceased developing. We may in the future spend our resources on other research programs and product candidates for specific indications that ultimately do not yield any commercially viable products. Furthermore, if we do not

accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights.

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

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

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

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

In particular, in one preclinical study of TC-1827 conducted with monkeys, two of ten monkeys that were given high doses of TC-1827 were found at the end of the study to have low levels of platelets in their blood, a condition known as thrombocytopenia. We plan to repeat the study in which thrombocytopenia was observed in the first half of 2005. If thrombocytopenia is observed when the study is repeated, we may have to discontinue further development of TC-1827.

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

Risks Related to Our Dependence on Third Parties

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

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

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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 terminated effective 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 may pursue the development and commercialization of our product candidates, including ispronidine, 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, in 2004, Sanofi-Synthelabo 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 expired in December 2004. 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. Aventis has informed us that it does not intend to extend the research term and desires to terminate the agreement.

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;

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- 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. For example, we have a pending patent application covering the composition of TC-2216, our product candidate for depression and anxiety disorders, but currently have no issued patent that covers that product candidate. 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-2696, our product candidate for pain, and TC-5214, one of our product candidates for depression. 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 currently rely on method of use patent coverage in the United States for TC-5214, one of our product candidates for depression. If we are unable to obtain patent protection for the actual composition of any compound that we seek to develop and commercialize and must rely on method of use patent coverage, we would likely be unable to prevent others from manufacturing or marketing that compound for any use that is not protected by our patent

rights. If a third party were to receive marketing approval for the 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 marketing, our product candidates may not gain market acceptance and may fail to generate significant revenues.

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

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

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

In addition, perceptions about the relationship or similarity between our product candidates and nicotine could limit their market potential. Our product candidates derive their medical effects by interacting with NNRs. Nicotine, which can have significantly negative health effects, also interacts with NNRs. Accordingly, our product candidates may be perceived by some to be nicotine or to be closely related to nicotine, particularly in light of the shared derivative names, "nicotine" and neuronal "nicotinic" 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.

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

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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. 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 either for AAMI or for cognitive impairment associated with schizophrenia. We believe that the primary competitive products for use in the other indications that we are currently targeting include:

- for mild to moderate 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 pain, non-steroidal anti-inflammatory drugs such as Celebrex from Pfizer and opioids such as OxyContin from Purdue Pharma;
- for depression, selective serotonin reuptake inhibitors such as Prozac from Eli Lilly, Paxil from GlaxoSmithKline, Zoloft from Pfizer, Celexa and Lexapro from Forest Laboratories and the dual uptake inhibitor Effexor from Wyeth;
- for schizophrenia, anti-psychotics such as Zyprexa from Eli Lilly, Risperdal from Johnson & Johnson and Abilify from Bristol-Myers Squibb; and
- for smoking cessation, Zyban from GlaxoSmithKline.

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

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

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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 any neuropsychiatric disorder. However, if we undertake any promotional activities in the future for Inversine or any other product candidate that we are able to commercialize and our activities fail to comply with these regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities.

Risks Related to Employees and Managing Growth

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

Our performance depends substantially on the performance of our senior management and key scientific, technical and managerial personnel, including our Chief Executive Officer and President, J. Donald deBethizy, and our Vice President, Clinical Development and Regulatory Affairs, Geoffrey C. Dunbar. Our executive officers, including these individuals, can terminate

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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 previously experienced extreme price and volume fluctuations. The market prices of securities of pharmaceutical and biotechnology companies have been extremely volatile and have experienced fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. These broad market fluctuations could result in extreme fluctuations in the price of our common stock, which could cause a decline in the value of your shares.

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

The offering price of our common stock will be substantially higher than the net tangible book value of \$(480.96) per share of our existing capital stock as of December 31, 2004. As a result, based on an assumed initial public offering price of \$12.00 per share, purchasers of our common stock in this offering will incur immediate and substantial dilution of \$6.24 per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the assumed initial public offering price, and will incur \$0.04 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 20,374,602 shares of common stock outstanding based on the number of shares outstanding as of January 31, 2005. 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

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the date of this prospectus, subject to a possible extension, without the prior written consent of Deutsche Bank Securities Inc. on behalf of the underwriters. However, Deutsche Bank Securities may, in its sole discretion, release all or any portion of the common stock from the restrictions of the lock-up agreements. Deutsche Bank Securities does not have any pre-established conditions to waiving the terms of the lock-up agreements. Any determination to release any shares subject to the lock-up agreements would be based on a number of factors at the time of determination, including but not necessarily limited to the market price of the common stock, the liquidity of the trading market for the common stock, general market conditions, the number of shares proposed to be sold and the timing, purpose and terms of the proposed sale.

Additionally, of the 986,073 shares of our common stock that may be issued upon the exercise of options outstanding as of January 31, 2005, approximately 735,835 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 37.9% 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 6,250,000 shares of our common stock in this offering will be approximately \$67.8 million, or approximately \$78.2 million if the underwriters exercise their over-allotment option in full, assuming an initial public offering price of \$12.00 per share and after deducting estimated underwriting discounts and commissions and offering expenses payable by us.

We estimate that we will use:

- approximately \$25 million of these net proceeds to fund further development of ispronidine, our product candidate for conditions marked by cognitive impairment that afflict the elderly, including Alzheimer's disease and AAMI;
- approximately \$2 million of these net proceeds to fund further development of TC-1827, our product candidate for cognitive impairment associated with schizophrenia;
- approximately \$12 million of these net proceeds to fund further development of TC-2696, our product candidate for acute post-operative pain;
- approximately \$3 million of these net proceeds to complete our ongoing Phase II clinical trial of Inversine as an add-on therapy in patients with major depressive disorder;
- approximately \$2 million of these net proceeds to conduct the additional preclinical toxicology studies necessary to support an IND for clinical trials of TC-2216; and
- approximately \$24 million of these net proceeds to fund general and administrative expenses, other research and development expenses, working capital needs and other general corporate purposes.

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

The amounts and timing of our actual expenditures may vary significantly depending upon numerous factors, including the progress and status of our development and commercialization efforts, the amount of proceeds actually raised in this offering, the amount of cash generated through our existing strategic collaborations, any additional strategic collaborations into which we may enter and sales of Inversine, and our operating costs and capital expenditures. Accordingly, our management will have significant flexibility in applying the net proceeds of this offering. We may change the allocation of use of these proceeds as a result of contingencies such as the progress and results of our clinical trials and other research and development activities, the establishment of collaborations, the results of our commercialization efforts, our manufacturing requirements and regulatory or competitive developments.

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 the net proceeds from this offering will be sufficient to enable us to initiate our planned Phase II clinical trial of ispronidine as an add-on therapy for mild to moderate Alzheimer's disease and to complete our planned Phase II clinical trial of ispronidine as a stand-alone treatment for mild Alzheimer's disease, our ongoing Phase II clinical trial of ispronidine for AAMI, our planned Phase I and Phase II clinical trials of TC-2696, our ongoing Phase II clinical trial of Inversine as an add-on therapy in patients with major depressive disorder and the additional preclinical toxicology studies necessary to support an IND for clinical trials of TC-2216. We also expect that the net proceeds from this offering, together with aggregate payments of \$4.25 million that we expect to receive under our development

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agreement with The Stanley Medical Research Institute upon our achievement of specified milestones, will be sufficient to enable us to complete a Phase I clinical development program and a Phase II clinical trial of TC-1827 for cognitive impairment associated with schizophrenia. It is possible that we will not make the progress that we expect because the actual costs and timing of drug development, particularly clinical trials, are highly uncertain, are subject to substantial risk and often change depending on the target indication, the particular development strategy and the results of earlier clinical trials. As a result, we may need to raise additional funds from external sources to make the development progress described in this paragraph.

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

DIVIDEND POLICY

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

CAPITALIZATION

The following table sets forth our capitalization at December 31, 2004:

- on an actual basis;
- on a pro forma basis to give effect to the conversion of all outstanding shares of our convertible preferred stock into 13,760,548 shares of common stock concurrently with the completion of this offering; and
- on a pro forma as adjusted basis to give further effect to:
 - our sale of 6,250,000 shares of common stock in this offering at an assumed initial public offering price of \$12.00 per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us; and
 - our issuance of 104,623 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 \$12.00 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 December 31, 2004		
	Actual	Pro Forma	Pro Forma As Adjusted
	(in thousands, except share and per share data)		
Total long-term obligations	\$ 4,557	\$ 4,557	\$ 3,307
Redeemable convertible preferred stock, \$0.001 par value, 88,009,433 shares authorized, issued and outstanding actual; no shares authorized, issued or outstanding pro forma and pro forma as adjusted	171,778	—	—
Stockholders' equity (deficit):			
Common stock, \$0.001 par value, 16,666,666 shares authorized actual and pro forma; 100,000,000 shares authorized pro forma as adjusted; 256,816 issued and outstanding actual; 14,017,364 shares issued and outstanding pro forma; 20,371,987 shares issued and outstanding pro forma as adjusted	—	14	20
Preferred stock, \$0.001 par value, no shares authorized, issued or outstanding actual and pro forma; 5,000,000 shares authorized and no shares issued and outstanding pro forma as adjusted	—	—	—
Capital in excess of par value	11,574	158,036	227,092
Common stock warrants	214	214	—
Accumulated deficit	(134,754)	(109,452)	(109,266)
Total stockholders' equity (deficit)	(122,966)	48,812	117,846
Total capitalization	\$ 53,369	\$ 53,369	\$ 121,153

The table above does not include:

- 987,800 shares of common stock issuable upon exercise of options outstanding as of December 31, 2004, at a weighted average exercise price of \$4.88 per share, of which options to purchase 586,707 shares were exercisable; and
- 40,286 shares of common stock reserved for future grant under our 2000 equity incentive plan as of December 31, 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 December 31, 2004 was approximately \$(123,517,000), or approximately \$(480.96) per share, based on 256,816 shares of common stock outstanding as of December 31, 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 December 31, 2004, the pro forma net tangible book value of our common stock was approximately \$49,517,000, or approximately \$3.51 per share. Pro forma net tangible book value per share represents our total tangible assets less total liabilities divided by the pro forma number of shares of our common stock outstanding, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into 13,760,548 shares of common stock concurrently with the completion of this offering and the issuance of 104,623 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 \$12.00 per share.

Assuming the sale of the shares of our common stock offered by this prospectus at an assumed initial public offering price of \$12.00 per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us, our pro forma net tangible book value as of December 31, 2004 would have been \$117,295,000, or \$5.76 per share. This represents an immediate increase in pro forma net tangible book value of \$2.25 per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of \$6.24 per share to new investors purchasing in this offering at the initial public offering price. The following table illustrates this dilution on a per share basis:

Assumed initial public offering price per share		\$12.00
Historical net tangible book value per share		\$(480.96)
Increase attributable to the conversion of convertible preferred stock and an outstanding promissory note		484.47
		<hr/>
Pro forma net tangible book value per share before this offering		3.51
Increase per share attributable to new investors		2.25
		<hr/>
Pro forma net tangible book value per share after this offering		5.76
		<hr/>
Dilution per share to new investors		\$ 6.24

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The following table summarizes, on a pro forma basis as of December 31, 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 \$12.00 per share, before deducting estimated underwriting discounts and commissions and offering expenses payable by us.

	Shares Purchased		Total Consideration		Average Price per Share
	Number	Percent	Amount	Percent	
Existing stockholders	14,121,987	69.3%	\$149,000,000	66.5%	\$ 10.55
New investors	6,250,000	30.7%	75,000,000	33.5%	\$ 12.00
Total	20,371,987	100.0%	\$224,000,000	100.0%	

The share data in the table above is based on shares outstanding as of December 31, 2004, counting as outstanding:

- 13,760,548 shares of common stock underlying all outstanding convertible preferred stock; and
- 104,623 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 \$12.00 per share.

The share data in the table above excludes:

- 987,800 shares of common stock issuable upon the exercise of options outstanding as of December 31, 2004, at a weighted average exercise price of \$4.88 per share, of which options to purchase 586,707 shares were exercisable;
- 40,286 shares of common stock reserved for future grant under our 2000 equity incentive plan as of December 31, 2004; and
- 215,054 shares of common stock subject to an outstanding warrant with an exercise price of \$14.63 per share that will expire if not exercised concurrently with the completion of this offering.

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

- the number of shares of our common stock held by existing stockholders would decrease to approximately 66.3% 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 7,187,500 shares, or approximately 33.7% 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, 2002, 2003 and 2004 and the balance sheet data as of December 31, 2003 and 2004 from our audited financial statements included in this prospectus. We have derived the statement of operations data for the years ended December 31, 2000 and 2001 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. Our historical results for any prior period are not necessarily indicative of the results to be expected for any future period.

The pro forma net loss attributable to common stockholders per share information is computed using the weighted average number of common shares outstanding, after giving pro forma effect to the conversion of all shares of our convertible preferred stock into 13,760,548 shares of common stock concurrently with the completion of this offering, as if the conversion had occurred at the date of the original issuance, and to the issuance of 104,167 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 \$12.00 per share, as if the conversion had occurred on the date of the original issuance.

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	Year ended December 31,				
	2000	2001	2002	2003	2004
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Net revenue	\$ 2,351	\$ 1,703	\$ 2,286	\$ 2,458	\$ 3,738
Operating expenses:					
Research and development	3,675	8,152	16,244	18,179	22,771
General and administrative	1,653	2,302	4,135	3,600	5,163
Cost of product sales	—	—	244	743	198
Purchased in-process research and development	—	—	2,666	—	—
Total operating expenses	5,328	10,454	23,289	22,522	28,132
Loss from operations	(2,977)	(8,751)	(21,003)	(20,064)	(24,394)
Interest and dividend income	536	1,449	88	791	505
Interest expense	—	—	(103)	(122)	(132)
Loss on disposal of fixed assets	—	—	(54)	—	(4)
Net loss	(2,441)	(7,302)	(21,072)	(19,395)	(24,025)
Deemed dividend—beneficial conversion feature for series C redeemable convertible preferred stock issued December 2004	—	—	—	—	(10,312)
Preferred stock accretion	(981)	(3,808)	(4,173)	(8,341)	(8,744)
Net loss attributable to common stockholders	\$ (3,422)	\$ (11,110)	\$ (25,245)	\$ (27,736)	\$ (43,081)
Basic and diluted net loss per share applicable to common stockholders	\$ (229.33)	\$ (200.97)	\$ (339.63)	\$ (254.33)	\$ (196.53)
Shares used to compute basic and diluted net loss per share	14,922	55,283	74,332	109,053	219,213
Pro forma basic and diluted net loss per share applicable to common stockholders (unaudited)					\$ (3.32)
Shares used to compute pro forma basic and diluted net loss per share (unaudited)					10,334,833

	As of December 31,				
	2000	2001	2002	2003	2004
	(in thousands, except share and per share data)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	\$ 28,053	\$ 21,180	\$ 49,361	\$ 42,977	\$ 53,075
Working capital	27,654	20,371	46,685	40,526	50,079
Total assets	29,338	24,396	54,379	47,390	58,204
Long-term debt, net of current portion	—	—	2,088	1,462	3,443
Redeemable convertible preferred stock	54,418	58,365	108,026	130,134	171,778
Accumulated deficit	(27,581)	(38,691)	(63,936)	(91,672)	(134,754)
Total stockholders' equity (deficit)	(27,314)	(38,268)	(63,335)	(90,796)	(122,966)

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 our most advanced product candidates as treatments for target indications in three therapeutic areas: cognitive impairment, pain and depression. Within these areas, we have three product candidates in clinical development and three preclinical product candidates. We expect to advance one of our preclinical product candidates into clinical development in the first half of 2005. We also have multiple preclinical programs for target indications outside these areas in which we believe that NNRs can be exploited for medical benefit. We have worldwide commercialization rights for all of our product candidates. Inversine, our product candidate currently in a Phase II clinical trial as an add-on therapy in patients with major depressive disorder, is approved in the United States for moderately severe to severe essential hypertension. We believe that Inversine is the only FDA-approved product 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 December 31, 2004, we had an accumulated deficit of \$134.8 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

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of this offering as we expand our clinical trial activity, as our product candidates advance through the development cycle and as we invest in additional product opportunities and research programs. We also expect our general and administrative expenses to increase substantially due to costs associated with being a public company. Clinical trials and preclinical studies are time-consuming, expensive and may never yield a product that will generate revenue. A substantial portion of our revenue for the next several years will depend on 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, we believe that Inversine is prescribed predominantly for the treatment of neuropsychiatric disorders, including Tourette's syndrome, autism and bipolar disorder, in children and adolescents. Sales of Inversine generated revenue of \$767,000 for the year ended December 31, 2004.

We have entered into two collaboration agreements with Aventis. One of those collaboration agreements with Aventis terminated effective 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 December 31, 2004, we had received a total of \$8.0 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 expired in December 2004. 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. Aventis has informed us that it does not intend to extend the research term and desires to terminate the agreement.

In December 2004, we 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, 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.

In January 2001, we entered into a collaboration agreement with Dr. Falk Pharma GmbH covering the development and commercialization of one of our compounds for the treatment of ulcerative colitis and other gastrointestinal and liver diseases. Upon effectiveness of the collaboration agreement, Dr. Falk Pharma paid us a \$1.0 million upfront license fee and purchased \$1.0 million of our common stock. We and Dr. Falk Pharma shared the development costs for the lead compound subject to the collaboration agreement. We and Dr. Falk Pharma discontinued the development of the lead compound in the fourth quarter of 2004. There are no compounds in development under this agreement.

Critical Accounting Policies and Estimates

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

While our significant accounting policies are more fully described in Note 2 to our financial statements 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;

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- 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 \$129,700 in 2002, \$65,300 in 2003 and \$50,600 in 2004. 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.

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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 \$866,400 greater and our diluted net loss per share attributable to common stockholders would have been approximately \$3.95 greater in 2004. For more information, you should refer to Note 2 to our financial statements included at the end of this prospectus.

Financial Operations Overview

Revenue

Inversine is our only commercial product generating revenue. Sales of Inversine generated revenue of \$815,000 for the year ended December 31, 2003 and \$767,000 for the year ended December 31, 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 \$1.3 million for the year ended December 31, 2003 and \$338,000 for the year ended December 31, 2004. The research term of our continuing agreement with Aventis ended in December 2004, and we do not expect to conduct further research for which we would receive research support payments from Aventis.

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 81% of our total operating expenses for each of the years ended December 31, 2002, 2003 and 2004.

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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 ispronidine and TC-2696:

Product Candidate	Year ended December 31,		
	2002	2003	2004
Ispronidine	\$976	\$3,557	\$4,135
TC-2696	—	893	1,145
Total:	\$976	\$4,450	\$5,280

At the end of 2004, we discontinued the development of two product candidates following the completion of Phase II clinical trials. We made total payments to third parties of \$2.7 million for the year ended December 31, 2002, \$2.1 million for the year ended December 31, 2003 and \$4.3 million for the year ended December 31, 2004 in connection with these discontinued programs.

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

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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 in 2005 and subsequent years due to increased payroll,

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expanded infrastructure, increased consulting, legal, accounting and investor relations expenses associated with being a public company.

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 \$63.3 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

Years ended December 31, 2004 and December 31, 2003

Revenue. Revenue increased by \$1.2 million, or 48%, to \$3.7 million for the year ended December 31, 2004, from \$2.5 million for 2003. The increase of \$1.2 million resulted principally from the acceleration in recognition of \$1.6 million of deferred license fee revenue and an increase in grant revenue of \$646,000, partially offset by a decrease in research fee revenue of \$965,000. The acceleration in recognition of \$1.6 million of deferred license fee revenue represented the remaining unamortized balance of upfront payments that we received when we entered into collaboration agreements with Aventis and Dr. Falk Pharma and were amortizing

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over the period of our expected research obligations under the agreements. In the fourth quarter of 2004, we concluded our research obligations under our collaboration agreement with Aventis that terminated effective January 2, 2005, and under our collaboration agreement with Dr. Falk Pharma. Grant revenue increased by \$646,000 to \$717,000 in 2004 as a result of a full year of work performed under a cooperative agreement awarded to us in the third quarter of 2003 by the National Institute of Standards and Technology through its Advanced Technology Program to fund the development of sophisticated molecular simulation software. Research fee revenue decreased to \$338,000 in 2004, from \$1.3 million in 2003. The decrease of \$965,000 resulted from less activity in 2004 under our collaboration agreement with Aventis relating to Aventis compounds as we completed the research requested by Aventis. The research term of that collaboration agreement with Aventis expired on December 31, 2004. In December 2004, we entered into a development agreement with The Stanley Medical Research Institute under which we may receive up to \$4.25 million from The Stanley Medical Research Institute if we achieve specified development milestones.

Research and Development Expense. Research and development expense increased by \$4.6 million, or 25%, to \$22.8 million for the year ended December 31, 2004, from \$18.2 million for 2003. The increase was primarily attributable to the costs associated with having four product candidates in clinical trials for most of 2004, compared to only two product candidates in clinical trials for most of 2003. For the year ended December 31, 2004, we estimate that approximately 18% of our total research and development expenses were payments made to third parties in connection with our ispronicline program for conditions marked by cognitive impairment that afflict the elderly, 5% were payments made to third parties in connection with our TC-2696 program for pain and 19% were made to third parties in connection with the two discontinued clinical development programs. We spent the remaining 58% of our total research and development expenses on salaries, benefits, and infrastructure costs associated with our internal research and development capabilities, including clinical programs, preclinical programs and research efforts, and on payments to third parties in connection with preclinical programs.

General and Administrative Expense. General and administrative expense increased by \$1.6 million, or 44%, to \$5.2 million for the year ended December 31, 2004, from \$3.6 million for 2003. This increase resulted from our investment in development of the administrative infrastructure necessary to enable us to expand our operations, to support our development efforts and to fulfill the additional reporting and regulatory requirements applicable to a public company. The increase was principally attributable to increased expenses of \$705,000 related to expansion of our business development staff and an increase in spending on business development pursuits, \$431,000 of additional patent related expenses and increases in our legal and other professional fees.

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

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

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interest income will increase in 2005 as compared to 2004 as a result of the increase in our cash following completion of the sale of \$32.9 million in shares of our series C convertible preferred stock in December 2004, net of offering expenses and the completion of this offering, and higher short-term interest rates.

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

Years ended December 31, 2003 and December 31, 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 2002 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 the elderly, 5% were payments made to third parties in connection with our TC-2696 program for pain and 12% were made to third parties in connection with the two discontinued clinical development programs. 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, including clinical programs, preclinical programs and research efforts, and on payments to third parties in connection with preclinical programs.

General and Administrative Expense. General and administrative expense 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 by \$499,000 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.

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

Liquidity and Capital Resources

Sources of Liquidity

Since we became an independent company in 2000, we have financed our operations and internal growth primarily through private placements of convertible preferred stock. As of December 31, 2004, we had derived aggregate net proceeds of \$121.3 million from these private placements. We have received additional funding from upfront license fees and payments for research and development services under collaboration agreements, equipment and building lease incentive financing, government grants and interest income. As of December 31, 2004, we had received \$9.9 million under our collaboration agreements. As of December 31, 2004, we are no longer conducting research under our collaboration agreements for which we would receive any research support payments. On December 31, 2004, we received loan proceeds of \$1.25 million 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. Under that development agreement, we may receive up to an additional \$4.25 million from The Stanley Medical Research Institute if we achieve specified development milestones. 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 \$53.1 million as of December 31, 2004, \$43.0 million as of December 31, 2003 and \$49.4 million as of December 31, 2002.

Cash Flows

Net cash used for operating activities was \$25.0 million for the year ended December 31, 2004. Net cash used for operating activities for 2004 consisted primarily of a net loss of \$24.0 million, which included acceleration of recognition of deferred license fee revenue of \$1.9 million that we received when we entered into collaboration agreements with Aventis and Dr. Falk Pharma. Net cash used for operating activities was \$19.3 million for the year ended December 31, 2003, primarily reflecting a net loss occurring for this period of \$19.4 million. Net cash used 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.

Net cash used in investing activities increased to \$622,000 for the year ended December 31, 2004, from \$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 provided by financing activities was \$35.9 million for the year ended December 31, 2004, and consisted principally of \$32.9 million in net proceeds from the issuance of shares of our series C convertible preferred stock in December 2004, \$2.0 million received under an equipment financing loan facility and \$1.3 million received from The Stanley Medical Research

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Institute in return for our issuance of a convertible promissory note in an equal principal amount, partially offset by \$731,000 of principal repayments on equipment financing. As of December 31, 2004, we did not have any borrowing facility or line of credit. Net cash provided by financing activities for the year ended December 31, 2003 was \$13.4 million and consisted principally of net proceeds of \$13.8 million from the issuance of shares of our series C convertible preferred stock and proceeds of \$239,000 received in connection with the purchase of our common stock upon the exercise of stock options, partially offset by \$637,000 of principal repayments on equipment financing. 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. We borrowed \$1.0 million in April 2004 and \$973,000 in December 2004 under the amended loan facility to finance equipment. The April 2004 borrowing bears a fixed interest rate of 5.9%, is payable in 48 equal monthly installments and matures in April 2008. The December 2004 borrowing bears a fixed interest rate of 6.9%, is payable in 48 monthly installments and matures in January 2009. All borrowings under the loan facility are secured by specified tangible fixed assets. As of December 31, 2004, the outstanding principal balance under the loan facility was \$2.8 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, 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 December 31, 2004, we had an accumulated deficit of \$134.8 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;

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- 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.

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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, 2004:

Contractual Obligations	Payments due by period (in thousands)				
	Total	2005	2006- 2008	2009- 2010	After 2010
Long-term debt obligations	\$4,557	\$1,113	\$3,083	\$202	\$ 159
Operating lease obligations	3,836	1,508	2,328	—	—
Other contractual obligations	2,512	2,483	29	—	—
Total	\$10,905	\$5,104	\$5,440	\$202	\$ 159

The amounts of long-term debt reflected in the above table include the \$1.25 million convertible promissory note that we issued on December 15, 2004. The outstanding principal and accrued interest under that note will automatically convert into shares of our common stock concurrently with the completion of this offering.

The amounts of other contractual obligations reflected in the above table include obligations to purchase product candidate material contingent on the delivery of the material and to compensate clinical investigators and clinical trial sites contingent on the performance of services in connection with clinical trials. The amount of other contractual obligations for 2005 reflected in the above table also includes annual maintenance fees or other fixed payments required under our technology license agreements. Our technology license agreements are generally terminable by us on short notice. As a result, the annual maintenance fees or other fixed payments under those agreements are not included in other contractual obligations in the above table after 2005. The amounts of other contractual obligations for all periods reflected in the above table exclude contingent royalty payments that we may be required to pay under our technology license agreements and other contingent payments that we may become required to make under our technology license agreements upon achievement of specified development, regulatory or commercial milestones.

Quantitative and Qualitative Disclosures about Market Risk

The primary objective of our investment activities is to preserve our capital to fund operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of cash equivalents and short-term investments in a variety of securities of high credit quality. As of December 31, 2004, we had cash, cash equivalents and short-term investments of \$53.1 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 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

SFAS No. 123 (Revised 2004), *Share-Based Payment*, issued in December 2004, is a revision of FASB Statement 123, *Accounting for Stock-Based Compensation*, and supersedes APB Opinion No. 25, *Accounting for Stock Issued to Employees*, and its related implementation guidance. The Statement focuses primarily on accounting for transactions in which an entity obtains employee services in share-based payment transactions. SFAS No. 123 (Revised 2004) requires a public entity to measure the cost of employee services received in exchange for an award of equity instruments based on the grant-date fair value of the award, with limited exceptions. That cost will be recognized over the period during which an employee is required to provide service in exchange for the award. This statement is effective as of the beginning of the first interim or annual reporting period that begins after June 15, 2005. We have not completed our assessment as to the impact on our financial position or results of operations.

In November 2004, the FASB issued SFAS No. 151, *Inventory Costs, an amendment of ARB No. 43, Chapter 4*, which clarifies the types of costs that should be expensed rather than capitalized as inventory. This statement also clarifies the circumstances under which fixed overhead costs associated with operating facilities involved in inventory processing should be capitalized. The provisions of SFAS No. 151 are effective for fiscal years beginning after June 15, 2005 and we will adopt this standard in fiscal 2006. We have not determined the impact, if any, that this statement will have on our financial position or 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 of the central 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. 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 central nervous system by selectively affecting specific NNR subtypes.

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

Cognitive Impairment

- *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 the elderly, including Alzheimer's disease and age associated memory impairment, commonly referred to as AAMI. In 2004, we completed two Phase II clinical trials of ispronicline, one in AAMI and one in mild cognitive impairment, commonly referred to as MCI. We are currently conducting a separate Phase II clinical trial of ispronicline in AAMI. We have two Phase II clinical trials of ispronicline in Alzheimer's disease planned. We expect the first of these trials, which we plan to initiate in mid-2005, to assess ispronicline as a stand-alone treatment for mild Alzheimer's disease. We expect the second of these trials, which we plan to initiate in the first quarter of 2006, to assess ispronicline as a complementary, or add-on, therapy to a currently approved treatment for mild to moderate Alzheimer's disease. We are also evaluating potential additional clinical development of ispronicline for indications such as cognitive impairment associated with schizophrenia, cognitive impairment following coronary artery bypass grafting, MCI, attention deficit hyperactivity disorder and various forms of dementia.
- *TC-1827*. TC-1827 is a novel small molecule that we are developing as an oral treatment for cognitive impairment associated with schizophrenia under a development agreement that we entered into in December 2004 with The Stanley Medical Research Institute. TC-1827 is currently a preclinical product candidate. We plan to file an investigational new drug application, or IND, and initiate a Phase I clinical trial of TC-1827 in the first half of 2005.

Pain

- *TC-2696*. TC-2696 is a novel small molecule that we are developing as an oral treatment for acute post-operative pain. Depending on clinical trial results, available resources and

other considerations, we may pursue development of TC-2696 for other classes of pain as well. In 2004, we completed a Phase I clinical trial of TC-2696. We plan to initiate a Phase I multiple rising dose clinical trial to further assess the safety and tolerability profile of TC-2696 in the second quarter of 2005. If the results of that trial are favorable, we plan to initiate a Phase II clinical trial of TC-2696 in hysterectomy or molar extraction patients in the first half of 2006.

Depression

- *Inversine and TC-5214.* Inversine, which we believe is the only FDA-approved product designed to target an NNR, is our only product approved by the FDA for marketing. Inversine is approved for the management of moderately severe to severe essential hypertension, a high blood pressure disorder with an unknown origin. However, we believe that Inversine is prescribed predominantly for the treatment of neuropsychiatric disorders, including Tourette's syndrome, autism and bipolar disorder. We are currently conducting a Phase II clinical trial of Inversine as an add-on therapy in patients with major depressive disorder. TC-5214 is one of the molecular components of mecamylamine hydrochloride, the active ingredient in Inversine. TC-5214 is currently a preclinical product candidate. We are evaluating the development of TC-5214 as an add-on therapy for depression.
- *TC-2216.* TC-2216 is a novel small molecule that we are developing as an oral treatment for depression and anxiety disorders. TC-2216 is currently a preclinical product candidate. In 2005, we plan to conduct the additional preclinical toxicology studies necessary to support an IND for clinical trials of TC-2216.

We also have preclinical programs for target indications outside these therapeutic areas in which we believe NNRs can be exploited for medical benefit, including schizophrenia, smoking cessation and obesity.

We develop product candidates using our proprietary databases and computer-based molecular design technologies, which we refer to collectively as Pentad. Pentad relies on extensive biological data for a library of diverse compounds that we have developed and gathered over more than 20 years. 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 and limit or potentially eliminate adverse side effects. We used Pentad to design or optimize ispronicline, TC-1827, TC-2696 and TC-2216.

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.

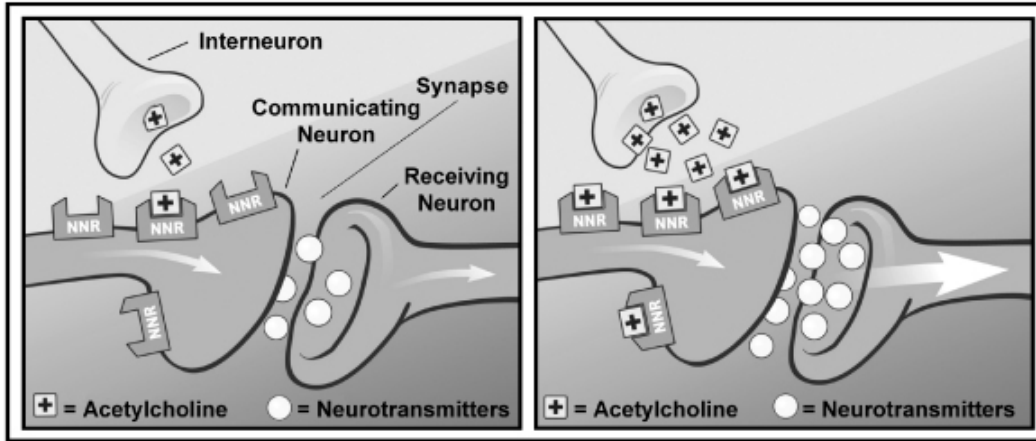
NNRs are a class of receptors found in the nervous system that play a critical role in modulating the release of neurotransmitters to regulate nervous system activity. When the

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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
$\alpha 7_5$	sensory gating; cognition	schizophrenia; cognitive impairment
$\alpha 4_2\beta 2_3$	cognition pain perception	Alzheimer’s disease; AAMI; MCI; ADHD
$\alpha 6\beta 3$	motor control	acute, chronic and neuropathic pain Parkinson’s disease

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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 $\alpha 4\beta 2$ NNR and the $\alpha 7$ 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 and limit or potentially eliminate adverse side effects.

Our Business Strategy

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

- *Develop and commercialize drugs that selectively target specific NNR subtypes.* Based on our understanding of the role of NNRs in the nervous system, we believe that drugs designed to selectively target specific NNR subtypes can have positive medical effects with limited or no adverse side effects. We use our scientific expertise and Pentad to identify compounds that selectively target specific NNR subtypes as potential treatments for diseases and disorders of the central nervous system.
- *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;
- 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 diseases and disorders. We are currently conducting clinical development of ispronicline for AAMI and TC-2696 for acute post-operative pain. We are also currently conducting a clinical trial of Inversine in patients with major depressive disorder. We plan to commence clinical trials of ispronicline for Alzheimer's disease and TC-1827 for cognitive impairment associated with schizophrenia in 2005.

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. Researchers have estimated that between 10% and 15% of persons with MCI are diagnosed

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with Alzheimer's disease each year. In addition, 80% of persons with MCI who participated in a third-party study were diagnosed with Alzheimer's disease within six years of being diagnosed with MCI.

Alzheimer's disease is a debilitating brain disorder for which there is no cure. The disease progresses in stages from mild to moderate to severe and gradually destroys a person's memory and ability to learn, reason, make judgments, communicate and carry out daily activities. Mild Alzheimer's disease is characterized by mild forgetfulness and difficulty acquiring basic information and communicating. Patients generally exhibit the symptoms of mild Alzheimer's disease for two to four years before progressing to the moderate stage. Moderate Alzheimer's disease is characterized by forgetfulness, failure to recognize friends and family, disorientation regarding time and place and personality changes. Patients generally exhibit the symptoms of moderate Alzheimer's disease for up to ten years before progressing to the severe stage. Severe Alzheimer's disease is characterized by difficulty performing simple tasks and activities associated with daily living. Patients with severe Alzheimer's disease require continuous care and generally do not survive for more than three years.

The Business Insights Healthcare Report 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. AAMI is not currently listed in *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, or DSM-IV, the manual published by the American Psychiatric Association to establish diagnostic criteria. However, DSM-IV does list the term "age related cognitive decline," which is often used by the medical community interchangeably with AAMI, as an "objectively identified decline in cognitive functioning consequent to the aging process that is within normal limits given the person's age." Although estimates of the prevalence of AAMI in the elderly vary greatly because of varying methodologies and definitions of AAMI, one published study indicates that AAMI may affect as many as 38% of people over age 65. Based on a 2000 report of the Federal Interagency Forum on Aging-Related Statistics, this represents over 13 million people in the United States alone. The Federal Interagency Forum report projects that the number of people in the United States age 65 or older will double by 2030.

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 is currently no product approved by the FDA for the treatment of AAMI. We believe that, when AAMI is treated at all, physicians typically prescribe acetylcholinesterase inhibitors. We believe that acetylcholinesterase inhibitors have limitations in that only about 25% 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.

Cognitive Impairment Associated with Schizophrenia

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

The Business Insights Healthcare Report estimates that schizophrenia affects over 9 million people in the world's seven major pharmaceutical markets, including approximately 3.7 million people in the United States. Scientists have estimated that up to 75% of schizophrenic patients are cognitively impaired. The Business Insights Healthcare Report estimates that the worldwide market for schizophrenia therapies was approximately \$9.7 billion in 2003.

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

Pain

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

According to the Business Insights Healthcare Report, the worldwide market for pain therapies was approximately \$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, another provider of business information for the pharmaceutical and other industries, 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 may result in addiction and abuse. As a result, physicians are often reluctant to prescribe opioids for an extended period of time or at all. Chronic pain is most often treated with a class of drugs known as non-steroidal anti-inflammatory drugs. These drugs are often not sufficiently effective. In a nationwide survey of over 1,000 adults conducted in the United States in August 2003, only 58% of chronic pain sufferers rated their prescription medications as very or somewhat effective. No class of drugs, including opioids and non-steroidal anti-inflammatory drugs, has demonstrated consistent effectiveness in treating neuropathic pain.

Depression

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

Datamonitor estimates that depression affects nearly 36 million people in the seven major pharmaceutical markets, including approximately 13 million people in the United States. Espicom Business Intelligence estimates that the worldwide market for depression therapies was approximately \$14.8 billion in 2003.

Depression is thought to be associated with the disruption and imbalance in the brain of the neurotransmitters dopamine, norepinephrine and serotonin. Medications currently used to treat depression, such as selective serotonin reuptake inhibitors, dual uptake inhibitors, and tricyclics, are designed to increase the levels of one or more of those neurotransmitters. However, these drugs may take two to four weeks to be effective, if at all, and may cause side effects like nausea, increased sweating, fatigue and sexual dysfunction that are experienced before any benefit. Moreover, experts have estimated that approximately 20% to 30% of patients with depression do not respond to anti-depressant medications.

Our Product Development Pipeline

We are developing our most advanced product candidates as treatments for target indications in three therapeutic areas: cognitive impairment, pain and depression. Within these areas, we have three product candidates in clinical development and three preclinical product candidates. We expect to advance one of our preclinical product candidates into clinical development in the first half of 2005. We also have multiple preclinical programs for target indications outside of these areas in which we believe that NNRs can be exploited for medical benefit. We have worldwide commercialization rights for all of our product candidates. Inversine, our product candidate currently in a Phase II clinical trial as an add-on therapy in patients with major depressive disorder, is approved in the United States for the management of moderately severe to severe essential hypertension. Except for Inversine for the treatment of hypertension, neither the FDA nor any foreign regulatory authority has approved any of our product candidates for marketing.

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The following table summarizes our product development pipeline.

<u>Area of Therapeutic Focus</u>	<u>Product Candidate</u>	<u>Target Indication</u>	<u>Status of Development</u>
Cognitive Impairment	Ispronnicline (TC-1734)	Alzheimer's disease	Phase II trial in MCI complete; two Phase II trials in Alzheimer's disease planned, one for initiation in mid-2005 and one for initiation in the first quarter of 2006
		AAMI	Initial Phase II trial complete; separate Phase II trial ongoing
	TC-1827	Cognitive impairment associated with schizophrenia	Preclinical; filing of IND and Phase I trial planned for initiation in the first half of 2005
Pain	TC-2696	Acute post-operative pain	Initial Phase I trial complete; separate Phase I trial planned for initiation in the second quarter of 2005
Depression	Inversine	Major depressive disorder	Phase II trial ongoing
	TC-5214	Depression	Preclinical
	TC-2216	Depression and anxiety disorders	Preclinical

We are currently conducting our Phase II clinical trial of ispronnicline in the United States and we have previously conducted two Phase II clinical trials of ispronnicline in the United Kingdom. We conducted our initial Phase I clinical trial of TC-2696 in France. We are currently conducting our Phase II clinical trial of Inversine in the United States. We plan to conduct a portion of this trial in India if we receive approval of a regulatory filing comparable to an IND that we have submitted.

Cognitive Impairment

We are developing two product candidates for conditions marked by cognitive impairment. We are developing ispronnicline for conditions that afflict the elderly, including Alzheimer's disease and AAMI. We are developing TC-1827 for cognitive impairment associated with schizophrenia.

Ispronnicline

Ispronnicline (TC-1734) is a novel small molecule that we are developing as an oral treatment for conditions marked by cognitive impairment that afflict the elderly, including Alzheimer's disease and AAMI. We are currently conducting a Phase II clinical trial of ispronnicline in AAMI. In 2004, we completed a Phase II clinical trial of ispronnicline in 76 elderly persons with AAMI and 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 ispronnicline in 84 healthy volunteers in four Phase I clinical trials.

While the exact causes of Alzheimer's disease, AAMI and MCI are unknown, the aging process is generally accompanied by a decline of cognitive function linked to a progressive

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

Published third-party studies have shown a reduced number of $\alpha 4\beta 2$ NNRs in persons with dementia, suggesting the involvement of $\alpha 4\beta 2$ in cognition. In our preclinical animal studies, ispronicline triggered activity of $\alpha 4\beta 2$, 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 $\alpha 4\beta 2$, we believe that ispronicline has the potential to prevent or delay neurodegeneration.

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

In addition to Alzheimer's disease and AAMI, we are evaluating potential additional clinical development of ispronicline for indications such as cognitive impairment associated with schizophrenia, cognitive impairment following coronary artery bypass grafting, MCI, attention deficit hyperactivity disorder 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 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

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exemption, the United Kingdom equivalent to an IND. The primary objective of this trial was to assess the safety and tolerability of ispronicline in elderly subjects compared to placebo. The secondary objectives of this trial were to assess the efficacy of ispronicline in improving cognitive function and changes in mood state.

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

In the AAMI trial, the subjects were divided into four 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 50mg, 100mg and 125mg arms of the AAMI trial, ispronicline was well tolerated, with no serious adverse events reported. 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. Because of these side effects, we ceased dosing new subjects at 150mg.

We used a computer-based test battery developed by CDR Ltd. in the AAMI and MCI trials to test for changes in cognitive function. 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. These measures are then used to make composite assessments on the following five factors:

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

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.

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Compared to subjects who received placebo, subjects in the 50mg dose group who received ispronicline showed improvements on four of the five factors: power of attention; continuity of attention; episodic memory and speed of memory. These results were statistically significant. 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. In the 50mg dose group, the power of attention factor had a p-value of 0.020, the continuity of attention factor had a p-value of 0.043, the episodic memory factor had a p-value of 0.010, and the speed of memory factor had a p-value of 0.008. These effects were consistent with the effects seen in our Phase I trials. Subjects in the 50mg dose group who received placebo performed better than subjects who received ispronicline on the working memory factor.

The positive effects that we observed in the 50mg dose group were less pronounced in the other dose groups. In the 100mg dose group, we observed improvement on the episodic memory factor. The result was statistically significant with a p-value of 0.049. In the 125mg dose group, we observed improvements on two of the factors. The result on the working memory factor, with a p-value of 0.038, was statistically significant. The other factor on which we observed improvement in the 125mg dose group was episodic memory, which had a p-value of 0.078. Subjects in the 100mg and 125mg dose groups who received placebo performed better than subjects who received ispronicline on the speed of memory factor. For those subjects in the 150mg dose group who completed the trial, improvements were shown on four of the factors. The results on the continuity of attention factor, with a p-value of 0.049, and the speed of memory factor, with a p-value of 0.018, were statistically significant. The other factors on which we observed improvement in the 150mg dose group were power of attention, with a p-value of 0.088, and working memory, with a p-value of 0.094. The results of the AAMI trial suggest that ispronicline is well tolerated at a dose range of up to 125mg, that 150mg is the maximum tolerated dose of ispronicline for this trial design and that the compound had positive effects on cognition at all tolerated doses tested.

To generate additional data related to the tolerability of ispronicline, we also tested eight elderly persons classified with AAMI at a dose of 150mg, after having eaten, using the same trial design. This enabled us to assess the impact of food on the tolerability of ispronicline by comparing it in subjects dosed at 150mg who had eaten and in subjects dosed at 150mg who had not eaten. As we expected, the results indicated that the 150mg dose of ispronicline was better tolerated in subjects who had eaten than in subjects who had not eaten. All but one of the subjects in the dose group who had eaten completed the trial, and we observed no serious adverse events. In addition, improvements were shown in this dose group on three of the CDR factors. The results on the continuity of attention factor, with a p-value of 0.029, and the speed of memory factor, with a p-value of 0.036, were statistically significant. The other factor on which we observed improvement in this dose group was episodic memory, which had a p-value of 0.079.

As in the AAMI trial, ispronicline was well tolerated in the MCI trial, with only one serious adverse event reported. A subject who had a history of an abnormally slow heart rate lost consciousness and was hospitalized approximately one-and-one-half weeks following the end of the dosing phase of the trial. We do not believe that this adverse event was related to ispronicline. Subjects in the 100mg dose group of the trial showed improvements on four of the CDR factors. The results on the power of attention factor, with a p-value of 0.042, and the episodic memory factor, with a p-value of 0.044, were statistically significant. The other factors on which we observed improvement in the 100mg dose group were working memory, with a p-value of 0.070, and speed of memory, with a p-value of 0.100. Subjects in the 50mg dose group

of the trial who received ispronicline did not show improvement and subjects who received placebo performed better than subjects who received ispronicline on the working memory and speed of memory factors.

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

We plan to initiate a double-blind, placebo controlled Phase II clinical trial of ispronicline for the treatment of mild Alzheimer's disease in mid-2005. We expect to include in the trial approximately 250 patients who were recently diagnosed with Alzheimer's disease for the first time, who have not previously taken medication for Alzheimer's disease and who score within specified ranges on the Mini-Mental Status Exam and the global Clinical Dementia Rating scale, standardized tests often used to characterize the severity of Alzheimer's disease. The co-primary outcome measures of the trial will be an updated 13-item version of the Alzheimer's Disease Assessment Scale-cognitive subscale, or ADAS-Cog, the measure most often used to assess the efficacy of drugs for Alzheimer's disease, and a subject global improvement scale. The updated version of ADAS-Cog contains three more items than the original version of ADAS-Cog. The additional three items are designed to enhance the sensitivity of the measure for evaluation of less impaired patients. We also plan to include a cognitive test battery in the trial as a secondary measure. We expect the results of the trial to be available in the second half of 2006.

In addition, we plan to initiate a double-blind, placebo controlled Phase II clinical trial of ispronicline as an add-on therapy to a currently approved treatment for mild to moderate Alzheimer's disease in the first quarter of 2006. We expect to include in this trial approximately 450 patients who have previously been diagnosed with Alzheimer's disease and have been taking a stable dose of the approved treatment for between six and 18 months. The co-primary outcome measures of the trial will be the original version of ADAS-Cog and the Clinician's Interview Based Impression of Change, which is a commonly used rating scale in which the investigator makes a global assessment of change in an Alzheimer's disease patient's condition based on clinical interviews of the patient, information provided by patient's caregiver and any testing of the patient that has been conducted. We expect the results of the trial to be available in the second half of 2007.

Plans for Future Development in AAMI. We are currently conducting a Phase II clinical trial to assess the efficacy of ispronicline in AAMI. The trial is designed to provide additional evidence that ispronicline improves cognitive performance in cognitively impaired elderly persons. We are conducting the trial at multiple sites in the United States. The trial design provides for 174 subjects with AAMI to be dosed once daily for 16 weeks with either ispronicline or a placebo. Those subjects dosed with ispronicline will receive 25mg for the first two weeks of

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the dosing phase, 37.5mg for the next two weeks and 50mg for the remaining 12 weeks. There are three co-primary efficacy endpoints for the trial:

- improvement on the power of attention factor of the CDR test battery as compared to placebo;
- improvement on the episodic memory factor of the CDR test battery as compared to placebo; and
- improvement in subject global impression, a standard seven-point overall cognitive improvement scale in which each subject rates himself on attention, memory and speed of thinking.

In addition, we will assess each subject's change from baseline on a number of other tests and scales as secondary endpoints. Also, to obtain additional information regarding the correlation between the amount of ispronicline present in the body and the compound's effects, we will make pharmacokinetic assessments at various points during the trial. We expect the results of the trial to be available in the first quarter of 2006.

In a recent letter that we received from the FDA in response to our submission of the protocol for our ongoing Phase II trial of ispronicline for the treatment of AAMI, the FDA informed us that it believes it is questionable whether AAMI satisfies the criteria necessary for AAMI to be recognized as a distinct clinical condition. However, we believe that the results of our Phase II clinical trials of ispronicline in AAMI and MCI and the neuroprotective effect that we observed in preclinical in vitro studies of ispronicline suggest the potential of ispronicline as an early treatment for progressive cognitive impairment. Based on feedback that we have received from researchers whom we believe to be leaders in this medical area and our belief that acceptance of the possibility and viability of a treatment for cognitive impairment associated with normal aging is emerging in the medical community, we believe that AAMI is an indication that the FDA may be willing to recognize in the future. While our Phase II clinical trial for AAMI is ongoing, we plan to consult with the FDA regarding the potential of AAMI as a distinct clinical condition for which the FDA would approve a drug. Based on the results of our Phase II AAMI trial and our planned consultation with the FDA, we will evaluate the continued clinical development of ispronicline for the treatment of AAMI. Even if the FDA were to be unwilling to recognize AAMI as a distinct clinical condition, we believe that our ongoing Phase II AAMI trial, if successful, would benefit us in our efforts to gain marketing approval of ispronicline for Alzheimer's disease by further establishing the safety profile of ispronicline and further demonstrating its cognitive effects in an expanded number of cognitively impaired elderly persons.

Additional Clinical Support. We are developing a salt form of ispronicline that is different from the salt form that we used in our completed trials, that we are currently using in our ongoing Phase II trial in AAMI and that we plan to use in our Phase II trial in mild Alzheimer's disease. We believe that the new salt form will cost less to make than the current salt form. We also believe that the new salt form will be more soluble than the current salt form, which could result in an improved pharmacokinetic profile. We plan to initiate a bioequivalence study designed to determine the dose of the new salt necessary to achieve the presence in the blood of the same amount of ispronicline as specified doses of the current salt in the second quarter of 2005. The study will include between six and eight healthy volunteers. We anticipate that we will use the new salt form of ispronicline in our Phase II trial of ispronicline as an add-on therapy for Alzheimer's disease that we plan to initiate in the first quarter of 2006 and in future clinical trials of ispronicline.

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In addition, we plan to initiate a clinical trial designed to determine the extent of any interaction between ispronicline and donepezil hydrochloride, which is marketed as Aricept and currently the leading treatment for mild to moderate Alzheimer's disease, in the second quarter of 2005. The trial will include between six and eight healthy volunteers. In the trial, we will assess the amounts of ispronicline and donepezil in the blood and make routine safety assessments. We will select the approved treatment with which we will conduct our planned Phase II clinical trial of ispronicline as an add-on therapy for Alzheimer's disease based in part on the results of this trial.

TC-1827

TC-1827 is a novel small molecule that we are developing as an oral treatment for cognitive impairment associated with schizophrenia under a development agreement that we entered into in December 2004 with The Stanley Medical Research Institute. We plan to file an IND and commence a Phase I clinical trial of TC-1827 in the first half of 2005.

In our preclinical in vitro studies, we found TC-1827 to be a potent activator of the $\alpha 4\beta 2$ NNR and to avoid interaction with nicotinic acetylcholine receptors in the muscles and ganglia that are associated with side effects. Published third-party studies in humans and animals have shown that compounds that act on $\alpha 4\beta 2$ have positive effects on cognition.

In our preclinical animal studies conducted under our terminated collaboration agreement with Aventis, TC-1827 demonstrated improvement in a variety of cognitive measures, including attention and vigilance and working memory. In a 2004 survey of 46 neuroscientists and neuropharmacologists conducted in connection with a National Institute of Mental Health schizophrenia initiative, deficits in attention and vigilance and working memory were identified as the most important cognitive deficits in schizophrenia. In other preclinical animal studies conducted under our agreement with Aventis, TC-1827 continued to demonstrate improvement following repeated oral administration without resulting in tolerance and was rapidly absorbed.

In one preclinical study conducted with monkeys, two of ten monkeys given high doses of TC-1827 were found at the end of the study to have low levels of platelets in their blood, a condition known as thrombocytopenia. Because TC-1827 was evaluated in several different preclinical studies involving a total of four different species and thrombocytopenia was seen only in one study with monkeys, we believe that the thrombocytopenia may have been caused by a viral infection in the particular monkeys used in the study. We plan to repeat the study in monkeys in which thrombocytopenia was observed at the same time as we initiate clinical development of TC-1827.

Plans for Future Development. We plan to file an IND and initiate a initial Phase I clinical trial of TC-1827 in the first half of 2005. We also plan to repeat the study of TC-1827 in monkeys described above at the same time as we conduct our initial Phase I trial. If the results of the Phase I trial and the study in monkeys are favorable, we expect to conduct additional Phase I clinical trials and, if the results of those trials are favorable, to conduct a Phase II clinical trial of TC-1827 for the treatment of cognitive impairment associated with schizophrenia.

Pain

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

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 a Phase I clinical trial of TC-2696. 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. In these studies, the compound was rapidly absorbed and demonstrated an acceptable toxicology profile.

In our preclinical in vitro studies of TC-2696, we found the compound to be a potent activator of the $\alpha_4\beta_2$ 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 $\alpha_4\beta_2$ have pain-relieving effects in animals. We believe these effects are caused in part by the activation of NNRs that are abundant in CNS pathways to block the transmission of pain signals to the brain. In contrast, opioids act through a different mechanism of action. In our preclinical animal studies, TC-2696 did not result in tolerance following repeated administration. This suggests a potential advantage of TC-2696 compared to existing treatments for acute post-operative pain.

Clinical Development of TC-2696

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

We included a surrogate measure in our Phase I clinical trial of TC-2696 to provide an indication of the potential efficacy of this product candidate as a treatment for pain. The surrogate measure involved the use of a metal probe, which emitted increasing amounts of heat. We asked participants to indicate when the heat became painful. We then assessed the amount of heat that was necessary at various time intervals following dosing with TC-2696 for participants to feel pain versus the amount of heat that was necessary for participants dosed with placebo to feel pain. Using this measure, we observed a drug effect in participants at one or more intervals in each of the 5mg, 10mg, 50mg and 150mg dose groups.

Plans for Future Development. We plan to initiate a Phase I multiple rising dose clinical trial to further assess the safety and tolerability profile of TC-2696 in the second quarter of 2005. If the results of trial are favorable, we plan to initiate a Phase II clinical trial of TC-2696 in hysterectomy or molar extraction patients in the first half of 2006.

Depression

We are currently conducting a clinical trial of Inversine as an add-on therapy in patients with major depressive disorder. In addition, we have two preclinical product candidates for depression, TC-5214, which is one of the molecular components of Inversine, and TC-2216, which we are developing both for depression and for anxiety disorders.

Inversine and TC-5214

Inversine is currently our only marketed product. Inversine is approved in the United States for the management of moderately severe to severe essential hypertension. We believe that

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

Preliminary results of a clinical trial conducted by researchers at Yale University and reported in 2004 showed that mecamylamine hydrochloride, the active ingredient in Inversine, had anti-depressant effects in patients who were not fully responding to fluoxetine hydrochloride, a commonly prescribed anti-depressant marketed as Prozac, when used as an add-on therapy to fluoxetine hydrochloride as compared to when patients were treated with fluoxetine hydrochloride and a placebo. In addition, in a third-party preclinical study published in 2004, rats lacking the $\beta 2$ NNR subunit did not respond to a known anti-depressant. We believe that this study suggests a correlation between abnormal $\beta 2$ activity and depression. We also believe that Inversine may act to normalize the activity of $\beta 2$. Based in part on these results, we initiated a clinical trial of Inversine as an add-on therapy to citalopram hydrobromide, a commonly prescribed anti-depressant marketed as Celexa, in patients with major depressive disorder. We are currently conducting the trial in the United States. We plan to conduct a portion of the trial in India if we receive approval of a regulatory filing comparable to an IND that we have submitted. The trial design provides for enrollment of 150 patients with major depressive disorder who have not responded, or who have only partially responded, to citalopram hydrobromide therapy. The primary efficacy endpoint of the trial is improvement on the Hamilton Rating Scale, an accepted rating scale for depression, as compared to placebo. We expect the results of the trial to be available in the first quarter of 2006.

TC-5214 is one of the enantiomers of mecamylamine hydrochloride. Enantiomers are chemical substances that are mirror images of each other and have the same chemical but different biological properties. We have licensed from the University of South Florida Research Foundation rights under a pending patent application that, if issued, would provide us with coverage for the composition of TC-5214 for use as a pharmaceutical and for the use of the enantiomer in the treatment of depression and other indications. TC-5214 has shown anti-depressant effects in several preclinical rodent models. If our ongoing Phase II clinical trial of Inversine as an add-on therapy for major depressive disorder is successful, we may accelerate the development of TC-5214 as an add-on therapy for depression.

TC-2216

TC-2216 is a novel small molecule that we are developing as an oral treatment for depression and anxiety disorders. Depression and anxiety disorders often occur together, and anti-depressants are often also used to treat anxiety disorders. In our preclinical studies, TC-2216 showed greater potency than, and anti-depressant effects comparable to, selective serotonin reuptake inhibitors and tricyclics, which are commonly used treatments for depression. In other preclinical studies that we conducted, TC-2216 showed anxiety-relieving effects. In addition, in our preclinical in vitro studies, we found TC-2216 to act on the $\alpha 4\beta 2$ NNR to inhibit the release of neurotransmitters that are involved in mood and to avoid interaction with nicotinic acetylcholine receptors in the muscles and ganglia that are associated with side

effects. In 2005, we plan to conduct the additional preclinical toxicology studies necessary to support an IND for clinical trials of TC-2216.

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

Recent Clinical Developments

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

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

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 preclinical research programs for schizophrenia, smoking cessation and obesity, in addition to our preclinical product candidates for depression. 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 $\alpha 7$ NNR and schizophrenia. In a 2004 survey of 46 cognitive neuroscientists and neuropharmacologists conducted in connection with a National Institute of Mental Health schizophrenia initiative, $\alpha 7$ 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 $\alpha 4\beta 2$ 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 $\alpha 7$ and others are designed to interact selectively with both $\alpha 7$ and $\alpha 4\beta 2$. In addition, as described above, we are developing our proprietary compound TC-1827, which interacts selectively with $\alpha 4\beta 2$, for the treatment of the cognitive impairment associated with schizophrenia.

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 $\beta 2$ NNR may be involved. These studies have shown that selectively blocking $\beta 2$ reduced the rewarding effects of nicotine in mice. Other studies have shown that mice deficient in $\beta 2$ 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 more than 20 years. To date, we have applied Pentad specifically in the discovery and optimization of NNR-targeted therapeutics, but we believe it has application to a wide range of targets.

Pentad's virtual screening enables us to more rapidly identify clinically-viable compounds than we believe could be achieved using traditional laboratory synthesis and screening methods. This allows us to reduce drug development time by focusing our resources on compounds that we believe have a greater likelihood of clinical success. We used Pentad to design or optimize ispronidine, TC-1827, TC-2696 and TC-2216.

Our use of Pentad to design new classes of compounds selective for the $\alpha 7$ NNR is another 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 $\alpha 7$ 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 terminated effective January 2, 2005. We also have a development agreement with The Stanley Medical Research Institute. In addition, we have a collaboration agreement with Dr. Falk Pharma GmbH.

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 any patent rights that claim methods or materials used for evaluating designated Aventis compounds and our know-how, excluding Pentad, to develop and commercialize those 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 under the agreement upon the achievement of specified pre-commercialization development and regulatory milestones related to Alzheimer's disease and up to \$8 million under the agreement 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

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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. The research term of the agreement expired in December 2004. We are only eligible to receive milestone payments and royalties from Aventis for any compounds that are selected for further development within six months after the expiration of the research term. Aventis has informed us that it does not intend to extend the research term and desires to terminate the agreement. As a result of research progress previously made under the agreement, we do not believe that the agreement is terminable by Aventis. We are currently in discussions with Aventis regarding the status of this agreement.

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 ispronidine, for the treatment or prevention of Alzheimer's disease. This agreement terminated effective January 2, 2005. As a result, we may 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 $\alpha 4\beta 2$ or $\alpha 7$ 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.

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

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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, 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.

Dr. Falk Pharma GmbH

In January 2001, we entered into a collaborative research, development and license agreement with Dr. Falk Pharma covering the development and commercialization of one of our compounds for the treatment of ulcerative colitis and other gastrointestinal and liver diseases. Upon the 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 and Dr. Falk Pharma have discontinued the development of the lead compound subject to the collaboration agreement after we determined that it failed to meet defined efficacy endpoints in a Phase II clinical trial. There are no compounds in development under this agreement.

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 January 31, 2005, our patent estate includes 60 patents issued in the United States, three patent applications allowed in the United States and not yet issued, 22 patent applications

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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. The actual protection afforded by a patent varies from country to country and depends upon many factors, including the type of patent, the scope of its coverage and the availability of legal remedies in a particular country.

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

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

<u>Area of Therapeutic Focus</u>	<u>Product Candidate</u>	<u>Patent Scope</u>	<u>Patent Expiration</u>
Cognitive Impairment	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
	TC-1827	Composition of matter for a family of compounds that includes TC-1827	April 2016
		Method of use of TC-1827 for treatment of CNS disorders, including schizophrenia	June 2018
Pain	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
Depression	Inversine	Methods of use of mecamylamine for nicotine-responsive psychiatric disorders, including depression	September 2017
	TC-5214	Methods of use of S-mecamylamine for neuropsychiatric disorders, including depression	December 2019

For TC-2216, our product candidate for depression and anxiety disorders, we have a patent application pending in the United States that claims the composition of TC-2216.

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

License Agreements

We are parties to 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 mecamlamine hydrochloride and other specified compounds. The licensed patents and patent applications include an issued patent covering methods of use for the treatment of depression, attention deficit hyperactivity disorder, Tourette's syndrome and nicotine-responsive neuropsychiatric disorders and pending patent applications covering the pharmaceutical composition of the molecular components of mecamlamine 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;

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- 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-1827, TC-2696 and other earlier-stage compounds in our portfolio. These patents were subsequently assigned by RJR to us in August 2000. Under the sponsored research agreement and a subsequent license agreement with UKRF, we are obligated to pay royalties to UKRF 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

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

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

clinical trials. We will ultimately depend on contract manufacturers for the manufacture of our products for commercial sale, as well as for process development. Contract manufacturers are subject to extensive governmental regulation.

Third parties currently manufacture Inversine and its active ingredient for us. Also, we have entered into a development and production agreement with Siegfried Ltd. Under this agreement, Siegfried has agreed to provide us with process development services and clinical trial material at specified rates for product candidates that we elect to introduce into the agreement. We have also agreed, following marketing approval or anticipated marketing approval of any product candidate for which Siegfried performs services under the agreement, to negotiate for a separate multi-year commercial supply agreement with Siegfried for a substantial percentage of our contracted supply needs for that product candidate, except in limited circumstances. 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-Synthelabo, Memory Pharmaceuticals, Critical Therapeutics and NeuroSearch A/S. We expect to face increased competition in the future if NNR-targeted therapeutics are further validated and if companies initiate or grow NNR-based programs or otherwise enter the CNS market.

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

- for mild to moderate 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 pain, non-steroidal anti-inflammatory drugs such as Celebrex from Pfizer and opioids such as OxyContin from Purdue Pharma;

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- for depression, selective serotonin reuptake inhibitors such as Prozac from Eli Lilly, Paxil/Seroxar from GlaxoSmithKline, Zoloft from Pfizer, Celexa from Forest Laboratories and Lexapro from Forest Laboratories and the dual uptake inhibitor Effexor from Wyeth;
- for schizophrenia, anti-psychotics such as Zyprexa from Eli Lilly, Risperdal from Johnson & Johnson and Abilify from Bristol-Myers Squibb; and
- for smoking cessation, Zyban from GlaxoSmithKline.

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

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

Government Regulation

Drug Regulation in the United States

The research, 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.

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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

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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 January 31, 2005, we had 72 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 exercisable until March 31, 2006 to lease additional space in this facility. The term of our lease expires August 1, 2007, and we have a renewal option for an additional five-year term. If we elect to renew the lease, we will have rights to lease additional space in this facility during the renewal term. The current monthly payment under our lease is approximately \$123,000. We believe that our leased facilities, together with our rights to lease additional space, are adequate to satisfy our current needs.

Legal Proceedings

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

MANAGEMENT

Executive Officers and Directors

The name, age and position of our executive officers and directors as of January 31, 2005 are as follows:

<u>Name</u>	<u>Age</u>	<u>Position</u>
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.	50	Vice President, Preclinical Research
Jeffrey P. Brennan	47	Vice President, Business and Commercial Development
William S. Caldwell, Ph.D.	51	Vice President, Drug Discovery and Development
Geoffrey C. Dunbar, M.D.	57	Vice President, Clinical Development and Regulatory Affairs
Alan A. Musso	43	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)	50	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 Icoria, 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.

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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., Pharmion Corporation and Inhibitex, Inc.

Charles A. Blixt has been a member of our board of directors since August 2000. Since January 1998, he has been executive vice president and general counsel of R.J. Reynolds Tobacco Company. Since June 1999, he has 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

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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 Icoria, 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.

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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 first annual meeting of stockholders following January 1, 2005;
- Class II, for a term expiring at the second annual meeting of stockholders following January 1, 2005; and
- Class III, for a term expiring at the third annual meeting of stockholders following January 1, 2005.

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

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- 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 3,333 shares of our common stock upon his or her initial election to our board of directors. Additionally, upon each non-employee director's annual reelection, he or she has been granted a nonqualified stock option to purchase 1,000 shares of common stock. However, our chairman received a nonqualified stock option to purchase 4,666 shares upon his or her initial election and a nonqualified stock option to purchase 1,666 shares upon his or her annual reelection. Each of these options:

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

In lieu of any such nonqualified stock option, each non-employee director could elect to receive a restricted stock award for the same number of shares of stock at a purchase price of \$0.08 per share. Each non-employee director 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.

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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 "Management—Stock Option and Other Compensation Plans—2005 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 2003 and 2004. We refer to these officers in this prospectus as our named executive officers.

Summary Compensation Table

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

(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 us in September 2003.

(4) Consists of our contribution of \$12,190 under our 401(k) plan and reimbursement of \$99,558 in relocation expenses.

(5) Salary amount includes compensation of \$1,731 in lieu of accrued vacation.

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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, 2004.

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 (2)	
					5%	10%
J. Donald deBethizy, Ph.D.	5,867 (1)	9.0%	\$ 5.63	1/26/2014	\$ 81,669	\$ 149,550
Merouane Bencherif, M.D., Ph.D.	—	—	—	—	—	—
Jeffrey P. Brennan	1,200 (1)	1.8	5.63	1/26/2014	16,704	30,588
William S. Caldwell, Ph.D.	2,588 (1)	4.0	5.63	1/26/2014	36,025	65,968
Geoffrey C. Dunbar, Ph.D.	3,948 (1)	6.1	5.63	1/26/2014	54,956	100,635
Alan A. Musso	2,880 (1)	4.4	5.63	1/26/2014	40,090	73,411

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

Option Exercises and Year-End Option Values

The following table sets forth information regarding the number of shares of our common stock issued upon option exercises by our named executive officers during the year ended December 31, 2004 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, 2004. There was no public trading market for our common stock as of December 31, 2004. 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

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and an assumed fair market value of our common stock as of December 31, 2004 equal to an assumed initial offering price of \$12.00 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, 2004		Value of Unexercised In-the-Money Options at December 31, 2004	
			Exercisable	Unexercisable	Exercisable	Unexercisable
J. Donald deBethizy, Ph.D.	53,223	\$ 67,031	124,700	127,291	\$ 868,013	\$ 878,308
Merouane Bencherif, M.D., Ph.D.	—	—	68,646	36,596	510,211	252,512
Jeffrey P. Brennan	—	—	11,422	11,111	78,184	76,666
William S. Caldwell, Ph.D.	—	—	67,028	31,398	497,684	216,651
Geoffrey C. Dunbar, Ph.D.	22,603	11,867	50,603	41,143	347,087	283,894
Alan A. Musso	1,600	840	52,051	38,705	357,639	267,067

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 2005, the base salary of Dr. deBethizy is \$310,000; the base salary of Dr. Dunbar is \$264,316; the base salary of Mr. Brennan is \$234,000; the base salary of Mr. Musso is \$205,000; the base salary of Dr. Bencherif is \$200,000; and the base salary of Dr. Caldwell is \$185,000.

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

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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 January 31, 2005, an aggregate of 1,228,888 shares of common stock had been authorized for issuance under our 2000 plan, of which options to purchase an aggregate of 986,073 shares of common stock were outstanding at a weighted average exercise price of \$4.88 per share, 13,000 shares of common stock were issued and outstanding in the form of restricted stock and 40,286 shares of common stock were available for future grant. Upon completion of this offering, 84,246 shares of common stock subject to unvested options outstanding as of January 31, 2005 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.

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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

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become immediately vested and exercisable because steps have been taken, such as the assumption of the awards or substitution of substantially equivalent awards by the other party, as it deems equitable to protect the rights of participants in our 2000 plan. Upon completion of this offering, all awards outstanding under our 2000 plan granted prior to August 20, 2003 will become immediately vested and exercisable.

Termination and Amendment. We may grant awards under our 2000 plan until August 21, 2010, unless our 2000 plan is terminated prior to that date. The board of directors may amend or terminate our 2000 plan at any time, subject to the rights of holders of outstanding awards. Our 2005 stock incentive plan, which we refer to as our 2005 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.

2005 Stock Incentive Plan

Introduction. Our 2005 plan is intended to serve as the successor equity incentive program to our 2000 plan. Our 2005 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 2005 plan and no further options will be granted under our 2000 plan.

Subject to adjustments as provided in our 2005 plan, the maximum number of shares that we may issue pursuant to awards granted under our 2005 plan may not exceed the sum of (i) 3,300,000 shares, plus (ii) up to 40,286 shares of common stock remaining available for issuance as of the effective date under our 2000 plan, plus (iii) up to 986,073 shares subject to any award granted under our 2000 plan that is forfeited, cancelled, terminated, expires or lapses for any reason without the issuance of shares pursuant to the award. The maximum number of shares of common stock that we may issue under our 2005 plan pursuant to the grant of incentive stock options is 4,326,359 or, if less, the maximum number of shares issuable under the 2005 plan. In addition, (i) we may not grant to any participant options and stock appreciation rights, or SARs, that are not related to an option for more than 500,000 shares of common stock in any calendar year; (ii) we may not grant to any participant awards for more than 500,000 shares of common stock in any calendar year; and (iii) participants may not be paid more than \$1,000,000 with respect to any cash-settled award granted in any calendar year, subject to adjustments as provided in our 2005 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 2005 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 2005 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.

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We may adjust the number of shares reserved for issuance under our 2005 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 2005 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 2005 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 2005 plan. In this discussion, we refer to our board of directors and the compensation committee collectively as the administrator. Under the terms of our 2005 plan, the administrator has full and final authority to take any action with respect to our 2005 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 2005 plan; (iii) establish, amend and rescind rules and regulations for the administration of our 2005 plan; and (iv) construe and interpret our 2005 plan, awards and award agreements made under the 2005 plan, interpret rules and regulations for administering the 2005 plan and make all other determinations deemed necessary or advisable for administering the 2005 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 2005 plan with respect to such awards.

Our board of directors may amend, alter or terminate our 2005 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 2005 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 amend the 2005 plan and any award, without participant consent and, except where required by applicable law, rule or regulation, without stockholder approval, in order to comply with applicable laws, rules or regulations or changes to such laws, rules or regulations. In addition, the administrator has the authority to make adjustments to awards upon the occurrence of certain unusual or nonrecurring events, if the administrator determines that such adjustments are appropriate in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under our 2005 plan or necessary or appropriate to comply with applicable laws, rules or regulations. The administrator may (subject to any requirements imposed by Section 409A of the Internal

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Revenue Code or related regulations or other guidance) cause any award or any portion of an award granted under our 2005 plan to be cancelled in consideration of an alternative award or cash payment of an equivalent cash value, as determined by the administrator, made to the holder of the cancelled award. The administrator also may determine, in its discretion, that a participant's rights, payments and/or benefits with respect to an award, including but not limited to any shares issued or issuable and/or cash paid or payable with respect to an award, will be subject to reduction, cancellation, forfeiture or recoupment upon the occurrence of certain specified events, in addition to any otherwise applicable vesting or performance conditions of an award. Subject to the requirements of Internal Revenue Code Section 409A or related regulations or guidance, the administrator also may, in its sole discretion, modify or extend the terms and conditions for exercise, vesting or earning of an award and/or accelerate the date that any award which was not otherwise exercisable, vested or earned may become exercisable, vested or earned, in whole or in part, without any obligation to accelerate such date with respect to any other award.

Options. Our 2005 plan authorizes the grant of both incentive stock options and nonqualified stock options, both of which are exercisable for shares of common stock, although incentive stock options may only be granted to our employees. The administrator will determine the option price at which a participant may exercise an option, and the option price must be:

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

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

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

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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 or service. The administrator has authority to establish other terms and conditions related to options.

Director Options. Each non-employee director who is first elected or appointed to our board of directors after the public offering date will receive an initial option to purchase 25,000 shares of common stock on the fifth business day after such director is first elected or appointed to our board of directors. A non-employee director who is first elected or appointed as chairman of the board also will receive an initial option for 10,000 shares. In addition, we will grant to each non-employee director, on an annual basis commencing with the 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 if the director is in service on that date. The option period of a director option is 10 years. Director options are also subject to certain restrictions on exercise if the director's service on our board of directors terminates. The administrator also has authority to establish other terms and conditions related to director options.

Stock Appreciation Rights. Under the terms of our 2005 plan, we may grant SARs to the holder of an option with respect to all or a portion of the shares of common stock subject to the option or we may grant SARs separately. The holder of an SAR may receive consideration paid either (i) in cash; (ii) shares of common stock valued at fair market value on the date of the SAR exercise; or (iii) a combination of cash and shares of common stock, as the administrator determines. Upon exercise of an SAR, a participant is entitled to receive from us consideration in an amount determined by multiplying:

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

Notwithstanding the foregoing, the administrator may limit the amount payable in its discretion. The base price may be no less than 100% of the fair market value per share of the common stock on the date the SAR is granted. To the extent required by Internal Revenue Code Section 409A and related regulations and guidance, (i) SARs will be settled solely for shares of our common stock, which is traded on an established securities market, and will not include any feature for the deferral of compensation other than the deferral of recognition of income until exercise; or (ii) SARs will be structured in a manner designed to be exempt from, or to comply with, the requirements of Internal Revenue Code Section 409A.

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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 2005 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 2005 plan and the discretion of the administrator.

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

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

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

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

Subject to the terms of the 2005 plan and the requirements of Internal Revenue Code Section 409A and related regulations and guidance, the administrator has authority to

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determine whether and to what degree restricted awards have vested and been earned and are payable. The administrator also may, subject to Internal Revenue Code Section 409A or related regulations or guidance, accelerate the date that any restricted award will be deemed vested or earned, without any obligation to accelerate such date with respect to other restricted awards. If a participant's employment or service is terminated for any reason and all or any part of a restricted award has not vested or been earned pursuant to the terms of our 2005 plan and the individual award, the participant will forfeit the award unless the administrator determines otherwise.

Performance Awards. Subject to the limitations of our 2005 plan, the administrator may in its discretion grant performance awards to such eligible individuals upon such terms and conditions and at such times as the administrator shall determine. Performance awards may be in the form of performance shares and/or performance units. An award of a performance share is a grant of a right to receive shares of our common stock, the cash value thereof or a combination thereof in the administrator's discretion, which is contingent upon the achievement of performance or other objectives during a specified period and which has a value on the date of grant equal to the fair market value of a share of our common stock. An award of a performance unit is a grant of a right to receive shares of our common stock or a designated dollar value amount of common stock that is contingent upon the achievement of performance or other objectives during a specified period, and that has an initial value determined in a dollar amount established by the administrator at the time of grant.

Subject to the terms of the 2005 plan and the requirements of Internal Revenue Code Section 409A and related regulations and guidance, the administrator has the authority to determine the nature, length and starting date of the period during which a participant may earn a performance award and will determine the conditions that must be met in order for a performance award to be granted or to vest or be earned. These conditions may include specific performance objectives, continued service or employment for a certain period of time, or a combination of such conditions. In the case of performance awards based on performance criteria, the administrator will determine the performance measures applicable to such awards, which performance measures may be based upon such corporate, business unit or division and/or individual performance factors and criteria as the administrator in its discretion may deem appropriate; provided, however, that such performance factors will be limited to the specific performance measures listed below.

The administrator has authority to determine whether and to what degree performance awards have been earned and are payable. The administrator also may, subject to Internal Revenue Code Section 409A or related regulations or guidance, accelerate the date that any performance award will be deemed to be earned in whole or in part, without any obligation to accelerate such date with respect to other performance awards. If a participant's employment or service is terminated for any reason and all or part of a performance award has not been earned pursuant to the terms of our 2005 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 2005 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.

Subject to the terms of the 2005 plan and the requirements of Internal Revenue Code Section 409A and related regulations and guidance, the administrator has the authority to

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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 2005 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 2005 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 2005 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 2005 plan, and unless an award agreement provides otherwise or Internal Revenue Code Section 409A or related regulations or guidance requires otherwise, our 2005 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, under certain conditions, our 2005 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 2005 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 are not generally transferable, including by sale, assignment, pledge or hypothecation, other than by will or the laws of intestate succession, and participants may not sell, transfer, assign, pledge or otherwise encumber shares subject to such awards until the restriction period and/or performance period has expired and until all conditions to vesting and/or earning the award have been met.

General Federal Income Tax Consequences. Under current federal laws, in general, recipients of awards and grants of nonqualified stock options, SARs, restricted stock, dividend equivalents, performance awards and stock payments under our 2005 plan are taxable under the Internal Revenue Code upon their actual or constructive receipt of common stock or cash with respect to such awards or grants and, subject to Section 162(m) of the Internal Revenue

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Code and certain reporting requirements, we will be entitled to an income tax deduction with respect to the amounts taxable as ordinary income to such recipients. Under Sections 421 and 422 of the Internal Revenue Code, recipients of incentive stock options are generally not taxed on their receipt of common stock upon their exercises of incentive stock options if the option stock is held for specified minimum holding periods and, in such event, we would not be entitled to income tax deductions with respect to such exercises. If Internal Revenue Code Section 409A is deemed to apply to the 2005 plan or any award, and the 2005 plan and award do not, when considered together, satisfy the requirements of Section 409A during a taxable year, the participant will have ordinary income on the amount of all deferrals subject to Section 409A in the year of non-compliance to the extent that the award is not subject to a substantial risk of forfeiture. The participant will be subject to an additional tax of 20 percent on all amounts includible in income and may also be subject to interest charges under Section 409A. Subject to Section 162(m) of the Internal Revenue Code and certain reporting requirements, we will be entitled to an income tax deduction with respect to the amount of compensation includible as income to the participant.

Internal Revenue Code Section 409A Requirements. The 2005 plan is intended to comply with Section 409A of the Internal Revenue Code and related regulations and other guidance. To the extent that Section 409A is deemed to apply to the 2005 plan or any award, the 2005 plan and all such awards will, to the extent practicable, be construed in accordance with Section 409A. Section 409A imposes certain requirements on compensation that is deemed under Section 409A to involve deferred compensation. The 2005 plan imposes certain conditions upon awards that may be subject to Section 409A. These include (but are not limited to) the following:

- Deferrals of shares issuable pursuant to options, SARs settled in shares, restricted awards or other awards otherwise exempt from Section 409A in a manner that would cause 409A to apply are not permitted.
- Awards that are deemed to involve the deferral of compensation under Section 409A are subject to additional restrictions (if and to the extent required under Section 409A):
 - Distributions may not be made earlier than upon the occurrence of one or more of the following: (i) separation from service; (ii) disability; (iii) death; (iv) a specified time or fixed schedule; (v) a change in control (as defined under Section 409A); or (vi) unforeseeable emergency.
 - Distributions to certain “key employees” (as defined in Section 409A of the Internal Revenue Code, related regulations or other guidance) due to separation from service may not be made for six months after termination (or, if earlier, upon death).
 - Acceleration of the time or schedule of payments due to awards subject to Section 409A is not permitted, unless permitted by the administrator and Section 409A and related guidance.
 - Distributions generally must be made within two and one-half months after the year in which an award is no longer subject to a substantial risk of forfeiture (unless otherwise permitted under the 2005 plan or by Section 409A or related guidance).
 - Deferral elections must generally be made (if at all) in the year before the year in which services for an award are performed (subject to certain exceptions permitted under the 2005 plan or Section 409A or related guidance). Additional restrictions apply to changes to deferral elections.

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Performance-Based Compensation—Section 162(m) Requirements. Our 2005 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 2005 plan to covered employees. Section 162(m) of the Internal Revenue Code generally denies an employer a deduction for compensation paid to covered employees, who are generally the named executive officers, of a publicly held corporation in excess of \$1,000,000 unless the compensation is exempt from the \$1,000,000 limitation because it is performance-based compensation.

In order to qualify as performance-based compensation, we must pay the compensation under our 2005 plan to covered employees under pre-established objective performance goals that a committee comprised of outside directors determines and certifies. In addition to other requirements for the performance-based exception (and subject to certain exceptions), Section 162(m) generally requires that companies disclose to stockholders, and stockholders approve, the material terms or changes in material terms of the performance goals under which compensation is to be paid. Material terms include the individuals eligible to receive compensation, a description of the business criteria on which the performance goals are based, and either the maximum amount of the compensation to be paid or the formula used to calculate the amount of compensation if the performance goals are met.

As proposed, our 2005 plan limits the maximum amount of awards that we may grant to any employee. In particular, (i) we may not grant to any participant options and SARs that are not related to an option for more than 500,000 shares of common stock in any calendar year; (ii) we may not grant to any participant awards for more than 500,000 shares of common stock in any calendar year; and (iii) we may not pay to any participant more than \$1,000,000 in cash with respect to awards granted in any single calendar year. Further, with respect to performance-based restricted awards and performance awards, and in some cases, certain other types of awards, payable to covered employees that are intended to be eligible for the compensation limitation exception available under Section 162(m) and related regulations, our 2005 plan limits performance measures to one or more of the following: cash flow, return on equity, return on assets, earnings per share, achievement of clinical development or regulatory milestones, operations expense efficiency milestones, consolidated earnings before or after taxes (including earnings before interest, taxes, depreciation and amortization), net income, operating income, book value per share, return on investment, return on capital, improvements in capital structure, expense management, profitability of an identifiable business unit or product, maintenance or improvement of profit margins, stock price or total stockholder return, market share, revenues or sales, costs, working capital, economic wealth created, strategic business criteria, efficiency ratios, achievement of division, group, function or corporate financial, strategic or operational goals and comparisons with stock market indices or performances of metrics of peer companies.

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

Targacept Retirement Savings Plan—401(k) Plan

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

Limitation of Liability and Indemnification

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

- a breach of the director's duty of loyalty to us or our stockholders;
- an act or omission not in good faith or involving intentional misconduct or a knowing violation of law;
- an improper distribution to stockholders; or
- a transaction from which the director derived an improper personal benefit.

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

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Since 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 41,258 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.

<u>Name</u>	<u>Number of Shares of Common Stock</u>	<u>Aggregate Purchase Price</u>
J. Donald deBethizy, Ph.D.	18,050	\$ 135
Merouane Bencherif, M.D., Ph.D.	7,736	58
William S. Caldwell, Ph.D.	7,736	58
Patrick M. Lippiello, Ph.D.	7,736	58

On August 8, 2002, we issued 6,333 shares of restricted stock to Mr. Skaletsky for an aggregate purchase price of \$475. On June 11, 2003, we issued 1,666 shares of restricted stock to Mr. Skaletsky for an aggregate purchase price of \$125. On October 15, 2004, we issued 1,666 shares of restricted stock to Mr. Skaletsky for an aggregate purchase price of \$125.

On April 18, 2003, we issued 3,333 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 215,054 shares of common stock at an exercise price of \$34.88 per share. As a result of price protection provisions contained in the warrant, the exercise price was reduced to \$14.63 per share upon our issuance of shares 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 0.133 shares 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 215,054 shares of common stock and receive cash proceeds of approximately \$3.1 million.

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.

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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.

<u>Name</u>	<u>Number of Shares of Series B Preferred Stock</u>	<u>Aggregate Purchase Price</u>
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 1,326,496 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.

<u>Name</u>	<u>Number of Shares of Series C Preferred Stock</u>	<u>Aggregate Purchase Price</u>
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 5,050,936 shares of our common stock concurrently with the completion of this offering.

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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.

<u>Name</u>	<u>Number of Shares of Series C Preferred Stock</u>	<u>Aggregate Purchase Price</u>
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 3,178,571 shares of our common stock concurrently with the completion of this offering.

Dr. Barrett, one of our directors, is a general partner of NEA Partners 10, Limited Partnership, the general partner of New Enterprise Associates 10, Limited Partnership, which is an affiliate of New Enterprise Associates. 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 that we had previously purchased. The borrowing bears a fixed interest rate of 6.6%, is payable in 48 equal monthly installments and matures in May 2006. In January 2004, we amended the terms of our loan facility to permit us to borrow up to an additional \$2.0 million in 2004 in up to three separate borrowings. Each borrowing would bear a fixed interest rate equal to a theoretical four-year U.S. Treasury Rate on the disbursement date plus 3.5%, be payable in 48 equal monthly installments and be secured by specified tangible fixed assets that the lender determined to be sufficient at the time of disbursement. We borrowed \$1.0 million in April 2004 and \$973,000 in December 2004 under the amended loan facility to finance equipment. The April 2004 borrowing bears a fixed interest rate of 5.9%, is payable in 48 equal monthly installments and matures in April 2008. The December 2004 borrowing bears a fixed interest rate of 6.9%, is payable in 48 equal monthly installments and matures in January 2009. All borrowings under the loan facility are secured by specified tangible fixed assets. We believe that the terms of the loan facility are no less favorable than those that we could have obtained from an unaffiliated third party. As of December 31, 2004, the outstanding principal balance under the loan facility was \$2.8 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 year ended December 31, 2004, we continued to use only the copy and printing services and paid \$79,000 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 January 31, 2005 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 January 31, 2005 through the exercise of any warrant, stock option or other right. Unless otherwise indicated, the address of all listed stockholders is c/o Targacept, Inc., 200 East First Street, Suite 300, Winston-Salem, North Carolina 27101. Each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned (1)	
		Before Offering	After Offering
5% Stockholders	2,920,999	20.8%	14.3%
Entities affiliated with New Enterprise Associates (2) 1119 St. Paul Street Baltimore, Maryland 21202			
Entities affiliated with EuclidSR Partners, L.P. (3) 45 Rockefeller Plaza, Suite 3240 New York, New York 10111	1,886,162	13.4%	9.3%
Entities affiliated with Nomura Phase4 Ventures Limited (4) Nomura House 1 St. Martin's-le-Grand London EC1A 4NP England	2,136,904	15.2%	10.5%
Entities affiliated with Oxford Bioscience Partners (5) 222 Berkeley Street, Suite 1650 Boston, Massachusetts 02116	897,189	6.4%	4.4%
R.J. Reynolds Tobacco Holdings, Inc. (6) 401 North Main Street Winston-Salem, North Carolina 27102	1,127,378	7.9%	5.5%
Entities affiliated with Burrill & Company LLC (7) One Embarcadero Center, Suite 2700 San Francisco, California 94111	783,395	5.6%	3.8%
Entities affiliated with Advent Private Equity Fund II (8) 25 Buckingham Gate London SW1E 6LD England	712,586	5.1%	3.5%

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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)	241,471	1.7%	1.2%
Merouane Bencherif, M.D., Ph.D. (10)	85,163	*	*
Jeffrey P. Brennan (11)	12,756	*	*
William S. Caldwell, Ph.D. (12)	83,072	*	*
Geoffrey C. Dunbar, M.D. (13)	84,710	*	*
Alan A. Musso (14)	69,901	*	*
Mark Skaletsky	9,666	*	*
M. James Barrett, Ph.D. (15)	2,920,999	20.8%	14.3%
Charles A. Blixt (16)	1,127,378	7.9%	5.5%
G. Steven Burrill (17)	783,395	5.6%	3.8%
Errol B. De Souza, Ph.D. (18)	3,333	*	*
Elaine V. Jones, Ph.D. (19)	1,886,162	13.4%	9.3%
John P. Richard (20)	4,333	*	*
Alan G. Walton, Ph.D. (21)	897,189	6.4%	4.4%
All executive officers and directors as a group (14 persons) (22)	8,209,536	55.8%	37.9%

* Indicates less than one percent.

- (1) Our calculation of the percentage of shares of common stock beneficially owned before this offering is based on 14,019,090 shares of our common stock and common stock equivalents outstanding as of January 31, 2005, 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 20,374,602 shares of common stock to be outstanding after this offering, including the 6,250,000 shares that we are selling in this offering and our issuance of 105,512 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 \$12.00 per share.
- (2) Includes 2,913,512 shares owned of record by New Enterprise Associates 10, Limited Partnership, for which voting and investment power is shared by M. James Barrett, Peter J. Barris, C. Richard Kramlich, Peter T. Morris, Charles W. Newhall, III, Mark W. Perry, Scott D. Sandell and Eugene A. Trainor, III, each of whom is a general partner of NEA Partners 10, Limited Partnership, the general partner of New Enterprise Associates 10, Limited Partnership; 3,154 shares owned of record by NEA Ventures 2002, Limited Partnership, for which voting and investment power is held by its general partner, Pamela J. Clark; and 4,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005 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 1,509,401 shares owned of record by, and 5,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005 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 Partners, L.P., the general partner of EuclidSR Partners, L.P.; and 371,428 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 1,190,476 shares owned of record by Nomura International plc and 946,428 shares owned of record by Nomura Phase4 Ventures LP. Nomura Phase4 Ventures Limited, as appointee of Nomura International plc and as manager of Nomura Phase4 Ventures LP, has voting and investment power over the shares held by Nomura International plc and Nomura Phase4 Ventures LP. Mr. Yoshiki Hashimoto, the Head of Merchant Banking, Nomura International plc, and Dr. Denise Pollard-Knight, the Head of Nomura Phase4 Ventures, are the only two members of the board of directors of Nomura Phase4 Ventures Limited and both of them, acting together,

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- exercise the voting and investment power of Nomura Phase4 Ventures Limited. Mr. Hashimoto exercises these powers in his capacity as director of Nomura Phase4 Ventures Limited and as Head of Merchant Banking, Nomura International plc. Mr. Hashimoto and Dr. Pollard-Knight disclaim beneficial ownership of these shares.
- (5) Includes 883,987 shares owned of record by Oxford Bioscience Partners IV L.P. and 8,869 shares owned of record by mRNA Fund II L.P., for which voting and investment power is shared by Alan G. Walton, Jonathan J. Fleming, Jeffrey T. Barnes, Mark P. Carthy and Michael Lytton, each of whom are general partners of OBP Management IV L.P., the sole general partner of Oxford Bioscience Partners IV L.P. and mRNA Fund II L.P.; and 4,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005 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 4,230 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005 and 215,054 shares issuable upon the exercise of an outstanding warrant, assuming that the warrant is exercised in full for cash. Voting and investment power is held by 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 778,062 shares owned of record by Burrill Biotechnology Capital Fund, L.P., for which voting and investment power is shared by G. Steven Burrill, John H. Kim, Roger E. Wyse, 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 5,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005 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 260,685 shares owned of record by Advent Private Equity Fund II 'A' Limited Partnership; 158,989 shares owned of record by Advent Private Equity Fund II 'B' Limited Partnership; 236,693 shares owned of record by Advent Private Equity Fund II 'C' Limited Partnership; and 56,219 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 147,636 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005.
- (10) Includes 77,428 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005.
- (11) Consists of 12,756 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005.
- (12) Includes 75,337 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005.
- (13) Includes 62,108 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005.
- (14) Includes 67,368 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005.
- (15) Includes 2,913,512 shares owned of record by New Enterprise Associates 10, Limited Partnership, for which voting and investment power is shared by M. James Barrett, Peter J. Barris, C. Richard Kramlich, Peter T. Morris, Charles W. Newhall, III, Mark W. Perry, Scott D. Sandell and Eugene A. Trainor, III, each of whom is a general partner of NEA Partners 10, Limited Partnership, the general partner of New Enterprise Associates 10, Limited Partnership; 3,154 shares owned of record by NEA Ventures 2002, Limited Partnership, for which voting and investment power is held by its general partner, Pamela J. Clark; and 4,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005 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.

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- (16) Includes 4,230 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005 and 215,054 shares issuable upon the exercise of an outstanding warrant, assuming that the warrant is exercised in full for cash. Voting and investment power is held by 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 778,062 shares owned of record by Burrill Biotechnology Capital Fund, L.P., for which voting and investment power is shared by G. Steven Burrill, John H. Kim, Roger E. Wyse, 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 5,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005 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 January 31, 2005.
- (19) Includes 1,509,401 shares owned of record by, and 5,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005 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 371,428 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 1,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005.
- (21) Includes 883,987 shares owned of record by Oxford Bioscience Partners IV L.P. and 8,869 shares owned of record by mRNA Fund II L.P., for which voting and investment power is shared by Alan G. Walton, Jonathan J. Fleming, Jeffrey T. Barnes, Mark P. Carthy and Michael Lytton, each of whom are general partners of OBP Management IV L.P., the sole general partner of Oxford Bioscience Partners IV L.P. and mRNA Fund II L.P.; and 4,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005 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 470,528 shares of common stock issuable upon exercise of stock options exercisable within 60 days of January 31, 2005 and 215,054 shares issuable upon the exercise of an outstanding warrant, assuming that the warrant is exercised in full for cash.

DESCRIPTION OF CAPITAL STOCK

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

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

As of January 31, 2005, we had outstanding:

- 258,542 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 January 31, 2005, 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 215,054 shares of common stock at an exercise price of \$14.63 per share.

All of our outstanding shares of preferred stock will convert into 13,760,548 shares of common stock concurrently with the completion of this offering. In addition, the convertible promissory note will convert into 105,512 shares of common stock concurrently with completion of this offering based on an assumed initial public offering price of \$12.00 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 215,054 shares of common stock and receive cash proceeds of approximately \$3.1 million.

Common Stock

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

Preferred Stock

Upon completion of this offering, our board of directors will be authorized, without stockholder approval, to issue up to an aggregate of 5,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, designation and powers granted to or imposed upon the preferred stock, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences. We cannot state with certainty the actual effects of the issuance of any shares of preferred stock upon the rights of holders of common stock until the board of directors determines the specific rights of the holders of the preferred stock. Some of these effects might potentially include:

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

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

Options

As of January 31, 2005, options to purchase 986,073 shares of common stock at a weighted average exercise price of \$4.88 per share were outstanding.

Registration Rights

After this offering, holders of approximately 13,971,611 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

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proper procedures are not followed. These provisions may also discourage or deter a potential acquirer from conducting a solicitation of proxies to elect the acquirer's own slate of directors or otherwise attempting to obtain control of us.

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

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

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

Transfer Agent and Registrar

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

NASDAQ National Market

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

SHARES ELIGIBLE FOR FUTURE SALE

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

Upon completion of this offering, we will have outstanding 20,374,602 shares of common stock, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into 13,760,548 shares of common stock concurrently with the completion of this offering, and our issuance of 105,512 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 \$12.00 per share.

All of the 6,250,000 shares sold in this offering will be freely tradable without restriction unless purchased by our “affiliates,” as that term is defined in Rule 144 under the Securities Act. The remaining 14,124,602 shares of common stock to be outstanding after this offering are “restricted securities” under Rule 144. Substantially all of these restricted securities will be subject to the 180-day lock-up period described below. Immediately after the 180-day lock-up period, 3,448,482 shares will be freely tradable under Rule 144(k) or Rule 701(g)(3) under the Securities Act and 6,642,062 shares will be eligible for resale under Rule 144 or Rule 701(g)(3), subject to volume limitations.

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

Rule 144

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

- 1% of the number of shares of common stock then outstanding, which will equal approximately 203,746 shares immediately after this offering; or
- the average weekly trading volume of the common stock on the NASDAQ National Market during the four calendar weeks preceding the filing of a notice on Form 144 with respect to the sale.

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

Rule 144(k)

Subject to the lock-up agreements described below, shares of our common stock eligible for sale under Rule 144(k) may be sold immediately after the completion of this offering. In general, under Rule 144(k), a person may sell shares of common stock acquired from us immediately

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after the completion of this offering, without regard to manner of sale, notice, availability of public information or volume, if:

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

Rule 701

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

Lock-up Agreements

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

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

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

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

Stock Options

After the completion of this offering, we intend to file a registration statement on Form S-8 under the Securities Act to register all of the shares of common stock subject to issuance upon exercise of outstanding options granted under, or reserved for future issuance under, our 2000 plan and our 2005 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 January 31, 2005, options to purchase 986,073 shares of common stock were outstanding under our 2000 plan with a weighted average exercise price of \$4.88 per share, of which approximately 588,321 were vested and exercisable with a weighted average exercise price of \$4.65 per share and an additional 40,286 shares were reserved for issuance under our 2000 plan. Upon completion of this offering, those shares reserved under our 2000 plan plus an additional 3,300,000 shares of common stock will become reserved for issuance under our 2005 plan.

Registration Rights

Upon completion of this offering, the holders of approximately 13,971,611 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."

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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 Deutsche Bank Securities on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus:

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

whether any transaction described above is to be settled by delivery of shares of our common stock or such other securities, in cash or otherwise.

The 180-day restricted period described in the preceding paragraph will be extended if:

- during the last 17 days of the 180-day restricted period we issue an earnings release or material news or a material event relating to our company occurs; or
- prior to the expiration of the 180-day restricted period, we announce that we will release earnings results during the 16-day period beginning on the last day of the 180-day period,

in which case the restrictions described in the preceding paragraph will continue to apply until the expiration of the 18-day period beginning on the issuance of the earnings release or the occurrence of the material news or material event.

These restrictions do not apply to:

- the sale of shares to the underwriters;
- the issuance by us of shares of our common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus of which the underwriters have been advised in writing;
- the issuance by us of shares or options to purchase shares of our common stock pursuant to our 2000 plan or our 2005 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.

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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 \$1,975,000.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell more shares than they are obligated to purchase under the underwriting agreement, creating a short position. A short sale is covered if the short position is no greater than the number of shares available for purchase by the underwriters under the over-allotment option. The underwriters can close out a covered short sale by exercising the over-allotment option or purchasing shares in the open market. In determining the source of shares to close out a covered short sale, the underwriters will consider, among other things, the open market price of shares compared to the price available under the over-allotment option. The underwriters may also sell shares in excess of the over-allotment option, creating a naked short position. The underwriters must close out any naked short position by purchasing shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the common stock in the open market after pricing that could adversely affect investors who purchase in this offering. In addition, to stabilize the price of the common stock, the underwriters may bid for, and purchase, shares of common stock in the open market. Finally, the underwriting syndicate may reclaim selling concessions allowed to an underwriter or a dealer for distributing the common stock in this offering, if the syndicate repurchases previously distributed common stock in transactions to cover syndicate short positions or to stabilize the price of the common stock. Any of these activities may stabilize or maintain the market price of the common stock above independent market levels. The underwriters are not required to engage in these activities, and may end any of these activities at any time.

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

We and the underwriters have agreed to indemnify each other against certain liabilities, including liabilities under the Securities Act.

Directed Share Program

At our request, the underwriters have reserved for sale, at the initial public offering price, up to 187,500 shares offered by this prospectus to directors, officers, employees and other individuals associated with us and members of their respective families and friends through a directed share program. The number of shares of our common stock available for sale to the general public in the offering will be reduced to the extent these persons purchase these reserved shares. Any reserved shares not purchased by these persons will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus.

Pricing of the Offering

Prior to the offering, there has been no public market for our common stock. The initial public offering price will be determined by negotiations between us and the representatives. Among the factors to be considered in determining the initial public offering price of the shares will be our future prospects and those of our industry in general, our sales, earnings and other financial operating information in recent periods, and the price-earnings ratios, price-sales ratios, market prices of securities and financial and operating information of companies engaged in activities similar to ours. The estimated initial public offering price range set forth on the cover page of this preliminary prospectus is subject to change as a result of market conditions and other factors.

LEGAL MATTERS

Certain legal matters with respect to the validity of the shares of common stock offered hereby will be passed upon for us by Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts and by Womble Carlyle Sandridge & Rice, PLLC, Winston-Salem, North Carolina. Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York, has acted as counsel for the underwriters in connection with certain legal matters related to this offering.

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, have audited our financial statements as of December 31, 2004 and 2003 and for each of the three years in the period ended December 31, 2004, 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. 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, 2003 and 2004, 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, 2004. 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 consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Targacept, Inc. at December 31, 2003 and 2004, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2004, in conformity with U.S. generally accepted accounting principles.

/S/ ERNST & YOUNG LLP

February 4, 2005
Greensboro, North Carolina

TARGACEPT, INC.
BALANCE SHEETS

	December 31,		Pro forma Stockholders' equity as of December 31, 2004 (unaudited)
	2003	2004	
ASSETS			
Current assets:			
Cash and cash equivalents	\$ 11,609,157	\$ 53,075,348	
Short-term investments	31,367,500	—	
Research fees and accounts receivable	818,618	484,565	
Inventories	118,520	102,640	
Prepaid expenses and accrued interest receivable	514,552	1,727,836	
Total current assets	44,428,347	55,390,389	
Property and equipment, net	2,373,035	2,262,698	
Intangible assets, net of accumulated amortization of \$53,499 and \$91,263 at December 31, 2003 and 2004, respectively	588,501	550,737	
Total assets	\$ 47,389,883	\$ 58,203,824	
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)			
Current liabilities:			
Accounts payable	\$ 1,246,975	\$ 1,854,138	
Accrued expenses	1,406,778	1,940,836	
Current portion of long-term debt	576,072	1,113,350	
Current portion of deferred rent incentive	402,647	402,647	
Current portion of deferred license fee revenue	269,537	—	
Total current liabilities	3,902,009	5,310,971	
Long-term debt, net of current portion	1,461,554	3,443,297	
Deferred rent incentive, net of current portion	1,040,171	637,524	
Deferred license fee revenue, net of current portion	1,647,687	—	
Total liabilities	8,051,421	9,391,792	
Commitments			
Redeemable convertible preferred stock:			
Series A, \$0.001 par value, 5,000,000 shares authorized, issued and outstanding, aggregate liquidation preference of \$28,496,497 and \$30,166,741 at December 31, 2003, and 2004, respectively, or \$4.65 per share plus accreted redemption value	28,496,497	30,166,741	
Series B, \$0.001 par value, 6,567,567 shares authorized, issued and outstanding, aggregate liquidation preference of \$37,484,419 and \$39,622,161 at December 31, 2003, and 2004, respectively, or \$4.65 per share, plus accreted redemption value	37,484,419	39,622,161	
Series C, \$0.001 par value, 49,169,138 and 76,441,866 shares authorized, issued and outstanding at December 31, 2003, and 2004, respectively, aggregate liquidation preference of \$64,153,421 and \$101,988,994 at December 31, 2003, and 2004, or \$1.21 per share, plus accreted redemption value	64,153,421	101,988,994	
Total redeemable convertible preferred stock	130,134,337	171,777,896	
Stockholders' equity (deficit):			
Common stock, \$0.001 par value, 11,333,333 and 16,666,666 shares authorized at December 31, 2003, and 2004, respectively, 144,370 and 256,816 shares issued and outstanding at December 31, 2003, and 2004, respectively	144	257	\$ 14,018
Capital in excess of par value	691,614	11,573,677	158,036,193
Common stock warrants	213,710	213,710	213,710
Accumulated deficit	(91,672,061)	(134,753,508)	(109,451,889)
Accumulated other comprehensive loss	(29,282)	—	—
Total stockholders' equity (deficit)	(90,795,875)	(122,965,864)	\$ 48,812,032
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	\$ 47,389,883	\$ 58,203,824	

See accompanying notes.

TARGACEPT, INC.
STATEMENTS OF OPERATIONS

	Year ended December 31,		
	2002	2003	2004
Revenue:			
Research fee revenue	\$ 1,388,824	\$ 1,302,500	\$ 337,500
License fee revenue	634,881	269,532	1,917,224
Product sales	242,861	814,724	766,583
Grant revenue	—	71,529	717,067
Other	19,792	—	—
Net revenue	2,286,358	2,458,285	3,738,374
Operating expenses:			
Research and development	16,243,888	18,179,542	22,770,881
General and administrative	4,135,262	3,599,673	5,162,474
Cost of product sales	243,718	742,941	198,446
Purchased in-process research and development	2,666,000	—	—
Total operating expenses	23,288,868	22,522,156	28,131,801
Loss from operations	(21,002,510)	(20,063,871)	(24,393,427)
Other income (expense):			
Interest and dividend income	87,691	791,339	504,986
Interest expense	(102,891)	(122,789)	(132,749)
Loss on disposal of fixed assets	(53,996)	—	(4,199)
Total other income (expense)	(69,196)	668,550	368,038
Net loss	(21,071,706)	(19,395,321)	(24,025,389)
Deemed dividend—beneficial conversion feature for Series C redeemable convertible preferred stock issued December 2004	—	—	(10,312,499)
Preferred stock accretion	(4,173,545)	(8,340,628)	(8,743,559)
Net loss attributable to common stockholders	\$ (25,245,251)	\$ (27,735,949)	\$ (43,081,447)
Basic and diluted net loss attributable to common stockholders per share	\$ (339.63)	\$ (254.33)	\$ (196.53)
Weighted average common shares outstanding—basic and diluted	74,332	109,053	219,213
Unaudited pro forma basic and diluted net loss per share attributable to common stockholders assuming conversion of preferred stock and conversion of convertible debt			\$ (3.32)
Unaudited pro forma weighted average shares outstanding—basic and diluted			10,334,833

See accompanying notes.

TARGACEPT, INC.

STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)

	Redeemable Convertible Preferred Stock			Common Stock		Capital in Excess of Par Value	Common Stock Warrants	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Deficit
	Series A	Series B	Series C	Shares	Amount					
Balances at January 1, 2002	\$25,156,009	\$33,208,932	\$ —	64,813	\$ 65	\$ 209,239	\$ 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 18,465 shares of common stock at \$0.001 per share par value, related to exercise of stock options	—	—	—	18,465	18	178,157	—	—	—	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	83,278	\$ 83	\$ 387,396	\$ 213,710	\$ (63,936,112)	\$ —	\$ (63,334,923)

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	Redeemable Convertible Preferred Stock			Common Stock		Capital in Excess of Par Value	Common Stock Warrants	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Deficit
	Series A	Series B	Series C	Shares	Amount					
Balances at December 31, 2002 (carried forward)	\$26,826,253	\$35,346,675	\$ 45,853,329	83,278	\$ 83	\$ 387,396	\$ 213,710	\$ (63,936,112)	\$ —	\$ (63,334,923)
Stock issuance costs	—	—	(32,548)	—	—	—	—	—	—	—
Issuance of 11,404,958 shares of Series C redeemable convertible preferred stock at \$1.21 per share	—	—	13,800,000	—	—	—	—	—	—	—
Issuance of 61,092 shares of common stock at \$0.001 per share par value, related to exercise of stock options	—	—	—	61,092	61	304,218	—	—	—	304,279
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock	42,744	—	—	—	—	—	—	(42,744)	—	(42,744)
Accreted redemption value for Series A, Series B, and Series C redeemable convertible preferred stock	1,627,500	2,137,744	4,532,640	—	—	—	—	(8,297,884)	—	(8,297,884)
Net change in unrealized holding loss on available-for-sale securities	—	—	—	—	—	—	—	—	(29,282)	(29,282)
Net loss	—	—	—	—	—	—	—	(19,395,321)	—	(19,395,321)
Comprehensive loss										(19,424,603)
Balances at December 31, 2003	\$28,496,497	\$37,484,419	\$ 64,153,421	144,370	\$ 144	\$ 691,614	\$ 213,710	\$ (91,672,061)	\$ (29,282)	\$ (90,795,875)
Stock issuance costs	—	—	(100,000)	—	—	—	—	—	—	—
Issuance of 27,272,728 shares of Series C redeemable convertible preferred stock at \$1.21 per share	—	—	33,000,000	—	—	—	—	—	—	—
Deemed dividend—beneficial conversion feature for Series C redeemable convertible preferred stock issued December 2004	—	—	—	—	—	10,312,499	—	(10,312,499)	—	—
Issuance of 112,446 shares of common stock at \$0.001 per share par value, related to exercise of stock options	—	—	—	112,446	113	569,564	—	—	—	569,677
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock	42,744	—	—	—	—	—	—	(42,744)	—	(42,744)
Accreted redemption value for Series A, Series B, and Series C redeemable convertible preferred stock	1,627,500	2,137,742	4,935,573	—	—	—	—	(8,700,815)	—	(8,700,815)
Net change in unrealized holding loss on available-for-sale securities	—	—	—	—	—	—	—	—	29,282	29,282
Net loss	—	—	—	—	—	—	—	(24,025,389)	—	(24,025,389)
Comprehensive loss										(23,996,107)
Balances at December 31, 2004	\$30,166,741	\$39,622,161	\$101,988,994	256,816	\$ 257	\$11,573,677	\$ 213,710	\$ (134,753,508)	\$ —	\$ (122,965,864)

See accompanying notes.

TARGACEPT, INC.

STATEMENTS OF REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)—(CONTINUED)

TARGACEPT, INC.
STATEMENTS OF CASH FLOWS

	Year ended December 31,		
	2002	2003	2004
Operating activities			
Net loss	\$ (21,071,706)	\$ (19,395,321)	\$ (24,025,389)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	958,105	672,927	766,335
Loss on disposal of equipment	53,996	—	4,199
Write-off of in-process research and development	2,666,000	—	—
Non-cash compensation expense	129,710	65,325	50,623
Recognition of deferred rent incentive	(167,769)	(402,647)	(402,647)
Realized loss on sale of investments	—	20,978	87,948
Amortization of discount on held-to-maturity investments	(48,446)	—	—
Changes in operating assets and liabilities, excluding the effects from acquired assets and liabilities:			
Research fees and accounts receivable	(713,109)	517,030	334,053
Inventories	22,464	51,016	15,880
Prepaid expenses and accrued interest receivable	158,605	(205,054)	(1,091,627)
Accounts payable and accrued expenses	1,503,132	(326,451)	1,141,221
Deferred license fee revenue	(634,881)	(269,532)	(1,917,224)
Net cash used in operating activities	\$ (17,143,899)	\$ (19,271,729)	\$ (25,036,628)
Investment activities			
Purchase of investments	(11,500,000)	(84,796,103)	(6,191,930)
Proceeds from sale of investments	26,400,000	58,500,000	37,379,107
Purchase of property and equipment	(1,281,840)	(545,254)	(660,624)
Proceeds from sale of property and equipment	—	—	38,191
Proceeds from rent incentive	2,013,234	—	—
Purchase of Inversine product	(3,500,000)	—	—
Net cash provided by (used in) investing activities	12,131,394	(26,841,357)	30,564,744
Financing activities			
Proceeds from borrowing of long-term debt	3,000,000	—	3,250,000
Principal payments on long-term debt	(324,891)	(637,483)	(730,979)
Proceeds from issuance of redeemable convertible preferred stock, net of transaction costs	45,487,771	13,767,452	32,900,000
Proceeds from issuance of common stock	48,465	238,954	519,054
Net cash provided by financing activities	48,211,345	13,368,923	35,938,075
Net increase (decrease) in cash and cash equivalents	43,198,840	(32,744,163)	41,466,191
Cash and cash equivalents at beginning of period	1,154,480	44,353,320	11,609,157
Cash and cash equivalents at end of period	\$ 44,353,320	\$ 11,609,157	\$ 53,075,348

See accompanying notes.

TARGACEPT, INC.
NOTES TO FINANCIAL STATEMENTS
DECEMBER 31, 2004

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 foreseeable future. As a result, the Company will require substantial additional funds, and plans to seek collaborative agreements, research funding, and private or public equity or debt financing to meet such needs. If such funds are not available, management may need to reassess its plans. Even if the Company does not have an immediate need for additional cash, it may seek access to the private or public equity markets if and when conditions are favorable. There is no assurance that such additional funds will be available for the Company to finance its operations on acceptable terms, if at all.

2. Summary of Significant Accounting Policies

Cash and Cash Equivalents

The Company considers cash equivalents to be those investments, which are highly liquid, readily convertible to cash, and which mature within three months from the date of purchase.

Investments

In accordance with the Company's investment policy, surplus cash is invested with high quality financial institutions in money market accounts, certificates of deposit, and 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 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.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

During 2002, 2003 and 2004, the Company recognized revenues of \$2,024,000, \$1,572,000 and \$2,255,000, respectively, or 89%, 64% and 60%, 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 5-10 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 December 31, 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 2002, 2003 and 2004, research and

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

development expenses were reduced by \$514,000, \$131,000 and \$23,000, respectively, for costs reimbursed primarily by Dr. Falk Pharma, GmbH and under the terms of the collaboration described in Note 15.

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 \$403,000 of the incentive during 2002, 2003 and 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 \$4,504,000 at December 31, 2002, 2003 and 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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

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 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. Revenues from grants are recognized as the Company performs the work and incurs reimbursable costs in accordance with the objectives of the governing grant agreement.

Shipping and Handling Costs

During 2002, 2003 and 2004, \$22,000, \$173,000 and \$174,000 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).

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

Reverse Stock Split

On February 2, 2005, the Company's Board of Directors adopted, and on February 2, 2005 the stockholders approved, a one for 7.5 reverse stock split of the Company's common stock effective as of February 3, 2005. All common stock and per common share amounts for all periods presented in the accompanying financial statements have been restated to reflect the effect of this reverse common stock split.

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 anticipated, all of the redeemable convertible preferred stock outstanding at the time of the IPO will automatically convert into 13,760,548 shares of common stock and the convertible promissory note described in Note 8 will convert to 104,623 shares of common stock based on an assumed IPO price per share of \$12.00. Pro forma stockholders' equity, as adjusted for the assumed conversion of the preferred stock and the convertible promissory note, 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, 2004, or the date of issuance, if later, and of the conversion of the outstanding convertible promissory note into shares of common stock as if such conversion had occurred on the date of issuance.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

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

	Year ended December 31,		
	2002	2003	2004
Historical			
Numerator:			
Net loss attributable to common stockholders	\$ (25,245,251)	\$ (27,735,949)	\$ (43,081,447)
Denominator:			
Weighted-average common shares outstanding	74,332	109,053	219,213
Basic and diluted net loss per share attributable to common stockholders	\$ (339.63)	\$ (254.33)	\$ (196.53)
Unaudited pro forma			
Numerator:			
Net loss attributable to common stockholders			\$ (34,332,409)
Denominator:			
Shares used above			219,213
Pro forma adjustment to reflect assumed conversion of convertible debt			4,554
Pro forma adjustment to reflect assumed conversion of preferred stock, on a weighted average basis			10,111,066
Shares used to compute pro forma basic and diluted net loss per share attributable to common stockholders			10,334,833
Unaudited pro forma basic and diluted net loss per share attributable to common stockholders			\$ (3.32)

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,		
	2002	2003	2004
Outstanding common stock options	286,753	613,503	1,010,716
Redeemable convertible preferred stock	2,130,673	9,373,431	10,111,066
Outstanding warrants	215,054	215,054	215,054
Total	2,632,480	10,201,988	11,336,836

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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

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,		
	2002	2003	2004
Dividend yield	—	—	—
Risk-free interest rate	3.5%	2.8%	3.0%
Volatility	0.8	0.8	0.8
Expected life	4 years	4 years	4 years

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,		
	2002	2003	2004
Net loss attributable to common stockholders, as reported	\$ (25,245,251)	\$ (27,735,949)	\$ (43,081,447)
Add: Stock-based employee compensation expense included in reported net income, net of related tax effects	129,710	65,325	50,623
Deduct: Stock-based employee compensation expense determined under fair value based method for all awards, net of related tax effects	(312,830)	(515,405)	(916,988)
Pro forma net loss	\$ (25,428,371)	\$ (28,186,029)	\$ (43,947,812)
Net loss per share:			
Basic and diluted, as reported	\$ (339.63)	\$ (254.33)	\$ (196.53)
Basic and diluted, pro forma	\$ (342.09)	\$ (258.46)	\$ (200.48)

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

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

On December 16, 2004, the Financial Accounting Standards Board (FASB) issued FASB Statement No. 123 (Revised 2004), *Share-Based Payment*, which is a revision of FASB Statement No. 123, *Accounting for Stock-Based Compensation*, Statement 123(R) supersedes APB Opinion No. 25, *Accounting for Stock Issued to Employees*, and amends FASB Statement No. 95, *Statement of Cash Flows*. Generally, the approach in Statement 123(R) is similar to the approach described in Statement 123. However, Statement 123(R) *requires* all share-based payments to employees, including grants of employee stock options, to be recognized in the income statement based on their fair values. Pro forma disclosure is no longer an alternative.

Statement 123(R) must be adopted no later than July 1, 2005. Early adoption will be permitted in periods in which financial statements have not yet been issued. The Company expects to adopt Statement 123(R) on July 1, 2005.

In November 2004, the FASB issued SFAS No. 151, *Inventory Costs, an amendment of ARB No. 43, Chapter 4*, which clarifies the types of costs that should be expensed rather than capitalized as inventory. This statement also clarifies the circumstances under which fixed overhead costs associated with operating facilities involved in inventory processing should be capitalized. The provisions of SFAS No. 151 are effective for fiscal years beginning after June 15, 2005 and we will adopt this standard in fiscal 2006. The Company has not determined the impact, if any, that this statement will have on its financial position or 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.

TARGACEPT, INC.
NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

3. Short-term investments

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

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 Company recognized \$88,000, \$591,000 and \$400,000 of interest income during 2002, 2003 and 2004, respectively. The Company recognized \$200,000 and \$193,000 of dividend income during 2003 and 2004, respectively. The Company recognized loss on sale of investments of \$88,000 in 2004.

4. Inventories

Inventories consisted of the following:

	December 31,	
	2003	2004
Raw materials	\$ 46,988	\$ 46,988
Work-in-process	6,892	6,400
Finished goods	64,640	49,252
	\$ 118,520	\$ 102,640

5. Property and equipment

Property and equipment consists of the following:

	December 31,	
	2003	2004
Lab equipment	\$ 5,057,345	\$ 4,795,050
Office furniture and fixtures	1,192,685	1,438,329
Leasehold improvements	87,875	138,790
	6,337,905	6,372,169
Less: accumulated depreciation	3,964,870	4,109,471
Property and equipment, net	\$ 2,373,035	\$ 2,262,698

The Company recorded \$577,000, \$635,000 and \$729,000 of depreciation expense during 2002, 2003 and 2004, respectively.

TARGACEPT, INC.
NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

6. Intangible Assets

Intangible assets consist of the following:

	December 31,	
	2003	2004
Patents (See Note 16)	\$642,000	\$642,000
Less: accumulated amortization	(53,499)	(91,263)
Total	\$588,501	\$550,737

The Company recognized amortization expense of \$16,000, \$38,000 and \$38,000 in 2002, 2003 and 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,	
	2003	2004
Clinical trials costs	\$ 623,158	\$ 965,407
Employee compensation	676,900	850,503
Other	106,720	124,926
	\$ 1,406,778	\$ 1,940,836

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 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 \$2,000,000, net of accumulated depreciation, at December 31, 2004. 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 was advanced the final tranche on December 23, 2004 in the amount of \$973,000. This tranche accrues interest at 6.89% and is repayable in monthly payments of \$23,000 through the maturity date of January 1, 2009. The Company paid \$91,000, \$135,000 and \$133,000 for interest under the RJRT note during 2002, 2003 and 2004, respectively.

TARGACEPT, INC.
NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

On December 15, 2004, the Company entered into a development 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 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 under the agreement.

Maturities of long-term debt are as follows:

	<u>Maturities as of December 31, 2004</u>
2005	\$ 1,113,350
2006	783,895
2007	1,843,330
2008	456,223
2009	121,748
Thereafter	238,101
	<u>\$ 4,556,647</u>

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.

In December 2004, the Company completed a private placement of an additional 27,272,728 shares of Series C and received cash of \$32,900,000 net of offering costs. Pursuant to EITF Issue No. 98-5, *Accounting for Convertible Securities with Beneficial Conversion Features*, and EITF 00-27, *Application of Issue No. 98-5 to Certain Convertible Instruments*, the Company recorded a deemed dividend at the date of issuance of \$10,312,499, which is the difference in the \$8.40 conversion price of the Series C and the underlying value of the common stock issuable upon conversion of the Series C of \$11.03.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

9. Redeemable Preferred Stock (continued)

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, 2004, conversion of the Series A, Series B and Series C would result in the issuance of 666,666, 2,082,623, and 11,011,258 shares of common stock, respectively. Future sales of equity at prices below the respective conversion prices could result in adjustments to the number of shares of common stock into which each series of preferred stock is convertible.

Automatic conversion of the Series A, Series B and Series C into fully paid and nonassessable shares of common stock, without the payment of additional consideration by the holders thereof, would occur immediately upon the closing of the sale of the Company's common stock in a firm commitment, underwritten public offering registered under the Securities Act of 1933 in which (i) the price per share equals or exceeds \$11.00 (subject to certain adjustments) or such lesser amount as is approved by the holders of (a) a majority of then outstanding shares of Series A and Series B, considered together as a single class on an as-converted basis, and (b) at least sixty-five percent (65%) of the then outstanding shares of Series C, and (ii) the gross proceeds to the Company are not less than \$50,000,000 or such lesser amount as is approved by the holders of (a) a majority of then outstanding shares of Series A and Series B, considered together as a single class on an as-converted basis, and (b) at least sixty-five percent (65%) of the then outstanding shares of Series C. The accrued but unpaid cumulative dividend on the Series C shall, if not yet declared, be forfeited upon conversion of the Series C.

Dividends

Dividends accrue daily on each share of Series C on a cumulative basis at the rate of 8% per annum and are recorded as an increase to Series C and an increase to accumulated deficit. Cumulative dividends may be declared and paid at any time and shall be payable upon liquidation or redemption. At December 31, 2003 and 2004, cumulative accrued dividends on the Series C stock totaled \$4,898,000 and \$9,834,000, 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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

9. Redeemable Preferred Stock (continued)

applicable record date. In addition, certain actions by the Company require the approval of one or more of (i) the holders of a majority of the outstanding shares of Series A, (ii) the holders of at least two-thirds of the outstanding shares of Series B, (iii) the holders of a majority of the outstanding shares of Series A and Series B, considered together on an as-converted basis, and/or (iv) the holders of at least 65% of the outstanding shares of Series C.

Liquidation Preference

In the event of any liquidation, dissolution or winding up of the Company, the holders of the Series C shares have preference and are entitled to receive an amount per share equal to the greater of (i) their initial purchase price per share plus any accrued or declared and unpaid dividends on such share or (ii) the amount per share of Series C that such holders would receive if all of the Series A, Series B and Series C were converted to common stock immediately prior to such liquidation, dissolution or winding up.

Next, the holders of Series A and Series B are entitled to receive, on a *pari passu* basis, an amount equal to their initial purchase price per share plus any declared and unpaid dividends on such shares. Any assets of the Company remaining after the payments specified above shall be distributed on a *pari passu* basis among the holders of common stock and, on an as-converted to common stock basis, Series A, Series B and Series C. Unless the holders of a prescribed number of shares of Series A, Series B and/or Series C otherwise elect, certain fundamental transactions involving the Company shall be treated as a liquidation for the Series A, Series B and/or Series C, as the case may be.

Mandatory Redemption

At any time after November 26, 2008, upon demand by the holders of at least 65% of the outstanding shares of Series C, all of the outstanding shares of Series C shall be redeemed in cash in an amount per share equal to the initial purchase price per share (subject to certain adjustments) plus any accrued or declared and unpaid dividends on such shares.

At any time after the later of August 22, 2005 or the date on which no shares of Series C are outstanding, a number of outstanding shares of Series A or Series B elected upon demand by 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.

TARGACEPT, INC.
NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

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 at \$4.65 per share and a warrant to purchase 215,054 shares of the Company's common stock at \$34.88 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 41,257 shares of the common stock to management 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 10,000,000 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 11,333,333 and preferred stock to 60,736,705 and issued 11,404,958 shares of Series C.

On December 6, 2004, the Company amended its Certificate of Incorporation to increase the number of authorized shares of common stock to 16,666,666 and preferred stock to 81,741,965 and issued 27,272,728 shares of Series C.

In conjunction with the issuance of Series A, the Company issued a warrant to purchase 215,054 shares of the Company's common stock at an original exercise price of \$34.88 per share (subject to certain adjustments). In connection with the Company's issuance of Series C and price adjustment provisions of the warrant, the conversion price of the warrant was adjusted to \$14.63. The warrant is exercisable only upon the earlier of an initial public offering or a change in control. The fair value of the warrant is a direct cost of obtaining capital. As such, the fair value has been recorded in stockholders' equity, with the offset recorded as a decrease in the redemption value of the Series A. The Company will accrete to the redemption value of the Series A at the earliest date of redemption, or until 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 215,054 shares of the Company's common stock was estimated at the grant date to be \$213,710 or \$3.98 per share. The Company considered the anti-dilution features, the contingencies surrounding the limited opportunities for exercise, and the warrant's priorities over common stock options in relation to the fair value of the Company's common stock at the date of issuance when estimating the fair value of the warrant.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

10. Stockholders' Equity (Deficit) (continued)

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

	December 31, 2003	December 31, 2004
Convertible preferred stock	9,831,987	13,760,548
Convertible promissory note	—	104,623
Warrant	215,054	215,054
Options	1,140,589	1,028,086
	<u>11,187,630</u>	<u>15,108,311</u>

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,		
	2002	2003	2004
Expected federal income tax benefit at statutory rate	(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	(4)	(5)	(5)
Net operating loss and credit limitations	14	3	—
Change in valuation allowance	21	41	42
Other	—	1	—
	<u>—%</u>	<u>—%</u>	<u>—%</u>

At December 31, 2003 and 2004, the Company had net operating loss carryforwards for federal income tax purposes of approximately \$17,637,000, \$38,409,000 and \$63,296,000, respectively, \$25,317,000, \$46,090,000 and \$70,976,000, respectively, for state income tax purposes, and research and development tax credits of approximately \$48,000, \$638,000 and \$1,357,000, 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.

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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

11. Income Taxes (continued)

credit carryforwards attributable to periods before the change. The Company completed a private placement of Series C in December 2004 but has not performed a detailed analysis to determine whether an ownership change under Section 382 of the Internal Revenue Code occurred.

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 2004, the valuation allowance increased approximately \$4,518,000, \$8,050,000 and \$9,600,000, respectively.

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

	December 31,	
	2003	2004
Deferred tax assets:		
Net operating loss carryforward	\$ 15,158,059	\$ 24,787,121
Research and development tax credit	638,153	1,357,135
Patents	641,008	577,974
Unearned revenue	739,167	—
Total gross deferred tax assets	17,176,387	26,722,230
Valuation allowance	(16,999,275)	(26,599,098)
Net deferred tax asset	177,112	123,132
Deferred tax liabilities:		
Equipment and other	(177,112)	(123,132)
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 268,168 shares under the Plan to attract and retain employees, directors and certain independent contractors, consultants and advisors and to allow them to participate in the growth of the Company. During 2001, the number of shares authorized for issuance under the Plan was increased to 348,168. In conjunction with the November 2002 Series C financing, the Company authorized the issuance of an additional 400,000 shares, increasing the number of authorized shares to 748,168. Upon the issuance of the additional Series C shares in March 2003, the number of authorized shares was increased to 1,228,888. Awards may be made to participants under the Plan in the form of incentive and nonqualified stock options, restricted stock, stock appreciation rights, stock awards, and performance awards.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

12. Equity Incentive Plan (continued)

Eligible participants under the Plan include employees, directors and certain independent contractors, consultants or advisors of the Company or a related corporation. The vesting periods for awards made under the Plan are determined at the discretion of the Plan administrator and range from 0 to 4 years. 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, 2002	210,362	\$ 3.53-34.88	\$ 4.43
Granted	111,807	0.08-5.10	4.35
Forfeited	(2,490)	4.20	4.20
Exercised	(12,131)	3.53-5.10	3.98
Outstanding at December 31, 2002	307,548	3.53-34.88	4.43
Granted	799,479	0.08-5.63	5.03
Forfeited	(4,797)	0.08-5.10	1.95
Exercised	(61,092)	0.08-5.10	3.90
Outstanding at December 31, 2003	1,041,138	0.08-34.88	4.88
Granted	65,200	0.08-5.63	5.33
Forfeited	(6,066)	3.53-34.88	21.53
Exercised	(112,472)	3.53-5.63	4.73
Outstanding at December 31, 2004	987,800	\$ 0.08-5.63	\$ 4.88

The weighted average fair value of options granted during 2002, 2003 and 2004 was \$3.45, \$3.08 and \$5.33, respectively. At December 31, 2002, 2003 and 2004, 127,741, 471,762 and 586,707 options, respectively, were exercisable at a weighted-average price of \$4.80, \$4.73 and \$4.65, respectively.

A summary of options outstanding as of December 31, 2004 is as follows:

Exercise Price	Options Outstanding			Options Exercisable	
	Number Outstanding	Weighted Average Remaining Contractual Exercise Life	Weighted Average Exercise Price	Number Exercisable	Weighted Average Price
\$0.08	27,897	8.1	\$ 0.08	24,563	\$ 0.08
3.53	92,461	5.7	3.53	92,448	3.53
5.10	803,051	8.5	5.10	430,561	5.10
5.63	64,391	9.2	5.63	39,135	5.63
	987,800	8.2	\$ 4.88	586,707	\$ 4.65

During 2002 and 2003, respectively, the Company granted 17,333 and 13,000 options below fair value at an exercise price of \$0.08 and fair value of \$5.10 per share. The fair value of these

TARGACEPT, INC.**NOTES TO FINANCIAL STATEMENTS—(CONTINUED)****12. Equity Incentive Plan (continued)**

shares was recorded as compensation expense in the amounts \$129,710 and \$65,325, during 2002 and 2003, respectively. During 2004, the Company granted 10,333 options below fair value at an exercise price of \$0.08 and a fair value of \$5.63 per share. The fair value of these shares was recorded as compensation expense in the amount of approximately \$51,000.

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 \$106,000 for the year ended December 31, 2002. The Company has no future minimum lease payments to RJRT as of December 31, 2004.

On March 1, 2002, the Company entered into an agreement with Wake Forest University to lease an office and research facility in Winston-Salem, North Carolina with an initial term that extends through July 31, 2007. The lease contains a renewal option for up to one additional five-year term, with a lease rate similar to the original agreement. In December 2004, the Company amended the terms of the lease to include 1,000 square feet and an option on additional space in this facility. The lease amendment increased annual rent by \$15,000 per year and included a \$37,000 hold fee in the first year. Rent expense incurred by the Company under this lease was approximately \$904,000, \$1,456,000 and \$1,456,000 for the years ended December 31, 2002, 2003 and 2004, respectively. Rent expense is offset by the monthly recognition of the deferred rent incentive discussed in Note 2. At December 31, 2004, the Company has the following future minimum lease payments in relation to this lease:

2005	\$ 1,507,566
2006	1,470,552
2007	857,822
2008 and thereafter	—
	<hr/>
	\$ 3,835,940

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 \$290,000, \$298,000 and \$368,000 to the plan for the years ended December 31, 2002, 2003 and 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,

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

15. Collaborative Research and License Agreements (continued)

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, 2002, 2003 and 2004, these fees were \$1,389,000, \$1,303,000 and \$338,000, 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 2002, 2003 or 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. During 2002, 2003 and 2004, the product candidate subject to the agreement had not completed the research and clinical development process. Accordingly, the Company has deferred recognition of the license fee and is amortizing it over the expected term of the research and development period. On December 3, 2004, Aventis provided the Company with 30 days advance written notice of Aventis' plans to terminate the collaborative research and license agreement between the companies entered into December 1998 and restated in January 2002. The agreement terminated effective January 2, 2005 and was within the provisions of termination clauses of the agreement. As a result of the termination of the agreement, the Company recognized the remaining deferred revenue of \$825,000 related to the agreement during the fourth quarter of 2004, as there were no further responsibilities or duties to be performed under the agreement as of December 3, 2004.

On January 21, 2002, the Company entered into a second collaborative research and license agreement with Aventis to discover and develop drugs, derived from the Aventis library of compounds for the treatment of Alzheimer's disease and other disorders of the central nervous system. The second agreement was structured similarly to the first agreement. The research term of the agreement expired in December 2004. The Company is eligible to receive milestone payments and royalties from Aventis for any compounds that are selected for further development within six months after the expiration of the research term.

Dr. Falk Pharma

On January 26, 2001, the Company entered into a collaborative research development and license agreement with Dr. Falk Pharma GmbH (“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 14,815 shares of the Company's common stock for \$1,000,000. The Company 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 \$1,000,000 in proceeds for the common stock, the Company used the estimated fair value of the

TARGACEPT, INC.**NOTES TO FINANCIAL STATEMENTS—(CONTINUED)****15. Collaborative Research and License Agreements (continued)**

common stock to value the shares issued to arrive at a total equity value of \$76,000, with the remaining proceeds of \$924,000 allocated to deferred revenue. This deferred revenue is also being amortized over the expected term of the research and development period.

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, 2002, 2003 and 2004, the Company did not pay or receive any royalties related to this agreement. The Company and Dr. Falk Pharma have mutually agreed to discontinue the development of the lead compound subject to the collaboration agreement resulting in the recognition of the remaining deferred revenue of \$890,000 during the fourth quarter of 2004. The Company recognized \$385,000, \$170,000 and \$1,017,000 of deferred revenue under this agreement during 2002, 2003, and 2004, respectively.

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:

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

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 666,666 shares of common stock, 1,652,893 shares of Series C redeemable preferred stock convertible to 238,095 shares of common stock, a warrant to purchase 215,054 shares of common stock, 3,333 shares of common stock, and options to purchase 4,230 shares of

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

17. Related Party Transactions (continued)

common stock. The Company has entered into the following transactions and agreements with RJRT in the ordinary course of business.

During 2002, the Company entered into an agreement to borrow \$2,500,000 from RJRT accruing interest at 6.6%. The note is repayable in monthly installments of \$59,000 through the maturity date of May 1, 2006. In January 2004, the Company amended the note agreement with RJRT to allow for up to three additional tranches to be advanced to the Company for up to a total of \$2,000,000. Each of the additional tranches will accrue interest at the 4-year U.S. Treasury rate plus 3.5% determined as at the day the additional tranche is advanced and will be repayable in 48 equal monthly installments. The Company was advanced an additional tranche on April 1, 2004 in the amount of \$1,027,000. This additional tranche accrues interest at 5.87% and is repayable in monthly payments of \$24,000 through the maturity date of April 1, 2008.

The Company was advanced the final tranche on December 23, 2004 in the amount of \$973,000. This tranche accrues interest at 6.89% and is repayable in monthly payments of \$23,000 through the maturity date of January 1, 2009. Under this related party note payable, the Company paid RJRT \$416,000, \$772,000 and \$846,000 during 2002, 2003 and 2004, respectively.

The notes are secured by equipment owned by the Company with a book value of approximately \$2,000,000, net of accumulated depreciation, at December 31, 2004.

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 \$106,000 for the year ended December 31, 2002. The Company has no future minimum lease payments to RJRT as of December 31, 2004.

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, 2002, 2003 and 2004 in connection with the director's services are 4,333, 1,000 and 2,103 shares, respectively. In addition, a stock option for an additional 4,333 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 2,103 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 \$43,550, \$2,512 and \$4,247 during 2002, 2003 and 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 \$525,000 and \$201,000 for these services during 2002, and 2003, respectively. During 2004, the Company continued to use copy and print services totaling \$79,000.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

18. Selected Quarterly Financial Data (unaudited)

	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)	\$ (71.09)	\$ (82.46)	\$ (53.63)	\$ (54.47)
Weighted average common shares outstanding—basic and diluted	85,809	96,012	121,758	131,983
	2004 Quarter			
	First	Second	Third	Fourth
Net revenue	\$ 496,939	\$ 528,026	\$ 555,583	\$ 2,157,826
Gross profit on product sales	6,060	494,780	55,697	11,600
Operating loss	(6,843,593)	(6,437,455)	(6,711,932)	(4,400,447)
Net loss	(6,637,935)	(6,433,767)	(6,665,238)	(4,288,449)
Net loss attributable to common stockholders	(8,779,826)	(8,575,657)	(8,807,125)	(16,918,839)
Basic and diluted net loss per share attributable to common stockholders(1)	\$ (59.18)	\$ (38.54)	\$ (35.13)	\$ (66.46)
Weighted average common shares outstanding—basic and diluted	148,345	222,504	250,710	254,556

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.

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You should rely only on the information contained in this prospectus. We have not authorized anyone to provide information different from that contained in this prospectus. We are offering to sell, and seeking offers to buy, shares of common stock only in jurisdictions where offers and sales are permitted. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock.

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Until _____, 2005 (25 days after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to unsold allotments or subscriptions.



6,250,000 Shares

Common Stock

Deutsche Bank Securities

Pacific Growth Equities, LLC

CIBC World Markets

Lazard

Prospectus

, 2005

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	\$ 11,774
NASDAQ National Market listing fee	100,000
NASD filing fee	9,844
Blue sky fees and expenses	5,000
Accounting fees and expenses	550,000
Legal fees and expenses	875,000
Transfer agent and registrar fees and expenses	3,500
Printing and engraving expenses	300,000
Miscellaneous	119,882
	<hr/>
Total	\$ 1,975,000

Item 14. Indemnification of Directors and Officers.

Our Third Amended and Restated Certificate of Incorporation, as amended and in effect as of the date of this registration statement, and our Fourth Amended and Restated Certificate of Incorporation to be in effect upon completion of this offering (as may be in effect from time to time, the "Certificate") provide that, except to the extent prohibited by the Delaware General Corporation Law, as amended (the "DGCL"), our directors shall not be personally liable to us or our stockholders for monetary damages for any breach of fiduciary duty while serving as our directors. Under the DGCL, our directors have a fiduciary duty to us that is not eliminated by this provision of the Certificate and, in appropriate circumstances, equitable remedies such as injunctive or other forms of non-monetary relief will remain available. In addition, each director will continue to be subject to liability under the DGCL for breach of the director's duty of loyalty to us or our stockholders, for acts or omissions that are found by a court of competent jurisdiction to be not in good faith or involving intentional misconduct, for knowing violations of law, for actions leading to improper personal benefit to the director and for payment of dividends or approval of stock repurchases or redemptions that are prohibited by the DGCL. This provision also does not affect our directors' responsibilities under any other laws, such as federal securities laws or state or federal environmental laws.

Section 145 of the DGCL empowers a corporation to indemnify its directors and officers against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by them in connection with any action, suit or proceeding brought by third parties by reason of the fact that they were or are directors or officers of the corporation, if they acted in good faith, in a manner they reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reason to believe that their conduct was unlawful. The DGCL provides further that the indemnification permitted thereunder shall not be deemed exclusive of any other rights to which the directors and officers may be entitled under the corporation's bylaws, any agreement, a vote of stockholders or otherwise. The Certificate provides that, to the fullest extent permitted by Section 145 of the DGCL, we shall indemnify any person who was or is a

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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 41,258 shares of our common stock at a purchase price per share of \$.0075 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 215,054 shares of common stock at an exercise price of \$34.88 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. As a result of price protection provisions contained in the warrant, the exercise price was reduced to \$14.63 per share upon our issuance of shares of series C convertible preferred stock in November 2002 and March 2003. Each share of series A convertible preferred stock will convert into 0.133 shares 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 0.318 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

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approximately \$3.0 million. These shares will convert into common stock at the rate of approximately 0.318 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 0.133 shares 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 14,814 shares of our common stock at a purchase price of \$67.50 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 9,666 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 0.144 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 0.144 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 3,333 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 0.144 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, 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 January 31, 2005, we have granted:

- options to purchase an aggregate of 1,206,225 shares of common stock at exercise prices ranging from \$0.08 to \$34.88 per share under our 2000 Equity Incentive Plan, as amended, with a weighted average exercise price of \$4.80 per share, to employees, directors and individual consultants;
- restricted stock awards for an aggregate of 13,000 shares of common stock at a purchase price of \$0.08 per share under our 2000 Equity Incentive Plan, as amended; and
- options to purchase an aggregate of 34,000 shares of common stock at an exercise price of \$0.08 per share to non-individual consultants under our 2000 Equity Incentive Plan, as amended.

The weighted average exercise price of all options to purchase shares of common stock granted since inception and outstanding on December 31, 2004 is \$4.88 per share. As of January 31, 2005, 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 benefit plans or arrangements with our employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

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Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

<u>Exhibit No.</u>	<u>Description</u>
1.1**	Form of Underwriting Agreement.
3.1(a)(1)**	Third Amended and Restated Certificate of Incorporation of the Company.
3.1(a)(2)**	Certificate of Amendment to 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.
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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**	Targacept, Inc. 2000 Equity Incentive Plan, as amended.
10.5(a)	Form of Incentive Stock Option Agreement under Targacept, Inc. 2000 Equity Incentive Plan
10.5(b)	Form of Nonemployee Director Nonqualified Stock Option Agreement under Targacept, Inc. 2000 Equity Incentive Plan
10.5(c)	Form of Restricted Stock Award Agreement under Targacept, Inc. 2000 Equity Incentive Plan
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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.

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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).
24.1**	Power of Attorney (included on signature page).

** Previously filed.

+ Confidential treatment has been granted with respect to certain portions of this Exhibit, which portions have been omitted and filed separately with the Securities and Exchange Commission as part of an application for confidential treatment pursuant to the Securities Act of 1933, as amended.

++ Portions of this Exhibit have been omitted and filed separately with the Securities and Exchange Commission as part of an application for confidential treatment pursuant to the Securities Act of 1933, as amended.

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(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.

EXHIBIT INDEX

<u>Exhibit No.</u>	<u>Description</u>
1.1**	Form of Underwriting Agreement.
3.1(a)(1)**	Third Amended and Restated Certificate of Incorporation of the Company.
3.1(a)(2)**	Certificate of Amendment to 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.
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24.1**	Power of Attorney (included on signature page).

** Previously filed.

+ Confidential treatment has been granted with respect to certain portions of this Exhibit, which portions have been omitted and filed separately with the Securities and Exchange Commission as part of an application for confidential treatment pursuant to the Securities Act of 1933, as amended.

++ Portions of this Exhibit have been omitted and filed separately with the Securities and Exchange Commission as part of an application for confidential treatment pursuant to the Securities Act of 1933, as amended.

**FOURTH 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.

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

3. This Fourth Amended and Restated Certificate of Incorporation was duly adopted in accordance with Sections 245(c), 242 and 228 of the DGCL and will be effective upon filing.

IN WITNESS WHEREOF, said Targacept, Inc. has caused this Fourth Amended and Restated Certificate of Incorporation to be signed by its President and Chief Executive Officer, this ____ day of February 2005.

TARGACEPT, INC.

By: _____
J. Donald deBethizy
President and Chief Executive Officer

EXHIBIT A

FOURTH 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 2711 Centreville Road, Suite 400, City of Wilmington 19808, 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, as the same now exists or may hereafter be amended.

FOURTH:

1. The total number of shares that the corporation is authorized to issue is One Hundred Five Million (105,000,000), of which: (1) One Hundred Million (100,000,000) shares shall be designated as Common Stock, \$0.001 par value per share (“**Common Stock**”); and (2) Five Million (5,000,000) shares shall be designated as Preferred Stock, \$0.001 par value per share (“**Preferred Stock**”).
2. The board of directors of the corporation (the “**Board**”) is authorized, subject to any limitations prescribed by law, to provide for the issuance of shares of Preferred Stock in one or more series, to establish from time to time the number of shares to be included in each such series, to increase or decrease the number of shares of any series subsequent to the issue of shares of that series, but not below the number or shares of such series then outstanding, and to fix the designation, powers, preferences, relative, participating optional or other special rights, and any qualifications, limitations and restrictions of the shares of each such series. In case the number of shares of any series shall be so decreased, the shares constituting such decrease shall resume the status that they had prior to the adoption of the resolution originally fixing the number of shares of such series.
3. Each outstanding share of Common Stock shall entitle the holder thereof to one vote on each matter properly submitted to the stockholders of the corporation for a vote; provided, however, that, except as otherwise required by law, holders of Common Stock shall not be entitled to vote on any amendment (including any certificate of designation relating to any series of Preferred Stock) to this certificate of incorporation that relates solely to the terms of one or more outstanding series of Preferred Stock if the holders of such affected series are entitled, either separately or together as a class with the holders of one or more other such series, to vote thereon by law or pursuant to this certificate of

incorporation (including any certificate of designation relating to any series of Preferred Stock).

FIFTH: The corporation is to have perpetual existence.

SIXTH: 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, it is further provided:

1. The business and the conduct of the affairs of the corporation shall be managed by or under the direction of the Board.
2. Any action required or permitted to be taken by the stockholders of the corporation must be effected at a duly called annual or special meeting of stockholders of the corporation and may not be effected by any written consent by such stockholders.
3. Special meetings of stockholders of the corporation may be called only by the Chairman of the Board, the Chief Executive Officer, the President or the Board acting pursuant to a resolution adopted by a majority of the Whole Board and any power of stockholders to call a special meeting of stockholders is specifically denied. Only such business as shall have been stated in the notice of a special meeting of stockholders shall be considered at such special meeting. For purposes of this certificate of incorporation, the "**Whole Board**" shall mean the total number of directors then fixed in accordance with this certificate of incorporation, whether or not there are any vacancies.

SEVENTH:

1. Subject to any rights of the holders of any series of Preferred Stock to elect additional directors under specified circumstances, the number of directors shall be fixed from time to time exclusively by the Board. The directors, other than those who may be elected by the holders of any series of Preferred Stock under specified circumstances, shall be divided into three classes, as nearly equal in number as possible, with the term of office of the first class to expire at the corporation's first annual meeting of stockholders following January 1, 2005, with the term of office of the second class to expire at the corporation's second annual meeting of stockholders following January 1, 2005 and with the term of office of the third class to expire at the corporation's third annual meeting of stockholders following January 1, 2005, and thereafter for each such term to expire at each third succeeding annual meeting of stockholders after such election and with each director to hold office until his or her successor shall have been duly elected and qualified. At each annual meeting of stockholders, directors elected to succeed those directors whose terms expire shall be elected for a term of office to expire at the

third succeeding annual meeting of stockholders after their election, with each director to hold office until his or her successor shall have been duly elected and qualified or until his or her death, retirement, resignation or removal.

2. Newly created directorships resulting from any increase in the authorized number of directors or any vacancies in the Board resulting from death, retirement, resignation, removal from office or other cause may be filled only by a majority vote of the directors then in office even though less than a quorum, or by a sole remaining director, and not by the stockholders. In the event of any increase or decrease in the authorized number of directors, (a) each director then serving as such shall nevertheless continue as a director of the class of which he or she is a member until the expiration of his or her current term or his or her prior death, retirement, resignation or removal and (b) the newly created or eliminated directorships resulting from such increase or decrease shall if reasonably possible be apportioned by the Board among the three classes of directors so as to ensure that no one class has more than one director more than any other class. To the extent reasonably possible, consistent with the foregoing rule, any newly created directorships shall be added to those classes whose terms of office are to expire at the latest dates following such allocation and newly eliminated directorships shall be subtracted from those classes whose terms of office are to expire at the earliest dates following such allocation, unless otherwise provided for from time to time by resolution adopted by a majority of the directors then in office, although less than a quorum. In the event of a vacancy in the Board, the remaining directors, except as otherwise provided by law or this certificate of incorporation, may exercise the powers of the full Board until the vacancy is filled. No decrease in the number of directors constituting the Board shall shorten the term of any incumbent director.
3. No election of directors need be by written ballot unless the Bylaws of the corporation so provide.
4. No stockholder will be permitted to cumulate votes at any election of directors.
5. Advance notice of stockholder nominations for the election of directors and of business to be brought by stockholders before any meeting of the stockholders of the corporation shall be given in the manner provided in the Bylaws of the corporation.
6. Subject to the rights of the holders of any series of Preferred Stock then outstanding and except as otherwise provided in this certificate of incorporation or required by law, any director, or all of the directors, may be removed from the Board with or without cause, but only by the

affirmative vote of the holders of at least 66 2/3% of the aggregate voting power of the then-outstanding shares of capital stock of the corporation entitled to vote in the election of directors, voting together as a single class.

EIGHTH: The power to adopt, amend or repeal the Bylaws of the corporation may be exercised by the Board. The stockholders shall also have the power to adopt, amend or repeal the Bylaws; provided, however, that, in addition to any vote of the holders of any class or series of stock of the corporation required by law or this certificate of incorporation, the affirmative vote of the holders of at least 66 2/3% of the aggregate voting power of the then-outstanding voting shares of voting stock entitled to vote generally in the election of directors, voting together as a single class, shall be required to adopt, amend or repeal all or any portion of Sections 13 or 14 of Article II, Section 2 of Article III, Article VIII and Section 6 of Article IX of the Bylaws.

NINTH: 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.

TENTH: 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.

ELEVENTH: From time to time any of the provisions of this 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; provided, however, that, notwithstanding any other provision of this certificate of incorporation, or any provision of law that might otherwise permit a lesser vote or no vote, but in addition to any vote of the holders of any class or series of the stock of this corporation required by law or by this certificate of incorporation, the affirmative vote of the holders of at least 66 2/3% of the voting power of the then-outstanding shares of voting stock entitled to vote generally in the election of directors, voting together as a single class, shall be required to amend or repeal Article SIXTH, Article SEVENTH, Article EIGHTH, Article NINTH, Article TENTH or this Article ELEVENTH. All rights conferred upon stockholders of the corporation by this certificate of incorporation are granted subject to the provisions of this Article ELEVENTH.

BYLAWS

OF

TARGACEPT, INC.

(as amended and restated on February __, 2005)

BYLAWS
OF
TARGACEPT, INC.

ARTICLE I

Offices

Section 1. Principal and Registered Offices. The principal office of the Corporation shall be located at such place as the Board of Directors (the “**Board**”) may specify from time to time. The registered office of the Corporation shall be located at such place as set forth in the Corporation’s Certificate of Incorporation, as may be amended or restated and in effect from time to time (the “**Charter**”).

Section 2. Other Offices. The Corporation may have offices at such other places, either within or without the State of Delaware, as the Board may from time to time determine.

ARTICLE II

Meetings of Stockholders

Section 1. Place of Meeting. Meetings of stockholders shall be held at the principal office of the Corporation or at such other place or places, either within or without the State of Delaware, as shall be designated in the notice of the meeting.

Section 2. Annual Meetings. The annual meeting of stockholders shall be held on the date and at the time fixed, from time to time, by the Board.

Section 3. Special Meetings. Except as otherwise provided in the Charter, and subject to the rights of holders of any series of preferred stock then outstanding, special meetings of the stockholders for any purpose or purposes may be called only by the Chairman of the Board, the Chief Executive Officer, the President or by the Board acting pursuant to a resolution adopted by a majority of the Whole Board. For purposes of these Bylaws, the “**Whole Board**” shall mean the total number of directors then fixed in accordance with the Charter, whether or not there are any vacancies. Only such business as shall have been stated in the notice of a special meeting of stockholders shall be considered at such special meeting.

Section 4. Cancellation of Meetings. Any previously scheduled meeting of stockholders may be postponed, and, unless the Charter provides otherwise, any special meeting of the stockholders may be cancelled by resolution duly adopted by a majority of the directors then in office upon public notice given prior to the date previously scheduled for such meeting of stockholders.

Section 5. Notice of Meetings. Written or printed notice shall be given not less than ten (10) or more than sixty (60) days before the date of the meeting, to each

stockholder of record entitled to vote at the meeting by delivering a written notice thereof to such stockholder personally or by depositing such notice in the United States mail, postage prepaid, directed to such stockholder at his last address as it appears on the stock records of the Corporation. The notice shall state the time and place of the meeting, the means of remote communications, if any, by which stockholders and proxy holders may be deemed to be present in person and vote at such meeting (if authorized by the Board in its sole discretion pursuant to the Delaware General Corporation Law, as may be amended from time to time the "DGCL") and, in the case of a special meeting, briefly describing the purpose or purposes of the meeting. It shall be the primary responsibility of the Secretary to give the notice, but notice may be given by or at the direction of the President or other person or persons calling the meeting. Notice of any adjourned meeting of the stockholders shall not be required to be given, except where expressly required by law.

Whenever notice is required to be given under any provision of the DGCL, the Charter or these Bylaws to any person with whom communication is unlawful, the giving of such notice to such person shall not be required and there shall be no duty to apply to any governmental authority or agency for a license or permit to give such notice to such person. Any action or meeting taken or held without notice to any such person with whom communication is unlawful shall have the same force and effect as if such notice had been duly given.

Whenever notice is required to be given under any provision of the DGCL, the Charter or these Bylaws to any stockholder to whom (a) notice of two (2) consecutive annual meetings or (b) all, and at least two (2) payments (if sent by first-class mail) of dividends or interest on securities during a twelve (12) month period, have been mailed addressed to such person at such person's address as shown on the records of the Corporation and have been returned undeliverable, the giving of such notice to such person shall not be required. Any actions or meeting taken or held without notice to such person shall have the same force and effect as if such notice had been duly given. If any such person shall deliver to the Corporation a written notice setting forth such person's then current address, the requirement that notice be given to such person shall be reinstated. The exception to the requirement that notice be given set forth in clause (a) above shall not be applicable to any notice returned as undeliverable if the notice was given by electronic transmission.

Section 6. Waiver of Notice. Whenever notice is required to be given under any provision of the DGCL, the Charter or these Bylaws, a written waiver thereof, signed by the person entitled to notice, or a waiver by electronic transmission by the person entitled to notice, whether before or after the time stated therein, shall be deemed equivalent to notice. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting, except when the person attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the stockholders need be specified in any written waiver of notice, or any waiver by electronic transmission, unless so required by the Charter.

Section 7. Proxies. Each stockholder entitled to vote at a meeting of stockholders may authorize another person or persons to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three (3) years from its date, unless the proxy provides for a longer period. A proxy may be granted in writing or otherwise as

permitted under Section 212(c) or any other provision of the DGCL. A duly executed proxy shall be irrevocable if it so states and it is coupled with an interest sufficient in law to support an irrevocable power.

Section 8. Quorum. Except as otherwise required by any provision of the DGCL or the Charter, the holders of a majority of the outstanding shares entitled to vote, present in person or represented by proxy, shall constitute a quorum at a meeting of stockholders. In the absence of a quorum, any officer entitled to preside at, or act as Secretary of, such meeting, shall have the power to adjourn the meeting from time to time until a quorum shall be constituted. At any such adjourned meeting at which a quorum shall be present any business may be transacted which might have been transacted at the meeting as originally called. When a quorum is once present to organize a meeting, the stockholders present may continue to do business at the meeting or at any adjournment thereof notwithstanding the withdrawal of enough stockholders to leave less than a quorum.

Section 9. Voting of Shares. Each outstanding share of capital stock of the Corporation shall, subject to Article II, Section 11, be entitled to one vote on each matter submitted to a vote at a meeting of the stockholders, except as otherwise provided in the Charter. In all matters other than the election of directors, the affirmative vote of the holders of a majority of the shares present in person or represented by proxy at a meeting of stockholders and entitled to vote on the subject matter shall be the act of the stockholders on that matter, unless the vote of a greater number is required by law, the Charter, or these Bylaws. Directors shall be elected by a plurality of the votes of the shares of capital stock present in person or represented by proxy at the meeting and entitled to vote on the election of directors.

Section 10. Action Without Meeting. Any action required or permitted to be taken by the stockholders of the Corporation must be effected at a duly called annual or special meeting of such holders and may not be effected by any consent in writing by such holders.

Section 11. Record Date. The Board may fix, in advance, a date as the record date for the purpose of determining stockholders entitled to notice of or to vote at any meeting of stockholders, or stockholders entitled to receive payment of any dividend or the allotment of any rights or to exercise any rights in respect of any change, conversion or exchange of stock, or in order to make a determination of stockholders for the purpose of any other lawful action. Such date, in any case, shall be not more than sixty (60) days, and in case of a meeting of stockholders not less than ten (10) days, prior to the date on which the particular action requiring such determination of stockholders is to be taken. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting unless the Board fixes a new record date for the adjourned meeting. If the Board does not so fix a record date, the record date for: (i) determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day next preceding the day on which notice is given, or, if notice is waived, at the close of business on the day next preceding the day on which the meeting is held; and (ii) any other purpose shall be at the close of business on the day on which the Board adopts the resolution relating thereto.

Section 12. List of Stockholders. It shall be the duty of the Secretary or other officer of the Corporation who shall have charge of the stock records, either directly or through a transfer agent appointed by the Board, to prepare and make, at least ten (10) days before every stockholders meeting, a complete list of stockholders entitled to vote at such meeting, arranged in alphabetical order and showing the address of each stockholder and the number of shares registered in the name of each stockholder. The Corporation shall not be required to include electronic mail addresses or other electronic contact information on such list. Such list shall be open to the examination of any stockholder for any purpose germane to the meeting for a period of at least ten (10) days prior to the meeting: (i) on a reasonably accessible electronic network, provided that the information required to gain access to such list is provided with the notice of the meeting; or (ii) during ordinary business hours at the principal place of business of the Corporation. The list shall be produced and kept at the time and place of the meeting during the whole time thereof and shall be subject to the inspection of any stockholder who may be present. The stock records of the Corporation shall be the only evidence of who are the stockholders entitled to examine such list or the books of the Corporation or to vote in person or by proxy at such meeting.

Section 13. Proposals by Stockholders at Annual Meeting. At an annual meeting of stockholders, only such business shall be conducted as shall have been properly brought before the meeting. To be properly brought before an annual meeting, business must be: (i) specified in the notice of meeting (or any supplement thereto) given in accordance with these Bylaws; (ii) properly brought before the meeting by or at the direction of the Board; or (iii) properly brought before the meeting by a stockholder that (A) is a stockholder of record on the date of the giving of notice provided for in this Article II, Section 13 and on the record date for the determination of stockholders entitled to vote at such annual meeting and (B) complies with the notice procedures set forth in this Article II, Section 13. For business to be properly brought before an annual meeting by a stockholder, the stockholder must have given timely notice thereof in writing to the Secretary of the Corporation. To be timely and unless waived by formal action of the Board, a stockholder's notice must be delivered to or mailed and received at the principal executive offices of the Corporation not fewer than sixty (60) and not more than ninety (90) calendar days in advance of the date that is the one year anniversary of the notice date in the Corporation's proxy statement for the previous year's annual meeting of stockholders; provided, however, that in the event that no annual meeting was held in the previous year or the date of the annual meeting has been advanced by more than thirty (30) days or delayed by more than sixty (60) days from the one year anniversary of the previous year's annual meeting of stockholders, notice by a stockholder to be timely must be so received not earlier than the ninetieth (90th) day prior to such annual meeting and not later than the close of business on the tenth (10th) day following the day notice of the date of the meeting was first mailed or public disclosure of the date of the meeting was first made (via press release reported by a national news service or via a filing with the Securities and Exchange Commission pursuant to the Securities Exchange Act of 1934, as amended (the "**Exchange Act**")), whichever occurs first; provided that public announcement of an adjournment of an annual meeting shall not commence a new time period for the giving of such notice by a stockholder.

To be properly brought before an annual meeting, a stockholder's notice must set forth (in addition to any information required by applicable law) : (1) a description of the business desired to be brought before the annual meeting and the reasons for conducting such business at the annual meeting; (2) the name and address, as they appear on the Corporation's

books, of the stockholder proposing such business and the beneficial owner, if any, on whose behalf such proposal is made; (3) the class and number of shares of the Corporation which are beneficially owned by the stockholder and the beneficial owner on whose behalf the proposal is made; (4) any material interest, direct or indirect, of the stockholder and such beneficial owner in such business; and (5) a representation that the stockholder is a holder of record of shares of the Corporation entitled to vote at the meeting and intends to appear in person or by proxy at the meeting to present the proposal.

Notwithstanding anything in these Bylaws to the contrary, no business shall be conducted at any annual meeting except in accordance with the procedures set forth in this Article II, Section 13. The officer presiding at such annual meeting shall, if the facts warrant, determine and declare at the meeting that business was not properly brought before the meeting and in accordance with the provisions of this Section 13 and that such business shall not be transacted.

In addition to the foregoing provisions of this Article II, Section 13, a stockholder shall also comply with all applicable requirements of the Exchange Act, the rules and regulations thereunder and the DGCL with respect to matters set forth in this Article II, Section 13. Nothing in this Section 13 shall be deemed to affect any rights of stockholders to request inclusion of proposals in the Corporation's proxy statement pursuant to Rule 14a-8 under the Exchange Act.

Section 14. Nominations by Stockholders at Annual Meeting. Only persons who are nominated in accordance with the procedures set forth in this Article II, Section 14 shall be eligible for election as directors, except as otherwise may be provided in the Charter with respect to the right of holders of any series of preferred stock then outstanding. Nominations of persons for election to the Board may be made at a meeting of stockholders by or at the direction of the Board (or any committee thereof) or by any stockholder of the Corporation entitled to vote in the election of directors at the meeting who complies with the notice procedures set forth in this Article II, Section 14. Any such nomination by a stockholder shall be made pursuant to timely notice in writing to the Secretary of the Corporation in accordance with the provisions of Article II, Section 13. For such nomination to be properly made, such stockholder's notice shall set forth: (i) as to each person whom the stockholder proposes to nominate for election or re-election as a director, (A) the name, age, business address and residence address of such person, (B) the principal occupation or employment of such person, (C) the class and number of shares of the Corporation that are beneficially owned by such person, (D) a description of all arrangements or understandings between the stockholder (or the beneficial owner, if any, on whose behalf such nomination is made) and each nominee and any other person or persons (naming such person or persons) pursuant to which the nominations are to be made by the stockholder, and (E) any other information relating to such person that is required to be disclosed in solicitations of proxies for elections, or is otherwise required, in each case pursuant to Regulation 14A under the Exchange Act (including without limitation such person's written consent to being named in the proxy statement, if any, as a nominee and to serving as a director if elected); and (ii) as to the stockholder giving notice, the information required to be provided pursuant to Article II, Section 13. At the request of the Board, any person nominated by a stockholder for election as a director shall furnish to the Secretary of the Corporation that information required to be set forth in the stockholder's notice of nomination that pertains to the nominee. No stockholder nominee shall be eligible for

election as a director of the Corporation unless nominated in accordance with the procedures set forth in this Article II, Section 14. The officer presiding at such annual meeting shall, if the facts warrant, determine and declare at the meeting that a nomination was not made in accordance with the procedures prescribed by these Bylaws and that the defective nomination shall be disregarded.

In addition to the foregoing provisions of this Article II, Section 14, a stockholder shall also comply with all applicable requirements of the Exchange Act and the rules and regulations thereunder with respect to matters set forth in this Article II, Section 14. Nothing in this Section 14 shall be deemed to affect any rights of stockholders to request inclusion of proposals in the Corporation's proxy statement pursuant to Rule 14a-8 under the Exchange Act.

Section 15. Conduct of Meetings. Meetings of stockholders shall be presided over by the Chairman of the Board or, in the absence thereof, (i) such person as the Chairman of the Board shall appoint or, in the absence thereof or in the event that the Chairman of the Board shall fail to make such appointment, (ii) any officer of the Corporation appointed by the Board. In the absence of the Secretary of the Corporation, the secretary of the meeting shall be such person as the officer presiding at the meeting appoints.

The Corporation shall, in advance of any meeting of stockholders, appoint one (1) or more inspector(s) to act at the meeting of stockholders and make a written report thereof. The Board may designate one (1) or more persons as alternate inspector(s) to replace any inspector who fails to act. If no inspector or alternate has been appointed or is able to act at a meeting of stockholders, the officer presiding at the meeting shall appoint one (1) or more inspector(s) to act at the meeting. Each inspector, before discharging his or her duties, shall take and sign an oath to faithfully execute the duties of inspector with strict impartiality and according to the best of his or her ability. The inspector(s) or alternate(s) shall have the duties prescribed pursuant to Section 231 of the DGCL or other applicable law.

The Board shall be entitled to make such rules or regulations for the conduct of meetings of stockholders as it shall deem necessary, appropriate or convenient. Subject to such rules and regulations, if any, the officer presiding at the meeting shall have the right and authority to prescribe such rules, regulations and procedures and to do all acts as, in his or her judgment, are necessary, appropriate or convenient for the proper conduct of the meeting, including without limitation establishing an agenda or order of business of the meeting, rules or regulations to maintain order and the safety of those present, limitations on the time allotted for questions or comments, restrictions on entry to the meeting after the time fixed for commencement thereof and the fixing of the date and time of the opening and closing of the polls for each matter upon which the stockholders will vote at a meeting (and shall announce such at the meeting). Unless and to the extent determined by the Board or the officer presiding at any meeting, meetings of stockholders shall not be required to be held in accordance with rules of parliamentary procedure.

Section 16. Notice by Electronic Transmission. Without limiting the manner by which notice otherwise may be given effectively to stockholders, any notice to stockholders given by the Corporation under any provision of the DGCL, the Charter or these Bylaws shall be effective if given by a form of electronic transmission consented to by the stockholder to which the notice is given. Any such consent shall be revocable by the

stockholder by written notice to the Corporation and shall be deemed revoked if (i) the Corporation is unable to deliver by electronic transmission two (2) consecutive notices given by the Corporation in accordance with such consent and (ii) such inability becomes known to the Secretary or an Assistant Secretary of the Corporation, the transfer agent or other person responsible for the giving of notice; provided, however, the failure to treat such inability as a revocation shall not invalidate any meeting or other action. This Article II, Section 16 shall not apply to those situations in which notice by electronic transmission is not permitted in accordance with Section 232 of the DGCL.

Notice given pursuant to the preceding paragraph shall be deemed given if by (i) facsimile telecommunication, when directed to a number at which the stockholder has consented to receive notice, (ii) electronic mail, when directed to an electronic mail address at which the stockholder has consented to receive notice, (iii) a posting on an electronic network together with a separate notice to the stockholder of such specific posting, upon the later of (A) such posting and (B) the giving of such separate notice and (iv) any other form of electronic transmission, when directed to the stockholder.

For purposes of these Bylaws, “**electronic transmission**” means any form of communication, not directly involving the physical transmission of paper, that creates a record that may be retained, retrieved and reviewed by a recipient thereof, and that may be directly reproduced in paper form by such a recipient through an automated process.

ARTICLE III

Board of Directors

Section 1. General Powers. The business and affairs of the Corporation shall be managed by the Board, except as otherwise provided by law, the Charter or these Bylaws.

Section 2. Number, Term and Qualification. The Board shall consist of not less than three or more than thirteen members as fixed from time to time in accordance with the terms of the Charter. Each director shall hold office until the expiration of the term for which elected and until his or her successor is elected and qualified or until his or her earlier death, resignation, retirement or removal. No reduction in the number of directors shall have the effect of removing any director before such director’s term of office expires. Directors need not be residents of the State of Delaware or stockholders of the Corporation.

Section 3. Removal. Except as otherwise provided in the Charter or required by law, directors may be removed from office with or without cause only by a vote of stockholders who hold at least 66 2/3% of the aggregate voting power of the then-outstanding shares of capital stock of the Corporation entitled to vote on the election of directors. If any directors are so removed, new directors may be elected at the same meeting.

Section 4. Resignation. Any director of the Corporation may resign at any time by giving notice in writing or by electronic transmission to the Chairman of the Board or the Secretary of the Corporation. The resignation of any director shall take effect upon receipt of notice thereof or at such later time as shall be specified therein. The acceptance of such resignation shall not be necessary to make it effective.

Section 5. Vacancies. Except as may otherwise be provided in the Charter or required by law, any newly created directorship resulting from any increase in the authorized number of directors and any vacancy in the Board resulting from death, resignation, retirement, removal or other cause shall, unless otherwise provided by resolution of the Board, be filled only by a majority vote of the directors then in office, whether or not less than a quorum, and each director so chosen shall hold office until expiration of the term for which elected and until his or her successor is elected and qualified or until his or her earlier death, resignation, retirement or removal.

Section 6. Compensation. The Board shall have the authority to fix the compensation of directors for service in such capacity and may provide for the payment or reimbursement of expenses incurred by the directors in connection with such service. Any director may serve the Corporation in any other capacity and receive compensation therefor.

ARTICLE IV

Meetings of Directors

Section 1. Annual and Regular Meetings. The annual meeting of the Board for the purpose of electing officers and transacting such other business as may be brought before the meeting shall be held immediately following, and at the same location as, the annual meeting of the stockholders, and no notice of such annual meeting shall be required; provided that the Board may fix another time and place for such annual meeting in which case it shall provide notice in the manner provided herein for special meetings. Regular meetings of the Board may be held without notice at such time and place as shall from time to time be determined by the Board.

Section 2. Special Meetings. Special meetings of the Board may be called by or at the request of the Chairman of the Board, the Chief Executive Officer, the President or a majority of the directors then in office. Such meetings may be held at the time and place designated in the notice of the meeting.

Section 3. Notice of Special Meetings. The Secretary or other person or persons calling a meeting for which notice is required shall give notice of each special meeting of the Board to each director personally, by telephone or by mail, electronic transmission, overnight mail, courier service or telegram, postage or charges prepaid, at his or her address as shown on the records of the Corporation. If the notice is: (i) given by telephone, electronic transmission, facsimile or hand delivery, it shall be deemed adequate if given at least twelve (12) hours prior to the time set for the meeting; (ii) mailed, it shall be deemed adequate if deposited in the United States mail at least four (4) calendar days before the date of the meeting; (iii) delivered by overnight mail, courier service or telegram, it shall be deemed adequate when delivered to the overnight mail or courier service company or telegraph company at least forty-eight (48) hours before such meeting. Any oral notice given personally or by telephone may be communicated either to the director or to a person at the office of the director who the person giving the notice has reason to believe will promptly communicate it to the director. The notice need not specify the purpose or the place of the meeting, if the meeting is to be held at the principal executive office of the Corporation. Whenever notice is required to be given under any provision of the DGCL, the Charter or

these Bylaws, a written waiver thereof, signed by the director entitled to notice, or a waiver by electronic transmission by the director entitled to notice, whether before or after the time stated therein, shall be deemed equivalent to notice. Attendance of a director at a meeting shall constitute a waiver of notice of such meeting, except when the director attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the stockholders need be specified in any written waiver of notice, or any waiver by electronic transmission, unless so required by the Charter or these Bylaws.

Section 4. Quorum. A majority of the directors then in office shall constitute a quorum for the transaction of business at a meeting of the Board. Any regular or special meeting may be adjourned from time to time by a majority of those present, whether or not a quorum.

Section 5. Manner of Acting. Except as otherwise provided by law, the Charter or these Bylaws, the act of the majority of the directors present at a meeting at which a quorum is present shall be the act of the Board.

Section 6. Action Without Meeting. Any action required or permitted to be taken at any meeting of the Board, or of any committee thereof, may be taken without a meeting if all members thereof consent thereto in writing or by electronic transmission and the writing(s) or electronic transmission(s) are filed with the minutes of proceedings of the Board or committee. Such unanimous written consent shall have the same force and effect as a unanimous vote at a meeting and may be stated as such in any articles, certificates or documents filed with the Secretary of State of Delaware, or any other state wherein the Corporation may do business.

Section 7. Meeting by Use of Conference Telephone. Any one or more directors or members of a committee may participate in a meeting of the Board or any of its committees by means of a conference telephone or similar communications equipment by means of which all persons participating in the meeting can hear each other, and such participation in a meeting shall be deemed presence in person at such meeting, except where a person participates in the meeting for the express purpose of objecting to the transaction of any business on the ground that the meeting is not lawfully called or convened.

ARTICLE V

Committees

Section 1. Designation of Committees. The Board may, by resolution passed by a majority of the directors then in office, designate one or more committees, each committee to consist of one or more of the directors of the Corporation. The Board may designate one or more directors as alternate members of any committee to replace any absent or disqualified member at any meeting of the committee. Any such committee, to the extent provided in these Bylaws or in a resolution of the Board, shall have and may exercise all the lawfully delegable powers and authority of the Board in the management of the business and affairs of the Corporation. Such committee or committees shall have such name or names as may be determined from time to time by resolution adopted by the Board.

Section 2. Executive Committee. There may be an Executive Committee of not more than three directors designated by resolution passed by a majority of the directors then in office. Such committee may meet at stated times, or on notice to all by any of their own number. During intervals between meetings of the Board, the Executive Committee shall have and may exercise the powers of the Board in the management of the business and affairs of the Corporation, except that the Executive Committee shall not have authority to authorize or approve, or to recommend to the stockholders, the following matters:

(a) Any action or matter required by law to be submitted to the stockholders for their approval.

(b) The designation of an Executive Committee or any other committee having power to exercise any of the authority of the Board in the management of the Corporation or the filling of vacancies in the Board or in such committee.

(c) The fixing of compensation of the directors for serving on the Board or on such committee.

(d) The amendment or repeal of any bylaw or the adoption of any new bylaw.

(e) The amendment or repeal of any resolution of the Board that by its terms shall not be so amendable or repealable.

Vacancies in the membership of the Executive Committee shall be filled by a majority of the directors then in office.

Section 3. Minutes. Each committee shall keep minutes of its proceedings and shall report thereon to the Board when required by the Board.

Section 4. Meetings and Action of Committees. Meetings and actions of committees shall be governed by, and held and taken in accordance with, the provisions of Article IV applicable to meetings and actions of the Board, with such changes in the context of those Bylaws as are necessary to substitute the committee and its members for the Board and its members; provided, however, that the time of regular and special meetings of committees may also be called by the Board and that the Board may adopt rules for any committee not inconsistent with the provisions of these Bylaws.

ARTICLE VI

Officers

Section 1. Titles. The officers of the Corporation shall be elected by the Board and shall consist of a President, a Secretary and a Treasurer. The Board may also elect a Chairman of the Board, a Vice Chairman of the Board, a Chief Executive Officer, a Chief Financial Officer, one or more Vice Presidents, a Controller, one or more Assistant Secretaries, one or more Assistant Treasurers, one or more Assistant Controllers and such

other officers as may be elected in accordance with Section 3 of this Article VI. Except as otherwise provided in these Bylaws, officers shall have the authority and perform the duties as from time to time may be prescribed by the Board or the officer electing such officer in accordance with Section 3 of this Article VI. Any two or more offices may be held by the same individual, but no officer may act in more than one capacity where action of two or more officers is required.

Section 2. Election and Term. The officers of the Corporation shall be elected by the Board at the regular meeting of the Board held each year immediately following the annual meeting of the stockholders. Each officer shall hold office until his or her successor is elected and qualified or until his or her death, resignation, retirement or removal.

Section 3. Subordinate Officers. The Board may elect, or empower the Chief Executive Officer or the President to elect, such other officers as the business of the Corporation may require, each of whom shall hold office for such period, have such authority, and perform such duties as are provided in these Bylaws or as the Board or the Chief Executive Officer or President may from time to time determine.

Section 4. Removal, Resignation and Vacancy. Any officer may be removed, with or without cause, by the Board, but removal shall be without prejudice to any contract rights of the officer removed. Election of an officer shall not of itself create contract rights. Any officer may resign at any time by giving written notice to the Corporation, effective as of the date of receipt of that notice or at any later time specified in that notice. Unless otherwise specified in such notice, the acceptance of the resignation shall not be necessary to make it effective. Any resignation is without prejudice to any rights of the Corporation under any contract to which the officer is a party. Any vacancy among the officers may be filled by the Board or otherwise in accordance with Section 3 of this Article VI.

Section 5. Chairman of the Board. The Chairman of the Board, if such officer is elected, shall preside at meetings of the Board and of stockholders and shall have such other authority and perform such other duties as the Board shall designate or as may be prescribed by these Bylaws. The Vice Chairman of the Board, if such officer is elected, shall fulfill the duties of the Chairman of the Board in his or her absence.

Section 6. Chief Executive Officer. The Chief Executive Officer, if such officer is elected, shall, subject to the control of the Board, have general supervision, direction and control of the business and affairs of the Corporation, shall report directly to the Board and shall have such other powers and perform such other duties as the Board shall designate or as may be provided by applicable law or prescribed by these Bylaws.

Section 7. President. In the absence or inability or refusal to act of the Chief Executive Officer, the President shall have all of the powers and duties of the Chief Executive Officer. The President shall have such other powers and duties as the Board or the Chief Executive Officer shall designate or as may be provided by applicable law or prescribed by these Bylaws.

Section 8. Vice Presidents. In the absence or inability or refusal to act of the President, the Vice President(s), if any are elected, in order of their rank as fixed by the Board or, if not ranked, a Vice President designated by the Board, shall have all of the powers and duties of the President. Each Vice President shall have such other powers and duties as the Board, the Chief Executive Officer or the President shall designate or as may be provided by applicable law or prescribed by these Bylaws.

Section 9. Chief Financial Officer. The Chief Financial Officer, if such officer is elected, shall keep and maintain, or cause to be kept and maintained, adequate and correct books and records of accounts of the properties and business transactions of the Corporation, including accounts of its assets, liabilities, receipts, disbursements, gains, losses, capital and retained earnings. The Chief Financial Officer shall deposit all money and other valuables in the name and to the credit of the Corporation with such depositories as may be designated by the Board or the Chief Executive Officer, disburse the funds of the Corporation as may be ordered by the Board, render to the Board and the Chief Executive Officer, upon request, an account of all of his or her transactions as Chief Financial Officer and of the financial condition of the Corporation, and have such other powers and duties as the Board or the Chief Executive Officer shall designate or as may be provided by applicable law or prescribed by these Bylaws.

Section 10. Treasurer. In the absence or inability or refusal to act of the Chief Financial Officer, the Treasurer shall have all of the powers and duties of the Chief Financial Officer. The Treasurer shall have such other powers and duties as the Board, the Chief Executive Officer or the Chief Financial Officer shall designate or as may be provided by applicable law or prescribed by these Bylaws.

Section 11. Assistant Treasurers. In the absence or inability or refusal to act of the Treasurer, the Assistant Treasurer(s), if any are elected, in the order determined by the Board (or if there be no such determination, then in the order of their election), shall have the powers and duties of the Treasurer. The Assistant Treasurer(s) shall have such other powers and duties as the Board or the Treasurer shall designate or as prescribed by these Bylaws.

Section 12. Controller and Assistant Controllers. The Controller shall have charge of the accounting affairs of the Corporation and shall have such other powers and duties as the Board or the Chief Executive Officer shall designate. In the absence or inability or refusal to act of the Controller, the Assistant Controller(s), if any, in the order determined by the Board (or if there be no such determination, then in the order of their election), shall have the powers and perform the duties of the Controller. The Assistant Controllers shall have such other powers and duties as the Board or the Controller shall designate.

Section 13. Secretary. The Secretary shall keep or cause to be kept accurate records of the acts and proceedings of all meetings of stockholders and of the Board and of all committees of the Board and shall give or cause to be given all notices required by law and by these Bylaws. The Secretary shall have general charge of the corporate books and records and of the corporate seal and shall affix the corporate seal to any lawfully executed instrument requiring it. The Secretary shall have general charge of the stock transfer books of the Corporation and shall keep at the principal office of the Corporation (or at the office of the Corporation's transfer agent or registrar) a record of stockholders,

showing the name and address of each stockholder and the number and class of the shares held by each. The Secretary shall have such other powers and duties as the Board or the Chief Executive Officer shall designate or as may be provided by applicable law or prescribed by these Bylaws.

Section 14. Assistant Secretaries. In the absence or inability or refusal to act of the Secretary, the Assistant Secretary(ies), if any, in the order determined by the Board (or if there be no such determination, then in the order of their election), shall have the powers and duties of the Secretary. The Assistant Secretaries shall have such other powers and perform such other duties as the Board or the Secretary shall designate or as prescribed by these Bylaws.

Section 15. Voting of Stock. Unless otherwise ordered by the Board, either the Chief Executive Officer or the President shall have full power and authority on behalf of the Corporation to attend, act and vote at meetings of the stockholders of any Corporation in which this Corporation may hold stock and, at such meetings shall possess and may exercise any and all rights and powers incident to the ownership of such stock and which, as the owner, the Corporation possesses. The Board may by resolution from time to time confer such power and authority upon any other person or persons.

ARTICLE VII

Capital Stock

Section 1. Certificates. Certificates for shares of the capital stock of the Corporation shall be in such form not inconsistent with the Charter as shall be approved by the Board. The certificates shall be consecutively numbered or otherwise identified. The name and address of the persons to whom they are issued, with the number of shares and date of issue, shall be entered on the stock transfer records of the Corporation. Each certificate shall be signed by the Chairman of the Board, Chief Executive Officer, President or any Vice President and by the Secretary, Assistant Secretary, Treasurer or Assistant Treasurer; provided, that where a certificate is signed by a transfer agent or assistant transfer agent of the Corporation, the signatures of such officers of the Corporation upon the certificate may be by facsimile, engraved or printed. In case any officer, transfer agent or registrar who has signed or whose facsimile signature has been placed upon a certificate has ceased to be such officer, transfer agent or registrar before such certificate is issued, it may be issued by the Corporation with the same effect as if he were such officer, transfer agent or registrar at the date of issue. Each certificate shall be sealed with the seal of the Corporation or a facsimile thereof. The Board may provide by resolution that some or all of any or all classes or series of its stock shall be uncertificated shares, provided that any such resolution shall not apply to shares represented by a certificate until such certificate is surrendered to the Corporation. Notwithstanding the adoption of such a resolution by the Board, every holder of stock represented by certificates and upon request every holder of uncertificated shares shall be entitled to have a certificate signed as set forth above.

Section 2. Transfer of Shares. Transfer of shares shall be made on the stock transfer books of the Corporation only upon surrender of the certificate for the shares sought to be transferred by the record holder or by a duly authorized agent, transferee or legal

representative to the Corporation or its transfer agent, duly endorsed or accompanied by proper evidence of succession, assignment or authority to transfer. All certificates surrendered for transfer shall be cancelled before new certificates for the transferred shares shall be issued.

Section 3. Transfer Agent and Registrar. The Board may appoint one or more transfer agents and one or more registrars of transfers and may require all stock certificates to be signed or countersigned by the transfer agent and registered by the registrar of transfers.

Section 4. Regulations. The Board shall have power and authority to make rules and regulations as it may deem expedient concerning the issue, transfer and registration of certificates for shares of capital stock of the Corporation.

Section 5. Lost Certificates. The Corporation may issue a new certificate in place of a certificate claimed to have been lost or destroyed, upon receipt of an affidavit from the person explaining the loss or destruction. The Corporation may require the claimant to give the Corporation a bond in a sum as it may direct to indemnify the Corporation against loss from any claim with respect to the certificate claimed to have been lost or destroyed or with respect to the issuance of such new certificate.

ARTICLE VIII

INDEMNIFICATION

Section 1. Right to Indemnification in Proceedings other than those by or in the Right of the Corporation. The Corporation shall indemnify any person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (a “**proceeding**”) (other than an action by or in the right of the Corporation) by reason of the fact that such person 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, 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 to the fullest extent permitted by the DGCL, as the same exists or as may be amended (but, in the case of any amendment, only to the extent such amendment permits broader indemnification rights than such law permitted the Corporation provided prior to such amendment). Such indemnification shall, unless otherwise provided when authorized or ratified, continue as to an indemnitee who has ceased to be a director or officer and shall inure to the benefit of the indemnitee’s heirs, executors and administrators; provided that, except as provided in Section 3 of this Article VIII with respect to proceedings to enforce rights to indemnification, the Corporation shall indemnify any such indemnitee in connection with a proceeding (or part thereof) initiated by such indemnitee only if such proceeding (or part thereof) was authorized by the Board. The right to indemnification conferred in this Section shall be a contract right and shall include the right to be paid by the Corporation the expenses (including attorneys’ fees) incurred in defending any such proceeding in advance of its final disposition (hereinafter, an “**advancement of expenses**”); provided, however, that if the DGCL so requires, an advancement of expenses incurred by an indemnitee in his or her capacity as a director or

officer (and not in any other capacity in which service was or is rendered by such indemnitee, including without limitation, service to an employee benefit plan) shall be made only upon delivery to the Corporation of an undertaking, by or on behalf of such indemnitee, to repay all amounts so advanced if it shall ultimately be determined that such indemnitee is not entitled to be indemnified by the Corporation under this Section or otherwise (hereinafter an “**undertaking**”).

Section 2. Right to Indemnification in Proceedings by or in the Right of the Corporation. The Corporation 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 or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that such person 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, against expenses (including attorneys’ fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit to the fullest extent permitted by the DGCL, as the same exists or as may be amended (but, in the case of any amendment, only to the extent such amendment permits broader indemnification rights than such law permitted the Corporation provided prior to such amendment).

Section 3. Right of Indemnitee to Bring Suit. If a claim under Section 1 or Section 2 of this Article VIII is not paid in full by the Corporation within sixty (60) days after a written claim has been received by the Corporation, except in the case of a claim for an advancement of expenses, in which case the applicable period shall be twenty (20) days, the indemnitee may at any time thereafter bring suit against the Corporation to recover the unpaid amount of the claim. If successful in whole or in part in any such suit or in a suit brought by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the indemnitee shall be entitled to be paid also the expense of prosecuting or defending such suit. In (i) any suit brought by the indemnitee to enforce a right to indemnification hereunder (but not in a suit brought by the indemnitee to enforce a right to an advancement of expenses) it shall be a defense that, and (ii) any suit by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking the Corporation shall be entitled to recover such expenses upon a final adjudication that, the indemnitee has not met the applicable standard of conduct set forth in the DGCL in order to empower the Corporation to indemnify him or her. Neither the failure of the Corporation (including, without limitation, its independent legal counsel, its stockholders or the Board) to have made a determination prior to the commencement of such suit that indemnification of the indemnitee is proper in the circumstances because the indemnitee has met the applicable standard of conduct set forth in the DGCL, nor an actual determination by the Corporation (including, without limitation, its independent legal counsel, its stockholders or the Board) that the indemnitee has not met such applicable standard of conduct, shall create a presumption that the indemnitee has not met the applicable standard of conduct or, in the case of such a suit brought by the indemnitee, be a defense to such suit. In any suit brought by the indemnitee to enforce a right hereunder, or by the Corporation to recover an advancement of expenses pursuant to the terms of an undertaking, the burden of proving that the indemnitee is not entitled to be indemnified or to such advancement of expenses hereunder or otherwise shall be on the Corporation.

Section 4. Nonexclusivity of Indemnification and Advancement of Expenses. The indemnification and advancement of expenses provided by, or granted pursuant to, this Article VIII shall not be deemed exclusive of any other rights to which those seeking indemnification or advancement of expenses may be entitled under the Charter, any Bylaw, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in such person's official capacity and as to action in another capacity while holding such office, it being the policy of the Corporation that indemnification of the persons specified in Sections 1 and 2 of this Article VIII shall be made to the fullest extent permitted by law. The provisions of this Article VIII shall not be deemed to preclude the indemnification of any person who is not specified in Section 1 or 2 of this Article VIII but whom the Corporation has the power or obligation to indemnify under the provisions of the DGCL or otherwise.

Section 5. Insurance. The Corporation may purchase and maintain insurance on behalf of any person who is or was a director, officer, employee or agent of the Corporation, or is or was serving at the request of the Corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise against any liability asserted against such person and incurred by such person in any such capacity, or arising out of such person's status as such, whether or not the Corporation would have the power or the obligation to indemnify such person against such liability under the provisions of this Article VIII.

Section 6. Certain Definitions. For purposes of this Article VIII, references to: (i) "the Corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors or officers, so that any person who is or was a director or officer of such constituent corporation, or is or was serving at the request of such constituent corporation as a director or officer of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, shall stand in the same position under the provisions of this Article VIII with respect to the resulting or surviving corporation as such person would have with respect to such constituent corporation if its separate existence had continued; (ii) "fines" shall include any excise taxes assessed on a person with respect to an employee benefit plan; and (iii) "serving at the request of the Corporation" shall include any service as a director or officer of the Corporation which imposes duties on, or involves services by, such director or officer with respect to an employee benefit plan, its participants or beneficiaries.

Section 7. Indemnification of Employees and Agents. The Corporation may, to the extent authorized from time to time by the Board, provide rights to indemnification and the advancement of expenses to any employee or agent of the Corporation, to any other person serving the Corporation or to any person who is or was serving at the request of the Corporation as an employee or agent of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, and such rights may be equivalent to, or greater or less than, the rights conferred in this Article VIII to directors and officers of the Corporation.

Section 8. Severability. If any provision or provisions of this Article VIII shall be held to be invalid, illegal or unenforceable for any reason whatsoever: (i) the

validity, legality and enforceability of the remaining provisions of this Article VIII (including, without limitation, each portion of any Section of this Article VIII containing any such provision held to be invalid, illegal or unenforceable, that is not itself held to be invalid, illegal or unenforceable) shall not in any way be affected or impaired thereby; and (ii) to the fullest extent possible, the provisions of this Article VIII (including, without limitation, each such portion of any Section of this Article VIII containing any such provision held to be invalid, illegal or unenforceable) shall be construed so as to give effect to the intent manifested by the provision held invalid, illegal or unenforceable.

ARTICLE IX

General Provisions

Section 1. Dividends. The Board may from time to time declare, and the Corporation may pay, dividends out of its earned surplus on its outstanding shares in the manner and upon the terms and conditions provided by law.

Section 2. Seal. The seal of the Corporation shall have inscribed thereon the name of the Corporation and "Delaware" around the perimeter, and the words "Corporate Seal" in the center and may be adopted or altered by or at the direction of the Board. The Corporation may use the seal by causing it or a facsimile thereof to be impressed, affixed or reproduced.

Section 3. Depositories and Checks. All funds of the Corporation shall be deposited in the name of the Corporation in such bank, banks, or other financial institutions as the Board or officers designated by the Board may from time to time designate and shall be drawn out on checks, drafts or other orders signed on behalf of the Corporation by such person or persons as the Board may from time to time designate.

Section 4. Bond. The Board may by resolution require any or all officers, agents and employees of the Corporation to give bond to the Corporation, with sufficient sureties, conditioned on the faithful performance of the duties of their respective offices or positions, and to comply with such other conditions as may from time to time be required by the Board.

Section 5. Fiscal Year. The fiscal year of the Corporation shall be the period ending on December 31 of each year or such other period as the Board shall from time to time determine.

Section 6. Amendments. Except as otherwise provided herein, these Bylaws may be amended or repealed and new Bylaws may be adopted at any annual meeting or at any special meeting of stockholders called for the purpose of considering such action by the affirmative vote of the holders of at least a majority of the aggregate voting power of the then-outstanding shares of capital stock of the Corporation, voting together as a single class; provided that the affirmative vote of the holders of at least 66 2/3% of the aggregate voting power of the then-outstanding shares of capital stock of the Corporation, voting together as a single class, shall be required to adopt, amend or repeal all or any portion of Section 13 or 14 of Article II, Section 2 of Article III, Article VIII and Section 6 of Article IX of these Bylaws.

These Bylaws may also be amended or repealed and new Bylaws may be adopted by the Board acting pursuant to Article IV, but the stockholders of the Corporation may adopt, amend or repeal any bylaw whether adopted by the Board or otherwise.



AMERICAN BANK NOTE COMPANY
 711 ARMSTRONG LANE
 COLUMBIA, TENNESSEE 38401
 (931) 388-3003
 SALES: J. NAPOLITANO 212-269-0339X14
 / ETHER 13 / LIVE JOBS / T / TARGACEPT 18440 FC

PRODUCTION COORDINATOR: TODD DEROSSETT
 931-490-1720
 PROOF OF JANUARY 18, 2005
 TARGACEPT, INC.
 TSB 18440 FC
 Operator: Ron
 New

PLEASE INITIAL THE APPROPRIATE SELECTION FOR THIS PROOF:
 ___ OK AS IS ___ OK WITH CHANGES ___ MAKE CHANGES AND SEND ANOTHER PROOF

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The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN COM – as tenants in common
TEN ENT – as tenants by the entireties
JT TEN – as joint tenants with right of survivorship and not as tenants in common

UNIF GIFT MIN ACT – _____ Custodian _____
(Cust) (Minor)
under Uniform Gifts to Minors
Act of _____
(State)

Additional abbreviations may also be used though not in the above list.

For Value Received, _____ hereby sell, assign and transfer unto

(PLEASE PRINT OR TYPEWRITE NAME AND ADDRESS, INCLUDING ZIP CODE, OF ASSIGNEE)

PLEASE INSERT SOCIAL SECURITY OR OTHER IDENTIFYING NUMBER OF ASSIGNEE

[Empty box for Social Security or other identifying number]

_____ Shares
of the capital stock represented by the within certificate, and do hereby irrevocably constitute and appoint

_____ Attorney
to transfer the said stock on the books of the within named Corporation with full power of substitution in the premises.

Dated _____

NOTICE: SIGNATURE MUST CORRESPOND TO THE NAME AS WRITTEN UPON THE FACE OF THIS CERTIFICATE IN EVERY PARTICULAR, WITHOUT ALTERATION OR ENLARGEMENT OR ANY CHANGE WHATSOEVER AND MUST BE GUARANTEED BY A BANK, BROKER OR ANY OTHER ELIGIBLE GUARANTOR INSTITUTION THAT IS AUTHORIZED TO DO SO UNDER THE SECURITIES TRANSFER AGENTS MEDALLION PROGRAM (STAMP) UNDER RULES PROMULGATED BY THE U.S. SECURITIES AND EXCHANGE COMMISSION

AMERICAN BANK NOTE COMPANY
711 ARMSTRONG LANE
COLUMBIA, TENNESSEE 38401
(931) 388-3003
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New

PLEASE INITIAL THE APPROPRIATE SELECTION FOR THIS PROOF: ___ OK AS IS ___ OK WITH CHANGES ___ MAKE CHANGES AND SEND ANOTHER PROOF

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
One Financial Center
Boston, MA 02111

_____, 2005

Targacept, Inc.
200 East First Street, Suite 300
Winston-Salem, NC 27101

Ladies and Gentlemen:

We have acted as counsel to Targacept, Inc., a Delaware corporation (the "Company"), in connection with the preparation and filing with the Securities and Exchange Commission (the "Commission") of a Registration Statement on Form S-1, Registration No. 333-115538 (the "Registration Statement"), as amended, pursuant to which the Company is registering under the Securities Act of 1933, as amended (the "Securities Act"), up to 7,187,500 shares (the "Shares") of its common stock, \$0.001 par value per share (the "Common Stock"). As used herein, the term "Shares" shall include any additional shares of Common Stock which may be registered pursuant to any subsequent registration statement that the Company may file with the Commission pursuant to Rule 462(b) under the Securities Act ("Rule 462(b)") in connection with the offering contemplated by the Registration Statement. The Shares are to be sold to a group of underwriters (the "Underwriters") who will be parties to an Underwriting Agreement with the Company, the form of which Agreement has been filed as an exhibit to the Registration Statement. The 7,187,500 shares of Common Stock covered by the Registration Statement are being sold by the Company and include 937,500 shares subject to an over-allotment option granted to the Underwriters by the Company. All of the shares being registered pursuant to the Registration Statement are being registered for sale to the Underwriters. This opinion is being rendered in connection with the filing of the Registration Statement. All capitalized terms used herein and not otherwise defined shall have the respective meanings given to them in the Registration Statement.

In connection with this opinion, we have examined the Company's Restated Certificate of Incorporation, as amended, and the Restated By-laws, as amended; the minutes of all pertinent meetings of stockholders and directors of the Company relating to the Registration Statement and the transactions contemplated thereby; such other records of the corporate proceedings of the Company and certificates of the Company's officers as we have deemed relevant; and the Registration Statement and the exhibits thereto filed with the Commission.

In our examination, we have assumed the genuineness of all signatures, the legal capacity of natural persons, the authenticity of all documents submitted to us as originals, the conformity to original documents of all documents submitted to us as certified, photostatic or facsimile copies and the authenticity of the originals of such copies.

Based upon the foregoing, and subject to the limitations set forth herein, we are of the opinion that the Shares, when issued by the Company and delivered by the Company against payment therefor as contemplated by the Underwriting Agreement, will be duly and validly issued, fully paid and non-assessable shares of the Common Stock.

Our opinion is limited to the General Corporation Law of the State of Delaware (including the applicable provisions of the Delaware Constitution and the reported judicial decisions

Targacept, Inc.

_____, 2004

Page 2

interpreting such laws) and the Federal laws of the United States, and we express no opinion with respect to the laws of any other jurisdiction. No opinion is expressed herein with respect to the qualification of the Shares under the securities or blue sky laws of any state or any foreign jurisdiction.

We hereby consent to the filing of this opinion as an exhibit to the Registration Statement in accordance with the requirements of Item 601(b) (5) of Regulation S-K promulgated under the Securities Act and to the use of this Firm's name therein under the caption "Legal Matters." In giving such consent, we do not hereby admit that we are in the category of persons whose consent is required under Section 7 of the Securities Act or the rules and regulations of the Commission.

Very truly yours,

MINTZ, LEVIN, COHN, FERRIS,
GLOVSKY AND POPEO, P.C.

INDEMNIFICATION AGREEMENT

THIS AGREEMENT (the "Agreement") is made and entered into as of February __, 2005 between Targacept, Inc., a Delaware corporation (the "Company"), and _____, a director, officer or member of the executive committee of the Company ("Indemnitee").

WITNESSETH THAT:

WHEREAS, Indemnitee performs a valuable service for the Company; and

WHEREAS, the Board of Directors of the Company (the "Board") has adopted bylaws (the "Bylaws") providing for or permitting the indemnification of officers, directors and employees of the Company to the fullest extent permitted by the Delaware General Corporation Law, as amended (the "DGCL"); and

WHEREAS, the Bylaws and the DGCL, by their nonexclusive nature, permit agreements between the Company and its officers, directors and employees with respect to indemnification; and

WHEREAS, in order to induce Indemnitee to continue to serve as a director, officer or member of the executive (management) committee of the Company, the Company has agreed to enter into this agreement with Indemnitee;

NOW, THEREFORE, in consideration of Indemnitee's continued service as a director, officer or member of the executive committee of the Company after the date hereof, the parties agree as follows:

1. Definitions. For purposes of this Agreement:

(a) "Change of Control" means:

(i) The acquisition by any Person of beneficial ownership (within the meaning of Rule 13d-3 promulgated under the Exchange Act) of twenty percent (20%) or more of (A) the then outstanding shares of common stock of the Company (the "Outstanding Company Common Stock") or (B) the combined voting power of the then outstanding voting securities of the Company entitled to vote generally in the election of directors (the "Outstanding Company Voting Securities"); provided that, notwithstanding the foregoing, none of the following acquisitions shall constitute a Change of Control: (1) an acquisition directly from the Company or from other stockholders that (x) was approved in advance by the Board and (y) would not constitute a Change of Control under Section 1(a)(iii); (2) an acquisition by the Company; (3) an acquisition by an employee benefit plan (or related trust) sponsored or maintained by the Company or any entity controlled by, or under common control with, the Company; or (4) an acquisition by an entity with respect to which the criteria set forth in Section 1(a)(iii)(A), (B) and (C) are met; or

(ii) Consummation of a reorganization, merger or consolidation or sale or other disposition of all or substantially all of the assets of the Company (a "Business Combination"); provided that, notwithstanding the foregoing, a Business Combination shall not constitute a Change of Control if: (A) the individuals and entities who are the beneficial owners of the Outstanding Company Common Stock and Outstanding Company Voting Securities, respectively, immediately prior to such Business Combination beneficially own, directly or indirectly, more than fifty percent (50%) of the then outstanding shares of common stock and of the combined voting power of the then outstanding voting securities entitled to vote generally in the election of directors of the resulting,

continuing or surviving entity in such Business Combination (including, if applicable, an entity that, as a result of such transaction, owns the Company or all or substantially all of the Company's assets either directly or through one or more subsidiaries) in substantially the same proportion as existed immediately prior to such Business Combination; (B) no Person (excluding the resulting, continuing or surviving entity in such Business Combination or any employee benefit plan (or related trust) of such resulting, continuing or surviving entity) beneficially owns, directly or indirectly, twenty percent (20%) or more of the then outstanding shares of common stock or of the combined voting power of the then outstanding voting securities of the resulting, continuing or surviving entity in such Business Combination, except to the extent that such ownership existed prior to the Business Combination; and (C) at least a majority of the members of the board of directors of the resulting, continuing or surviving entity in such Business Combination are members of the Board at the time of the execution of the definitive agreement providing for such Business Combination or of its authorization and approval by the Board; or

(iii) Approval by the stockholders of the Company of a complete liquidation or dissolution of the Company.

(b) "Company Position" means the status of a person as a present or former director, officer, employee or agent of the Company or any other Enterprise.

(c) "Disinterested Director" means a director of the Company who is not and was not a party to the matter in respect of which indemnification or advancement of Expenses is sought by Indemnitee.

(d) "Enterprise" shall mean the Company or any other corporation, partnership, joint venture, trust, employee benefit plan or other enterprise for which Indemnitee serves, or did serve, at the request of the Company as a director, officer, employee or agent.

(e) "Exchange Act" means the Securities Exchange Act of 1934, as amended.

(f) "Expenses" shall include all judgments, fines, ERISA excise taxes or penalties, amounts paid in settlement, reasonable attorneys' fees, retainers, court costs, transcript costs, fees of experts, witness fees, travel expenses, duplicating costs, printing and binding costs, telephone charges, postage, delivery service fees and all other disbursements or expenses of a type customarily incurred in connection with prosecuting, defending, preparing to prosecute or defend, investigating, participating in, or being or preparing to be a witness in a Proceeding.

(g) "Independent Counsel" means a law firm, a partner or member of a law firm or an independent practitioner who (i) is experienced in matters of corporate law and (ii) would not, under the applicable standards of professional conduct then prevailing, have a conflict of interest in representing either the Company or the Indemnitee in an action to determine the Indemnitee's rights under this Agreement.

(h) "Person" means any individual, entity or group (within the meaning of Section 13(d)(3) or 14(d)(2) of the Exchange Act).

(i) "Proceeding" includes any threatened, pending or completed action, suit, arbitration, alternate dispute resolution mechanism, investigation, inquiry, administrative hearing or any other actual, threatened or completed proceeding in which Indemnitee was, is or will be involved as a party or otherwise, whether brought by or in the right of the Company or otherwise, whether civil, criminal, administrative or investigative, whether pending before or after the date of this

Agreement and whether or not he is acting or serving in any such capacity at the time any liability or expense is incurred for which indemnification can be provided under this Agreement, but specifically excluding an action initiated by an Indemnitee pursuant to Section 8 to enforce his rights under this Agreement.

2. Indemnity of Indemnitee. The Company hereby agrees to indemnify and hold harmless Indemnitee to the fullest extent permitted by the provisions of the DGCL, as may be amended from time to time. Without limiting the generality of the foregoing:

(a) *Proceedings Other Than Proceedings by or in the Right of the Company*. If Indemnitee was, is or is threatened to be made a party to, or a participant in, any Proceeding (other than a Proceeding by or in the right of the Company) by reason of his Company Position, the Company shall indemnify him against all Expenses actually and reasonably incurred by him, or on his behalf, in connection with such Proceeding (including, without limitation, any claim, issue or matter included therein) if he acted in good faith and in a manner he reasonably believed to be in, or not opposed to, the best interests of the Company, and with respect to any criminal Proceeding, had no reasonable cause to believe his conduct was unlawful.

(b) *Proceedings by or in the Right of the Company*. If Indemnitee was, is or is threatened to be made a party to, or a participant in, any Proceeding by or in the right of the Company by reason of his Company Position, the Company shall indemnify him against all Expenses actually and reasonably incurred by him, or on his behalf, in connection with the defense or settlement of such Proceeding if he acted in good faith and in a manner he reasonably believed to be in, or not opposed to, the best interests of the Company; provided, however, if required by applicable law, no indemnification against such Expenses shall be made in respect of any claim, issue or matter in such Proceeding as to which Indemnitee shall have been adjudged to be liable to the Company unless and to the extent that the Court of Chancery of the State of Delaware shall determine that such indemnification may be made.

(c) *Indemnification for Expenses of a Party who is Wholly or Partially Successful*. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Company Position, a party to, and is successful in defending (on the merits or otherwise), any Proceeding, the Company shall indemnify him to the maximum extent permitted by law against all Expenses actually and reasonably incurred by him, or on his behalf, in connection therewith. If Indemnitee is not wholly successful in such Proceeding but is successful, on the merits or otherwise, as to one or more but less than all claims, issues or matters in such Proceeding, the Company shall indemnify Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf in connection with each successfully resolved claim, issue or matter. For purposes of this Section 2(c) and without limitation, the termination of any claim, issue or matter in such a Proceeding by dismissal, with or without prejudice, shall be deemed to be a successful result as to such claim, issue or matter.

3. Additional Indemnity. In addition to, and without regard to any limitations on, the indemnification provided for in Section 2, the Company shall indemnify and hold harmless Indemnitee against all Expenses actually and reasonably incurred by him or on his behalf if, by reason of his Company Position, he was, is or is threatened to be made, a party to, or participant in, any Proceeding (including a Proceeding by or in the right of the Company), including, without limitation, all liability arising out of the negligence or active or passive wrongdoing of Indemnitee. The only limitation that shall exist upon the Company's obligations pursuant to this Agreement, other than those specified in Section 12, shall be that the Company shall not be obligated to make any

payment to Indemnitee that is finally determined (under the procedures, and subject to the presumptions, set forth in Sections 7 and 8) to be unlawful under Delaware law.

4. Contribution in the Event of Joint Liability.

(a) Whether or not the indemnification provided in Sections 2 and 3 is available, in respect of any Proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such Proceeding), the Company shall pay, in the first instance, the entire amount of any judgment or settlement of such Proceeding without requiring Indemnitee to contribute to such payment and the Company hereby waives and relinquishes any right of contribution it may have against Indemnitee. The Company shall not enter into any settlement of any Proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such Proceeding) unless such settlement provides for a full and final release of all claims asserted against Indemnitee.

(b) Without diminishing or impairing the obligations of the Company set forth in Section 4(a), if, for any reason, Indemnitee shall elect or be required to pay all or any portion of any judgment or settlement in any Proceeding in which the Company is jointly liable with Indemnitee (or would be if joined in such Proceeding), the Company shall contribute to the amount of Expenses actually and reasonably incurred and paid or payable by Indemnitee in proportion to the relative benefits received by the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such Proceeding), on the one hand, and Indemnitee, on the other hand, from the transaction from which such Proceeding arose; provided, however, that the proportion determined on the basis of relative benefit may, to the extent required by law, be further adjusted by reference to the relative fault of the Company and all officers, directors or employees of the Company other than Indemnitee who are jointly liable with Indemnitee (or would be if joined in such Proceeding), on the one hand, and Indemnitee, on the other hand, in connection with the events that resulted in such Expenses, as well as any other equitable considerations which are required to be considered under applicable law. The relative fault of the Company and all officers, directors or employees of the Company, other than Indemnitee, who are jointly liable with Indemnitee (or would be if joined in such Proceeding), on the one hand, and Indemnitee, on the other hand, shall be determined by reference to, among other things, the degree to which their respective actions were motivated by intent to gain personal profit or advantage, the degree to which their liability is primary or secondary and the degree to which their conduct is active or passive.

(c) The Company shall fully indemnify and hold harmless Indemnitee from any claims of contribution that may be brought by any one or more officers, directors or employees of the Company, other than Indemnitee, who may be jointly liable with Indemnitee.

5. Indemnification for Expenses of a Witness. Notwithstanding any other provision of this Agreement, to the extent that Indemnitee is, by reason of his Company Position, a witness in any Proceeding to which Indemnitee is not a party, he shall be indemnified against all Expenses actually and reasonably incurred by him or on his behalf in connection therewith.

6. Advancement of Expenses. Notwithstanding any other provision of this Agreement, the Company shall advance all Expenses incurred in connection with any Proceeding by or on behalf of Indemnitee by reason of his Company Position within twenty (20) calendar days after the receipt by the Company of a statement or statements from Indemnitee requesting such advance or advances from time to time, whether prior to or after final disposition of such Proceeding; provided that: (i) no determination has been made that the facts then known would preclude indemnification pursuant to the terms of this Agreement; and (ii) Indemnitee (A) affirms in such written request that he acted in

good faith and in a manner which he reasonably believed to be in, or not opposed to, the best interests of the Company (and, in the case of a criminal Proceeding, that he had no reasonable cause to believe his conduct was unlawful), (B) undertakes in such written request to repay such amount to the extent that it is ultimately determined that Indemnitee is not entitled to be indemnified against such Expenses and (C) provides appropriate supporting documentation for the Expenses for which he is seeking indemnification. Any advances and undertakings to repay pursuant to this Section 6 shall be unsecured and interest free. Notwithstanding the foregoing, the obligation of the Company to advance Expenses pursuant to this Section 6 shall be subject to the condition that, if, when and to the extent that the Company determines that Indemnitee would not be permitted to be indemnified under applicable law, the Company shall be entitled to be reimbursed by Indemnitee (who hereby expressly agrees to reimburse the Company) within thirty (30) days of such determination for all such amounts theretofore paid; provided, however, that if Indemnitee has commenced or thereafter commences legal proceedings in a court of competent jurisdiction to secure a determination that Indemnitee should be indemnified under applicable law, any determination made by the Company that Indemnitee would not be permitted to be indemnified under applicable law shall not be binding and Indemnitee shall not be required to reimburse the Company for any advance of Expenses until a final judicial determination is made with respect thereto (and as to which all rights of appeal therefrom have been exhausted or lapsed).

7. Procedures and Presumptions for Determination of Entitlement to Indemnification. It is the intent of this Agreement to secure for Indemnitee rights of indemnity that are as favorable as may be permitted under the DGCL and public policy of the State of Delaware. Accordingly, the parties agree that the following procedures and presumptions shall apply in the event of any question as to whether Indemnitee is entitled to indemnification under this Agreement:

(a) To obtain indemnification under this Agreement (including, without limitation, the advancement of Expenses and contribution by the Company), Indemnitee shall submit to the Company a written request, including therein or therewith such documentation and information as is reasonably available to Indemnitee and is reasonably necessary to determine whether and to what extent Indemnitee is entitled to indemnification. The Secretary of the Company shall, promptly upon receipt of such a request for indemnification, advise the Board in writing that Indemnitee has requested indemnification.

(b) Upon written request by Indemnitee for indemnification pursuant to the first sentence of Section 7(a), a determination, if required by applicable law, with respect to Indemnitee's entitlement thereto shall be made: (i) by Independent Counsel, if requested by Indemnitee with its written request for indemnification; or (ii) if no request is made by the Indemnitee for a determination by Independent Counsel, (A) by the Board (or the Board of Directors of the resulting, continuing or surviving entity following a Change of Control), by a majority vote of a quorum consisting of Disinterested Directors, (B) if such a quorum is not obtainable or if such quorum of Disinterested Directors so directs, by Independent Counsel in a written opinion to the Board (or the Board of Directors of the resulting, continuing or surviving entity following a Change of Control), a copy of which shall be delivered to the Indemnitee, or (C) if a quorum of Disinterested Directors so directs, by the stockholders of the Company.

(c) In the event the determination of entitlement to indemnification or advancement of Expenses is to be made by Independent Counsel at the request of the Indemnitee, the Independent Counsel shall be selected by the Board, unless there shall have occurred, within two (2) years prior to the date of the commencement of the Proceeding with respect to which indemnification or advancement of Expenses is claimed, a Change of Control, in which case the Independent Counsel shall be selected by the Indemnitee, unless the Indemnitee shall request that such selection be made

by the Board. Indemnitee or the Company, as the case may be, may, within ten (10) days after such written notice of selection shall have been given, deliver to the Company or to Indemnitee, as the case may be, a written objection to such selection; provided, however, that such objection may be asserted only on the ground that the Independent Counsel so selected does not meet the criteria of "Independent Counsel" as defined in Section 1, and the objection shall set forth with particularity the factual basis of such assertion. Absent a proper and timely objection, the person so selected shall act as Independent Counsel. If a written objection is made and substantiated, the Independent Counsel selected may not serve as Independent Counsel unless and until such objection is withdrawn or a court has determined that such objection is without merit. If, within twenty (20) days after submission by Indemnitee of a written request for indemnification pursuant to Section 7(a), no Independent Counsel shall have been selected without objection, either the Company or Indemnitee may petition the Court of Chancery of the State of Delaware or other court of competent jurisdiction for resolution of any objection which shall have been made by the Company or Indemnitee to the other's selection of Independent Counsel and/or for the appointment as Independent Counsel of a person selected by the court or by such other person as the court shall designate, and the person with respect to whom all objections are so resolved or the person so appointed shall act as Independent Counsel under Section 7(b). The Company shall pay any and all reasonable fees and expenses incurred by such Independent Counsel in connection with acting pursuant to Section 7(b), and the Company shall pay all reasonable fees and expenses incident to the procedures of this Section 7(c), regardless of the manner in which such Independent Counsel was selected or appointed.

(d) In making a determination with respect to entitlement to indemnification hereunder, the person or persons or entity making such determination shall presume that Indemnitee is entitled to indemnification under this Agreement. Anyone seeking to rebut this presumption shall have the burden of proof.

(e) Indemnitee shall be deemed to have acted in good faith if his action is based on the records or books of account of the Enterprise, including financial statements, or on information supplied to Indemnitee by the officers or other employees of the Enterprise in the course of their duties, or on the advice of legal counsel for the Enterprise or on information or records given or reports made to the Enterprise by an independent certified public accountant or by an appraiser or other expert selected with reasonable care by the Enterprise. The parties acknowledge and agree that the foregoing does not represent an exclusive list of the means by which Indemnitee may be deemed to have acted in good faith and in a manner he reasonably believed to be in, or not opposed to, the best interests of the Company. In addition, the knowledge or actions, or failure to act, of any director, officer, agent or employee of the Enterprise shall not be imputed to Indemnitee for purposes of determining the right to indemnification under this Agreement.

(f) If the person, persons or entity empowered or selected under Section 7 to determine whether Indemnitee is entitled to indemnification shall not have made a determination within thirty (30) days after receipt by the Company of the request therefor, the requisite determination of entitlement to indemnification shall be deemed to have been made and Indemnitee shall be entitled to such indemnification absent (i) a misstatement by Indemnitee of a material fact, or an omission of a material fact necessary to make Indemnitee's statement, in light of the context in which it was made, not materially misleading, in connection with the request for indemnification, or (ii) a prohibition of such indemnification under applicable law; provided, however, that (A) such 30-day period may be extended for a reasonable time, not to exceed an additional fifteen (15) days, if the person, persons or entity making such determination with respect to entitlement to indemnification in good faith requires such additional time to obtain or evaluate documentation or information relating thereto and (B) the foregoing provisions of this Section 7(f) shall not apply if the determination of entitlement to indemnification is to be made by the stockholders pursuant to Section 7(b) and (1)

within fifteen (15) days after receipt by the Company of the request for such determination, the Board or the Disinterested Directors, if appropriate, resolve to submit such determination to the stockholders for their consideration at an annual meeting thereof to be held within seventy-five (75) days after such receipt and such determination is made at such meeting, or (2) a special meeting of stockholders is called within fifteen (15) days after such receipt for the purpose of making such determination, such meeting is held for such purpose within sixty (60) days after having been so called and such determination is made at such meeting.

(g) Indemnitee shall cooperate with the person, persons or entity making such determination with respect to Indemnitee's entitlement to indemnification, including providing to such person, persons or entity upon reasonable advance request any documentation or information that is not privileged or otherwise protected from disclosure, available to Indemnitee without undue effort or expense and reasonably necessary to such determination. Any Independent Counsel, member of the Board or stockholder of the Company shall act reasonably and in good faith in making a determination regarding the Indemnitee's entitlement to indemnification under this Agreement. Any costs or expenses (including attorneys' fees and disbursements) incurred by Indemnitee in so cooperating with the person, persons or entity making such determination shall be borne by the Company (irrespective of the determination as to Indemnitee's entitlement to indemnification) and the Company hereby indemnifies and agrees to hold Indemnitee harmless therefrom.

(h) The Company acknowledges that a settlement or other disposition short of final judgment may be successful if it permits a party to avoid expense, delay, distraction, disruption and uncertainty. In the event that any Proceeding to which Indemnitee is a party is resolved in any manner other than by adverse judgment against Indemnitee (including, without limitation, settlement of such Proceeding with or without payment of money or other consideration), it shall be presumed that Indemnitee has been successful on the merits or otherwise in such Proceeding. Anyone seeking to rebut this presumption shall have the burden of proof.

8. Remedies of Indemnitee.

(a) In the event that (i) a determination is made pursuant to Section 7 that Indemnitee is not entitled to indemnification under this Agreement, (ii) advancement of Expenses is not timely made pursuant to Section 6, (iii) no determination of entitlement to indemnification is made pursuant to Section 7(b) within ninety (90) days after receipt by the Company of the written request for indemnification, or (iv) payment of indemnification is not made within ten (10) days after a determination has been made that Indemnitee is entitled to indemnification or such determination is deemed to have been made pursuant to Section 7, Indemnitee shall be entitled to an adjudication in an appropriate court of the State of Delaware, or in any other court of competent jurisdiction, of his entitlement to such indemnification or advancement of Expenses. Indemnitee shall commence such proceeding seeking an adjudication within one hundred eighty (180) days following the date on which Indemnitee first has the right to commence such proceeding pursuant to this Section 8(a). The Company shall not oppose Indemnitee's right to seek any such adjudication.

(b) In the event that a determination shall have been made pursuant to Section 7(b) that Indemnitee is not entitled to indemnification, any judicial proceeding commenced pursuant to this Section 8 shall be conducted in all respects as a de novo trial on the merits, and Indemnitee shall not be prejudiced by reason of the adverse determination under Section 7(b).

(c) If a determination shall have been made pursuant to Section 7(b) that Indemnitee is entitled to indemnification, the Company shall be bound by such determination in any

judicial proceeding commenced pursuant to this Section 8, absent a prohibition of such indemnification under applicable law.

(d) In the event that Indemnitee, pursuant to this Section 8, seeks a judicial adjudication of his rights under, or to recover damages for breach of, this Agreement, or to recover under any directors' and officers' liability insurance policies maintained by the Company, the Company shall pay on his behalf, in advance (but subject to the same conditions as are set forth in Section 6 with regard to the advancement of Expenses), any and all expenses (of the types described in the definition of Expenses in Section 1) actually and reasonably incurred by him in connection with such judicial adjudication.

(e) The Company shall be precluded from asserting in any judicial proceeding commenced pursuant to this Section 8 that the procedures and presumptions of this Agreement are not valid, binding and enforceable and shall stipulate in any such court that the Company is bound by all the provisions of this Agreement.

9. Nonexclusivity; Survival of Rights; Insurance; Subrogation.

(a) The rights of indemnification provided by this Agreement shall not be deemed exclusive of any other rights to which Indemnitee may at any time be entitled under applicable law, the certificate of incorporation of the Company (as may be amended or restated from time to time), the Bylaws, any agreement, a vote of stockholders, a resolution of directors or otherwise. No amendment, alteration or repeal of this Agreement or of any provision hereof shall limit or restrict any right of Indemnitee under this Agreement in respect of any action taken or omitted by such Indemnitee in his Company Position prior to such amendment, alteration or repeal. To the extent that a change in the DGCL, whether by statute or judicial decision, permits greater indemnification than would be afforded currently under this Agreement, it is the intent of the parties that Indemnitee shall enjoy by this Agreement the greater benefits so afforded by such change. No right or remedy herein conferred is intended to be exclusive of any other right or remedy, and every other right and remedy shall be cumulative and in addition to every other right and remedy given hereunder or now or hereafter existing at law or in equity or otherwise. The assertion or employment of any right or remedy hereunder, or otherwise, shall not prevent the concurrent assertion or employment of any other right or remedy.

(b) To the extent that the Company maintains an insurance policy or policies providing liability insurance for directors, officers, employees, or agents or fiduciaries of the Company or of any other Enterprise, Indemnitee shall be covered by such policy or policies in accordance with its or their terms to the maximum extent of the coverage available for any director, officer, employee, agent or fiduciary under such policy or policies.

(c) Except as provided in the last sentence of this Section 9(c), in the event of any payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnitee, who shall execute all papers and take all action reasonably necessary to secure such rights, including execution of such documents as are reasonably necessary to enable the Company to bring suit to enforce such rights. Notwithstanding the foregoing, no right of recovery of Indemnitee pursuant to any (i) director liability insurance policy that covers Indemnitee and is purchased separately by Indemnitee, by any fund or other entity of which Indemnitee is a partner, member or stockholder or that employs Indemnitee (excluding the Company) or by any of their respective affiliates or (ii) indemnification from any fund or other entity of which Indemnitee is a partner, member or stockholder or that employs Indemnitee or from any of its affiliates shall be subject to subrogation under this Section 9(c).

(d) The Company shall not be liable under this Agreement to make any payment of amounts otherwise indemnifiable hereunder if and to the extent that Indemnitee has otherwise actually received such amount under any insurance policy, contract, agreement or otherwise.

10. Mutual Acknowledgment. The Company and Indemnitee acknowledge that, in certain instances, Federal law or applicable public policy (pursuant to the immediately following sentence) may prohibit the Company from indemnifying its directors, officers, employees, controlling persons, fiduciaries or other agents or affiliates under this Agreement or otherwise. Indemnitee understands and acknowledges that the Company may be required in the future to undertake with the Securities and Exchange Commission to submit the question of indemnification to a court in certain circumstances for a determination of the Company's rights under public policy to indemnify Indemnitee.

11. Duration of Agreement. All agreements and obligations of the Company contained herein shall continue during the period Indemnitee is a director, officer or member of the executive committee of the Company (or is or was serving at the request of the Company as a director, officer, employee or agent of any other Enterprise) and shall continue thereafter if and while Indemnitee shall be subject to any Proceeding (or any proceeding commenced under Section 8) by reason of his Company Position, whether or not he is acting or serving in any such capacity at the time of initiation of the Proceeding, while the Proceeding is pending or at the time any liability or expense is incurred for which indemnification can be provided under this Agreement. This Agreement shall be binding upon and inure to the benefit of and be enforceable by the parties hereto and their respective successors (including any direct or indirect successor by purchase, merger, consolidation or otherwise to all or substantially all of the business or assets of the Company), assigns, spouses, heirs, executors and personal and legal representatives.

12. Exceptions. Notwithstanding any other provision of this Agreement, the Company shall not be obligated pursuant to the terms of this Agreement:

(a) *Excluded Action or Omissions*. To indemnify the Indemnitee in respect of any intentional malfeasance by the Indemnitee or any act undertaken by the Indemnitee where the Indemnitee did not in good faith believe the Indemnitee was acting in the best interests of the Company, or for any other acts, omissions or transactions from which the Indemnitee may not be relieved of liability under applicable law.

(b) *Claims Initiated by Indemnitee*. To indemnify or advance Expenses to Indemnitee with respect to any Proceeding initiated or brought voluntarily by Indemnitee and not by way of defense, except (i) with respect to a Proceeding to establish or enforce a right to indemnity under any agreement or insurance policy or under the Company's certificate of incorporation or Bylaws now or hereafter in effect relating to indemnification, (ii) in specific cases if the Board has approved the initiation or bringing of such Proceeding, or (iii) as otherwise required under Section 145 of the DGCL, regardless of whether such Indemnitee ultimately is determined to be entitled to such indemnification, advance expense payment or insurance recovery, as the case may be.

(c) *Lack of Good Faith*. To indemnify Indemnitee with respect to any (i) Proceeding instituted by Indemnitee as contemplated by Section 12(b)(i) or (ii) proceeding instituted by Indemnitee under Section 8 to enforce its rights under this Agreement, if a court of competent jurisdiction determines that each of the material assertions made by the Indemnitee in such proceeding was not made in good faith or was frivolous; or

(d) *Claims Under Section 16(b)*. To indemnify Indemnitee for any Expenses and disgorgement of profits arising from the purchase and sale by Indemnitee of securities in violation of Section 16(b) of the Exchange Act or any similar successor statute.

13. Enforcement.

(a) The Company expressly (i) confirms and agrees that it has entered into this Agreement and assumes the obligations imposed on it hereby in order to induce Indemnitee to serve as a director, officer or member of the executive committee of the Company and (ii) acknowledges that Indemnitee is relying upon this Agreement in serving as a director, officer or member of the executive committee of the Company.

(b) This Agreement constitutes the entire agreement between the parties hereto with respect to the subject matter hereof and supersedes all prior agreements and understandings, oral, written and implied, between the parties hereto with respect to the subject matter hereof.

14. Severability. If any provision or provisions of this Agreement shall be held by a court of competent jurisdiction to be invalid, void, illegal or otherwise unenforceable for any reason whatsoever: (i) the validity, legality and enforceability of the remaining provisions of this Agreement (including without limitation, each portion of any section of this Agreement containing any such provision held to be invalid, illegal or unenforceable that is not itself invalid, illegal or unenforceable) shall not in any way be affected or impaired thereby and shall remain enforceable to the fullest extent permitted by law; and (ii) to the fullest extent possible, the provisions of this Agreement (including, without limitation, each portion of any section of this Agreement containing any such provision held to be invalid, illegal or unenforceable that is not itself invalid, illegal or unenforceable) shall be construed so as to give effect to the intent manifested thereby. Without limiting the generality of the foregoing, this Agreement is intended to confer upon Indemnitee indemnification rights to the fullest extent permitted by applicable law. In the event any provision hereof conflicts with any applicable law, such provision shall be deemed modified, consistent with the aforementioned intent, to the extent necessary to resolve such conflict.

15. Modification and Waiver. No supplement, modification, termination or amendment of this Agreement shall be binding unless executed in writing by both parties. No waiver of any of the provisions of this Agreement shall be deemed or shall constitute a waiver of any other provisions hereof (whether or not similar) nor shall such waiver constitute a continuing waiver.

16. Notice By Indemnitee. Indemnitee agrees promptly to notify the Company in writing upon being served with or otherwise receiving any summons, citation, subpoena, complaint, indictment, information or other document relating to any Proceeding or matter that may be subject to indemnification hereunder. The failure to so notify the Company shall not relieve the Company of any obligation which it may have to Indemnitee under this Agreement or otherwise unless and only to the extent that such failure or delay materially prejudices the Company.

17. Notices. All notices, requests, demands and other communications hereunder shall be in writing and shall be deemed to have been duly given if (i) delivered by hand and received by the party to whom said notice or other communication shall have been directed, or (ii) mailed by certified or registered mail with postage prepaid, on the third business day after the date on which it is so mailed:

(a) If to Indemnitee, to the address set forth below Indemnitee's signature hereto.

(b) If to the Company, to:

Targacept, Inc.
200 East First Street, Suite 300
Winston-Salem, NC 27101-4165
Attention: Chief Financial Officer

or to such other address as may have been furnished to Indemnitee by the Company or to the Company by Indemnitee, as the case may be.

18. Counterparts. This Agreement may be executed in two counterparts, each of which shall for all purposes be deemed to be an original and both of which together shall constitute one and the same agreement. Only one such counterpart signed by the party against whom enforceability is sought needs to be produced to evidence the existence of this Agreement.

19. Headings. The headings of the paragraphs of this Agreement are inserted for convenience only and shall not be deemed to constitute part of this Agreement or to affect the construction thereof.

20. Governing Law. The parties agree that this Agreement shall be governed by, and construed and enforced in accordance with, the laws of the State of Delaware without application of the principles of conflicts of laws thereof.

21. Gender. Use of the masculine pronoun herein shall be deemed to include also the corresponding feminine pronoun.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement on and as of the day and year first above written.

COMPANY:

TARGACEPT, INC.

By: _____

Name: _____

Title: _____

INDEMNITEE:

Name: _____

Address: _____

**2000 EQUITY INCENTIVE PLAN
OF
TARGACEPT, INC.**

**Stock Option Agreement
(Employees)**

THIS AGREEMENT (the "Agreement"), made the _____ day of _____, between Targacept, Inc., a Delaware corporation (the "Corporation"), and _____, an employee of the Corporation or a related corporation (the "Participant");

R E C I T A L S :

In furtherance of the purposes of the 2000 Equity Incentive Plan of Targacept, Inc., as it may be hereafter amended (the "Plan"), and in consideration of the services of the Participant and such other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Corporation and the Participant hereby agree as follows:

1. **Incorporation of Plan.** The rights and duties of the Corporation and the Participant under this Agreement shall in all respects be subject to and governed by the provisions of the Plan, a copy of which is delivered herewith or has been previously provided to the Participant and the terms of which are incorporated herein by reference. In the event of any conflict between the provisions in the Agreement and those of the Plan, the provisions of the Plan shall govern. Unless otherwise defined herein, capitalized terms in this Agreement shall have the same definitions as set forth in the Plan.

2. **Grant of Option; Term of Option.** The Corporation hereby grants to the Participant pursuant to the Plan, as a matter of separate inducement and agreement in connection with his or her employment or service to the Corporation, and not in lieu of any salary or other compensation for his or her services, the right and Option (the "Option") to purchase all or any part of an aggregate of _____ (_____) shares (the "shares") of the common stock (the "Common Stock") of the Corporation, at a purchase price (the "option price") of _____ (\$_____) per share. The Option to purchase all of the shares shall be designated as an Incentive Option. To the extent that the Option is designated as an Incentive Option and such Option does not qualify as an Incentive Option, the Option (or portion thereof) shall be treated as a Nonqualified Option. Except as otherwise provided in the Plan, the Option will expire if not exercised in full before _____.

3. **Exercise of Option.** The Option shall become exercisable on the date or dates and subject to such conditions set forth in the Plan, this Agreement and Schedule A, which is attached hereto and expressly made a part of this Agreement. To the extent that the Option is exercisable but is not exercised, the Option shall accumulate and be exercisable by the Participant in whole or in part at any time prior to expiration of the Option, subject to the terms

of the Plan and this Agreement. Upon the exercise of an Option in whole or in part, payment of the option price in accordance with the provisions of the Plan and this Agreement and satisfaction of such other conditions as may be established by the Administrator, the Corporation shall as soon thereafter as practicable deliver to the Participant a certificate or certificates for the shares purchased. Payment of the option price may be made: (i) in cash or by check; (ii) by delivery (by either actual delivery or attestation) of shares of Common Stock owned by the Participant at the time of exercise for a period of at least six months and otherwise acceptable to the Administrator; (iii) in the event that a public market for the Common Stock exists (as defined in the Plan), by delivery of written notice of exercise to the Corporation and delivery to a broker of written notice of exercise and irrevocable instructions to promptly deliver to the Corporation the amount of sale or loan proceeds to pay the option price; (iv) by such other methods as may be permitted by the Administrator in its sole discretion in accordance with Section 6(c)(ii) of the Plan; or (v) by a combination of the foregoing methods. Shares delivered in payment of the option price shall be valued at their fair market value on the date of exercise, as determined by the Administrator by applying the provisions of the Plan.

4. No Right of Continued Employment or Service. Nothing contained in this Agreement or the Plan shall confer upon the Participant any right to continue in the employment or service of the Corporation or a related corporation or interfere with the right of the Corporation or a related corporation to terminate the Participant's employment or service at any time. Except as otherwise expressly provided in the Plan, all rights of the Participant under the Plan with respect to the Option shall terminate upon termination of the employment or service of the Participant with the Corporation or a related corporation.

5. Nontransferability of Option. To the extent that this Option is designated as an Incentive Option, the Option shall not be transferable other than by will or the laws of intestate succession. To the extent that this Option is designated as a Nonqualified Option, the Option shall not be transferable other than by will or the laws of intestate succession, except as may be permitted by the Administrator of the Plan in its sole discretion in a manner consistent with the registration provisions of the Securities Act of 1933, as amended (the "Securities Act"). Except as may be permitted by the preceding sentence, this Option shall be exercisable during the Participant's lifetime only by the Participant.

6. Superseding Agreement; Binding Effect. This Agreement supersedes any statements, representations or agreements of the Corporation with respect to the grant of the Option or any related rights, and the Participant hereby waives any rights or claims related to any such statements, representations or agreements. This Agreement shall be binding upon and shall inure to the benefit of the parties hereto and their respective executors, administrators, next-of-kin, successors and assigns.

7. Representations and Warranties of Participant. The Participant represents and warrants to the Corporation that:

- (a) Agrees to Terms of the Plan and Agreement. The Participant has received a copy of the Plan, has read and understands the terms of the Plan and this Agreement, and agrees to be bound by their terms and conditions. The Participant

acknowledges that there may be adverse tax consequences upon acquisition or disposition of the shares subject to the Option, and that the Participant should consult a tax advisor prior to such exercise or disposition.

- (b) Purchase for Own Account for Investment. Any shares of Common Stock acquired pursuant to the Option shall be acquired for the Participant's own account for investment purposes only and not with a view to, or for sale in connection with, a distribution of the shares within the meaning of the Securities Act. The Participant has no present intention of selling or otherwise disposing of all or any portion of the shares subject to the Option.
- (c) Access to Information. The Participant has had access to all information regarding the Corporation and its present and prospective business, assets, liabilities and financial condition that the Participant reasonably considers important in making a decision to acquire the shares subject to the Option, and the Participant has had ample opportunity to ask questions of the Corporation's representatives concerning such matters and this investment.
- (d) Understanding of Risks. The Participant is fully aware of: (i) the speculative nature of the investment in the shares of Common Stock; (ii) the financial hazards involved in investment of the Common Stock; (iii) the lack of liquidity of the shares subject to the Option and the restrictions on transferability of such shares; (iv) the qualifications and backgrounds of the management of the Corporation; and (v) the tax consequences of investment in the shares of Common Stock. The Participant is capable of evaluating the merits and risks of this investment, has the ability to protect his or her own interests in this transaction and is financially capable of bearing a total loss from this investment.
- (e) No General Solicitation. At no time was the Participant presented with or solicited by any publicly issued or circulated newspaper, mail, radio, television or other form of general advertising or solicitation in connection with the offer, sale or purchase of the shares subject to the Option.
- (f) Compliance with Securities Laws. The shares subject to the Option have not been registered with the Securities and Exchange Commission ("SEC") under the Securities Act and, notwithstanding any other provision of this Agreement or the Plan to the contrary, the right to acquire any shares subject to this Option is expressly conditioned upon compliance with the Securities Act and all applicable state securities laws. The Participant agrees to cooperate with the Corporation to ensure compliance with such laws.
- (g) No Transfer Unless Registered or Exempt. The Participant understands that he or she may not transfer any shares subject to the Option unless such shares are registered under the Securities Act and qualified under applicable state securities laws or unless, in the opinion of counsel to the Corporation, exemptions from such registration and qualification requirements are available. The Participant

understands that only the Corporation may file a registration statement with the SEC and that the Corporation is under no obligation to do so with respect to the shares subject to the Option. The Participant has also been advised that exemptions from registration and qualification may not be available or may not permit the Participant to transfer all or any of the shares subject to the Option in the amounts or at the times proposed by him. The Participant also agrees in connection with any registration of the Corporation's securities that, upon the request of the Corporation or the underwriters managing any public offering of the Corporation's securities, the Participant will not sell or otherwise dispose of any shares without the prior written consent of the Corporation or such underwriters, as the case may be, for such period of time (not to exceed 180 days) after the effective date of such registration requested by such managing underwriters and subject to all restrictions as the Corporation or the underwriters may specify.

8. Other Restrictions on Option and Shares.

- (a) As a condition to the issuance and delivery of shares subject to the Option, or the grant of any benefit pursuant to the terms of the Plan, the Corporation may require the Participant or other person to become a party to a stockholders agreement, buy-sell agreement, redemption agreement, repurchase agreement or other agreement between the Corporation and stockholders of the Corporation or among stockholders of the Corporation or such other agreements imposing such restrictions as may be required by the Corporation. Without in any way limiting the effect of the foregoing, the Participant hereby expressly acknowledges and agrees that the Corporation shall require, prior to the issuance of any shares pursuant to this Agreement, that the Participant become a party to that certain 2nd Amended and Restated Stockholders Agreement dated as of November 26, 2002, by and among Targacept, Inc. and the stockholders thereof, as it may be amended.
- (b) The Corporation may impose such restrictions on the Option and any shares issuable pursuant to the exercise of the Option as it may deem advisable, including without limitation restrictions under the federal securities laws, or the requirements of any stock exchange or similar organization or any blue sky or state securities laws applicable to such shares. Notwithstanding any other provision in the Plan or the Agreement to the contrary, the Corporation shall not be obligated to issue, deliver or transfer shares of Common Stock, to make any other distribution of benefits, or to take any other action, unless such delivery, distribution or action is in compliance with all applicable laws, rules and regulations (including but not limited to the requirements of the Securities Act). The Corporation will be under no obligation to register the shares of Common Stock with the SEC or to effect compliance with the exemption, registration, qualification or listing requirements of any state securities laws, stock exchange or similar organization, and the Corporation will have no liability for any inability or failure to do so. The Corporation may cause a restrictive legend to be placed

on any certificate issued pursuant to the exercise of the Option in such form as may be prescribed from time to time by applicable laws and regulations or as may be advised by legal counsel.

9. Governing Law. Except as otherwise provided in the Plan or herein, this Agreement shall be construed and enforced according to the laws of the State of Delaware, without regard to the principles of conflict of laws.

10. Amendment and Termination; Waiver. Subject to the terms of the Plan, this Agreement may be modified or amended only by the written agreement of the parties hereto. The waiver by the Corporation of a breach of any provision of the Agreement by the Participant shall not operate or be construed as a waiver of any subsequent breach by the Participant.

11. No Rights as a Stockholder. The Participant and his or her legal representatives, legatees or distributees shall not be deemed to be the holder of any shares subject to the Option and shall not have any rights of a stockholder unless and until certificates for such shares have been issued and delivered to him, her or them.

12. Withholding. The Participant acknowledges that the Corporation shall require the Participant to pay the Corporation the amount of any federal, state, local or other tax or other amount required by any governmental authority to be withheld and paid over by the Corporation to such authority for the account of the Participant, and the Participant agrees, as a condition to the grant of the Option and delivery of the shares, to satisfy such obligations.

13. Administration. The authority to construe and interpret this Agreement and the Plan, and to administer all aspects of the Plan, shall be vested in the Administrator (as such term is defined in the Plan), and the Administrator shall have all powers with respect to this Agreement as are provided in the Plan. Any interpretation of the Agreement by the Administrator and any decision made by it with respect to the Agreement is final and binding.

14. Notices. Except as may be otherwise provided by the Plan, any written notices provided for in this Agreement or the Plan shall be in writing and shall be deemed sufficiently given if either hand delivered or if sent by fax or overnight courier, or by postage paid first class mail. Notices sent by mail shall be deemed received three business days after mailed but in no event later than the date of actual receipt. Notices shall be directed, if to the Participant, at the Participant's address indicated by the Corporation's records, or if to the Corporation, at the Corporation's principal office.

15. Severability. The provisions of this Agreement are severable and if any one or more provisions may be determined to be illegal or otherwise unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

IN WITNESS WHEREOF, this Agreement has been executed in behalf of the Corporation and by the Participant effective as of the day and year first above written.

TARGACEPT, INC.

By: _____
Name: _____
Title: _____

Attest:

Secretary

[Corporate Seal]

PARTICIPANT

**2000 EQUITY INCENTIVE PLAN
OF
TARGACEPT, INC.**

**Stock Option Agreement
(Employees)**

SCHEDULE A

Date Option granted: _____
Date Option expires: _____
Number of shares subject to Option: _____ shares
Option price (per share): \$ _____
Class of Option: Incentive.

Date Installment First Exercisable

Number of Shares in Installment

**2000 EQUITY INCENTIVE PLAN
OF
TARGACEPT, INC.**

**Stock Option Agreement
(Non-Employee Directors)**

THIS AGREEMENT (the "Agreement"), made the _____ day of _____ between Targacept, Inc., a Delaware corporation (the "Corporation"), and _____, a director of the Corporation or a related corporation (the "Participant");

R E C I T A L S :

In furtherance of the purposes of the 2000 Equity Incentive Plan of Targacept, Inc., as it may be hereafter amended (the "Plan"), and in consideration of the services of the Participant and such other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Corporation and the Participant hereby agree as follows:

1. **Incorporation of Plan.** The rights and duties of the Corporation and the Participant under this Agreement shall in all respects be subject to and governed by the provisions of the Plan, a copy of which is delivered herewith or has been previously provided to the Participant and the terms of which are incorporated herein by reference. In the event of any conflict between the provisions in the Agreement and those of the Plan, the provisions of the Plan shall govern. Unless otherwise defined herein, capitalized terms in this Agreement shall have the same definitions as set forth in the Plan.

2. **Grant of Option; Term of Option.** The Corporation hereby grants to the Participant pursuant to the Plan, as a matter of separate inducement and agreement in connection with his service to the Corporation, and not in lieu of any salary or other compensation for his services, the right and Option (the "Option") to purchase all or any part of an aggregate of _____ (_____) shares (the "shares") of the common stock (the "Common Stock") of the Corporation, at a purchase price (the "option price") of Zero Dollars and 01/100 (\$0.01) per share. The Option shall be designated as a Nonqualified Option. Except as otherwise provided in the Plan, the Option will expire if not exercised in full before _____.

3. **Exercise of Option.** The Option shall become exercisable on the date or dates and subject to such conditions set forth in the Plan, this Agreement and Schedule A, which is attached hereto and expressly made a part of this Agreement. To the extent that the Option is exercisable but is not exercised, the Option shall accumulate and be exercisable by the Participant in whole or in part at any time prior to expiration of the Option, subject to the terms of the Plan and this Agreement. Upon the exercise of an Option in whole or in part, payment of the option price in accordance with the provisions of the Plan and this Agreement, and satisfaction of such other conditions as may be established by the Administrator, the Corporation shall as soon thereafter as practicable deliver to the Participant a certificate or certificates for the shares purchased. Payment of the option price may be made: (i) in cash or by check; (ii) by delivery (by either actual delivery or attestation) of shares of Common Stock owned by the Participant at the time of exercise for a period of at least six months and otherwise acceptable to the Administrator; (iii) in the event that a public market for the Common Stock exists (as defined in the Plan), by delivery of written notice of exercise to the Corporation and delivery to a broker of written notice of exercise and irrevocable instructions to promptly deliver to

the Corporation the amount of sale or loan proceeds to pay the option price; (iv) by such other methods as may be permitted by the Administrator in its sole discretion in accordance with Section 6(c)(ii) of the Plan; or (v) by a combination of the foregoing methods. Shares delivered in payment of the option price shall be valued at their fair market value on the date of exercise, as determined by the Administrator by applying the provisions of the Plan.

4. No Right of Continued Service. Nothing contained in this Agreement or the Plan shall confer upon the Participant any right to continue in the service of the Corporation or a related corporation or interfere with the right of the Corporation or a related corporation to terminate the Participant's service at any time. Except as otherwise expressly provided in the Plan or Schedule A, all rights of the Participant under the Plan with respect to the Option shall terminate upon termination of the services of the Participant with the Corporation or a related corporation.

5. Nontransferability of Option. This Option shall not be transferable other than by will or the laws of intestate succession, except as may be permitted by the Administrator of the Plan in its sole discretion in a manner consistent with the registration provisions of the Securities Act of 1933, as amended (the "Securities Act"). Except as may be permitted by the preceding sentence, this Option shall be exercisable during the Participant's lifetime only by the Participant.

6. Superseding Agreement; Binding Effect. This Agreement supersedes any statements, representations or agreements of the Corporation with respect to the grant of the Option or any related rights, and the Participant hereby waives any rights or claims related to any such statements, representations or agreements. This Agreement shall be binding upon and shall inure to the benefit of the parties hereto and their respective executors, administrators, next-of-kin, successors and assigns.

7. Representations and Warranties of Participant. The Participant represents and warrants to the Corporation that:

- (a) Agrees to Terms of the Plan and Agreement. The Participant has received a copy of the Plan, has read and understands the terms of the Plan and this Agreement, and agrees to be bound by their terms and conditions. The Participant acknowledges that there may be adverse tax consequences upon acquisition or disposition of the shares subject to the Option, and that the Participant should consult a tax advisor prior to such exercise or disposition.
- (b) Purchase for Own Account for Investment. Any shares of Common Stock acquired pursuant to the Option shall be acquired for the Participant's own account for investment purposes only and not with a view to, or for sale in connection with, a distribution of the shares within the meaning of the Securities Act. The Participant has no present intention of selling or otherwise disposing of all or any portion of the shares subject to the Option.
- (c) Access to Information. The Participant has had access to all information regarding the Corporation and its present and prospective business, assets, liabilities and financial condition that the Participant reasonably considers important in making a decision to acquire the shares subject to the Option, and the Participant has had ample opportunity to ask questions of the Corporation's representatives concerning such matters and this investment.

- (d) Understanding of Risks. The Participant is fully aware of: (i) the speculative nature of the investment in the shares of Common Stock; (ii) the financial hazards involved in investment of the Common Stock; (iii) the lack of liquidity of the shares subject to the Option and the restrictions on transferability of such shares; (iv) the qualifications and backgrounds of the management of the Corporation; and (v) the tax consequences of investment in the shares of Common Stock. The Participant is capable of evaluating the merits and risks of this investment, has the ability to protect his own interests in this transaction and is financially capable of bearing a total loss from this investment.
- (e) No General Solicitation. At no time was the Participant presented with or solicited by any publicly issued or circulated newspaper, mail, radio, television or other form of general advertising or solicitation in connection with the offer, sale or purchase of the shares subject to the Option.
- (f) Compliance with Securities Laws. The shares subject to the Option have not been registered with the Securities and Exchange Commission ("SEC") under the Securities Act and, notwithstanding any other provision of this Agreement or the Plan to the contrary, the right to acquire any shares subject to this Option is expressly conditioned upon compliance with the Securities Act and all applicable state securities laws. The Participant agrees to cooperate with the Corporation to ensure compliance with such laws.
- (g) No Transfer Unless Registered or Exempt. The Participant understands that he may not transfer any shares subject to the Option unless such shares are registered under the Securities Act and qualified under applicable state securities laws or unless, in the opinion of counsel to the Corporation, exemptions from such registration and qualification requirements are available. The Participant understands that only the Corporation may file a registration statement with the SEC and that the Corporation is under no obligation to do so with respect to the shares subject to the Option. The Participant has also been advised that exemptions from registration and qualification may not be available or may not permit the Participant to transfer all or any of the shares subject to the Option in the amounts or at the times proposed by him. The Participant also agrees in connection with any registration of the Corporation's securities that, upon the request of the Corporation or the underwriters managing any public offering of the Corporation's securities, the Participant will not sell or otherwise dispose of any shares without the prior written consent of the Corporation or such managing underwriters, as the case may be, for such period of time (not to exceed 180 days) after the effective date of such registration requested by such managing underwriters and subject to all restrictions as the Corporation or the underwriters may specify.

8. Other Restrictions on Option and Shares.

- (a) As a condition to the issuance and delivery of shares subject to the Option, or the grant of any benefit pursuant to the terms of the Plan, the Corporation may require the Participant or other person to become a party to a stockholders agreement, buy-sell agreement, redemption agreement, repurchase agreement or other agreement between the Corporation and stockholders of the Corporation or among stockholders of the Corporation or such other agreements imposing such restrictions as may be required

by the Corporation. Without in any way limiting the effect of the foregoing, the Participant hereby expressly acknowledges and agrees that the Corporation shall require, prior to the issuance of any shares pursuant to this Agreement, that the Participant become a party to that certain Second Amended and Restated Stockholders Agreement dated as of November 26, 2002, by and among Targacept, Inc. and the stockholders thereof, as amended.

- (b) The Corporation may impose such restrictions on the Option and any shares issuable pursuant to the exercise of the Option as it may deem advisable, including without limitation restrictions under the federal securities laws, or the requirements of any stock exchange or similar organization or any blue sky or state securities laws applicable to such shares. Notwithstanding any other provision in the Plan or the Agreement to the contrary, the Corporation shall not be obligated to issue, deliver or transfer shares of Common Stock, to make any other distribution of benefits, or to take any other action, unless such delivery, distribution or action is in compliance with all applicable laws, rules and regulations (including but not limited to the requirements of the Securities Act). The Corporation will be under no obligation to register the shares of Common Stock with the SEC or to effect compliance with the exemption, registration, qualification or listing requirements of any state securities laws, stock exchange or similar organization, and the Corporation will have no liability for any inability or failure to do so. The Corporation may cause a restrictive legend to be placed on any certificate issued pursuant to the exercise of the Option in such form as may be prescribed from time to time by applicable laws and regulations or as may be advised by legal counsel.

9. Governing Law. Except as otherwise provided in the Plan or herein, this Agreement shall be construed and enforced according to the laws of the State of Delaware, without regard to the principles of conflict of laws.

10. Amendment and Termination; Waiver. Subject to the terms of the Plan, this Agreement may be modified or amended only by the written agreement of the parties hereto. The waiver by the Corporation of a breach of any provision of the Agreement by the Participant shall not operate or be construed as a waiver of any subsequent breach by the Participant.

11. No Rights as a Stockholder. The Participant and his legal representatives, legatees or distributees shall not be deemed to be the holder of any shares subject to the Option and shall not have any rights of a stockholder unless and until certificates for such shares have been issued and delivered to him or them.

12. Withholding. The Participant acknowledges that the Corporation shall require the Participant to pay the Corporation the amount of any federal, state, local or other tax or other amount required by any governmental authority to be withheld and paid over by the Corporation to such authority for the account of the Participant, and the Participant agrees, as a condition to the grant of the Option and delivery of the shares, to satisfy such withholding obligations.

13. Administration. The authority to construe and interpret this Agreement and the Plan, and to administer all aspects of the Plan, shall be vested in the Administrator (as such term is defined in the Plan), and the Administrator shall have all powers with respect to this Agreement as are provided in the Plan. Any interpretation of the Agreement by the Administrator and any decision made by it with respect to the Agreement is final and binding.

14. Notices. Except as may be otherwise provided by the Plan, any written notices provided for in this Agreement or the Plan shall be in writing and shall be deemed sufficiently given if either hand delivered or if sent by fax or overnight courier, or by postage paid first class mail. Notices sent by mail shall be deemed received three business days after mailed but in no event later than the date of actual receipt. Notices shall be directed, if to the Participant, at the Participant's address indicated by the Corporation's records, or if to the Corporation, at the Corporation's principal office.

15. Severability. The provisions of this Agreement are severable and if any one or more provisions may be determined to be illegal or otherwise unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

IN WITNESS WHEREOF, this Agreement has been executed in behalf of the Corporation and by the Participant effective as of the day and year first above written.

TARGACEPT, INC.

By: _____

Attest:

[Corporate Seal]

PARTICIPANT

2000 EQUITY INCENTIVE PLAN
OF
TARGACEPT, INC.

Stock Option Agreement
(Non-Employee Directors)

SCHEDULE A

Date Option granted: _____, _____.

Date Option expires: _____, _____.

Number of shares subject to Option: _____ shares.

Option price (per share): \$0.01.

Type of Option: Nonqualified Stock Option

Date Installment First Exercisable

Percentage of Option Which Is Exercisable

100%

Other Conditions to Exercise:

**2000 EQUITY INCENTIVE PLAN
OF TARGACEPT, INC.**

**Restricted Stock Award Agreement
(Service-Based Award)**

Name of Participant: _____

Grant Date: _____

Number of Shares: _____

Vesting Begins: _____

THIS AGREEMENT (together with Schedule A attached hereto, this "Agreement"), made the _____ day of _____ (as defined below, the "Grant Date"), between Targacept, Inc., a Delaware corporation (the "Corporation"), and _____, an employee of, or a director or other individual in service to, the Corporation or a related corporation (the "Participant");

RECITALS:

In furtherance of the purposes of the 2000 Equity Incentive Plan of Targacept, Inc., as amended and as may be hereafter amended (the "Plan"), and in consideration of _____ Dollars (\$_____) paid to the Corporation and such other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Corporation and the Participant hereby agree as follows:

1. Incorporation of Plan. The rights and duties of the Corporation and the Participant under this Agreement shall in all respects be subject to and governed by the provisions of the Plan, the terms of which are incorporated herein by reference. In the event of any conflict between the provisions in the Agreement and those of the Plan, the provisions of the Plan shall govern. Unless otherwise defined herein, capitalized terms in this Agreement shall have the same definitions as set forth with the Plan.

2. Terms of Award. The following terms used in this Agreement shall have the meanings set forth in this Section 2:

- (a) The "Participant" is _____.
- (b) The "Grant Date" is _____.
- (c) The "Restriction Period" is the period beginning on the Grant Date and ending on _____.
- (d) The number of shares of Restricted Stock subject to the restricted award granted under this Agreement shall be _____ shares (the "Shares").

3. Grant of Restricted Award. Subject to the terms of this Agreement and the Plan, the Corporation hereby grants the Participant an award (the "Award") for that number of Shares of Restricted Stock as is set forth in Section 2.

4. Certificates; Dividends and Voting Rights. A certificate evidencing the Shares shall be issued by the Corporation in the Participant's name, or at the option of the Corporation, in the name of a nominee of the Corporation, pursuant to which the Participant shall have voting rights and shall be entitled to receive all dividends unless and until the Shares are forfeited pursuant to the provisions of this Agreement. The certificate shall bear a legend evidencing the nature of the Shares, and the Corporation may cause the certificate to be delivered upon issuance to the Secretary of the Corporation or to such other depository as may be designated by the Corporation as a depository for safekeeping until the forfeiture occurs or the Award is vested and earned pursuant to the terms of the Plan and this Award. Upon request of the Administrator, the Participant shall deliver to the Corporation a stock power, endorsed in blank, relating to the Shares. Upon the vesting of the Award, the Corporation shall cause a new certificate or certificates to be issued without legend in the name of the Participant for the Shares.

5. Vesting of Award.

- (a) Subject to the terms of the Plan and the Agreement, the Award shall be deemed earned and vested upon such date or dates, and subject to such conditions, as are described on Schedule A. Without limiting the effect of the foregoing, the Shares subject to the Award may vest in installments over a period of time, if so provided in Schedule A.
- (b) Notwithstanding any other provision of Section 5 herein, the Administrator has sole authority to determine whether and to what degree the Award has vested and been earned and to interpret the terms and conditions of this Agreement and the Plan.

6. Forfeiture of Award. Except as may be otherwise provided in the Plan, in the event that (i) the employment or service of the Participant is terminated or (ii) the Participant fails to attend (either in person or by conference telephone) at least 75% of the regular meetings of the Board of Directors in the one-year period ending _____, and the Participant has not yet earned all or part of the Award pursuant to Section 5 and Schedule A herein, then the Award, to the extent not earned as of the Participant's termination date, shall be forfeited immediately upon such termination, and the Participant shall have no further rights with respect to the Award or the Shares underlying that portion of the Award that has not yet been earned and vested. The Participant expressly acknowledges and agrees that the termination of his employment or service for any reason other than death or disability shall result in forfeiture of the Award and the Shares to the extent the Award has not been earned and vested as of the date of his termination of service or employment.

7. No Right of Continued Employment or Service. Nothing contained in this Agreement or the Plan shall confer upon the Participant any right to continue in the employment or service of the Corporation or a related corporation or to interfere in any way with the right of the Corporation or a related corporation to terminate the Participant's employment or service at any time. Except as otherwise expressly provided in the Plan or Section 6 or any other provision of this Agreement, all rights of the Participant with respect to the Award shall terminate upon termination of the employment or service of the Participant with the Corporation or a related corporation.

8. Nontransferability of Award. The Award shall not be transferable other than by will or the laws of intestate succession. The designation of a beneficiary does not constitute a transfer. The Participant shall not sell, transfer, assign, pledge or otherwise encumber ("transfer") the Shares

subject to the Award unless and until all conditions to vesting have been met and such Shares have been issued and any such proposed transfer is permitted pursuant to the Plan and this Agreement.

9. Representations and Warranties of Participant. The Participant represents and warrants to the Corporation that:

- (a) Agrees to Terms of the Plan and Agreement. The Participant has received a copy of the Plan, has read and understands the terms of the Plan and this Agreement, and agrees to be bound by their terms and conditions. The Participant acknowledges that there may be adverse tax consequences upon acquisition or disposition of the shares subject to the Award, and that the Participant should consult a tax advisor prior to such acquisition or disposition.
- (b) Purchase for Own Account for Investment. Any Shares of Common Stock acquired pursuant to the Award shall be acquired for the Participant's own account for investment purposes only and not with a view to, or for sale in connection with, a distribution of the Shares within the meaning of the Securities Act of 1933, as amended (the "Securities Act"). The Participant has no present intention of selling or otherwise disposing of all or any portion of the Shares subject to the Award.
- (c) Access to Information. The Participant has had access to all information regarding the Corporation and its present and prospective business, assets, liabilities and financial condition that the Participant reasonably considers important in making a decision to acquire the Shares subject to the Award, and the Participant has had ample opportunity to ask questions of, and to receive answers from, the Corporation's representatives concerning such matters and this investment.
- (d) Understanding of Risks. The Participant is fully aware of: (i) the highly speculative nature of the investment in the shares of Common Stock; (ii) the financial hazards involved in investment in the Common Stock; (iii) the lack of liquidity of the Shares subject to the Award and the restrictions on transferability of such Shares; (iv) the qualifications and backgrounds of the management of the Corporation; and (v) the tax consequences of investment in the shares of Common Stock. The Participant is capable of evaluating the merits and risks of this investment, has the ability to protect his own interests in this transaction and is financially capable of bearing a total loss from this investment.
- (e) No General Solicitation. At no time was the Participant presented with or solicited by any publicly issued or circulated newspaper, mail, radio, television or other form of general advertising or solicitation in connection with the offer, sale or purchase of the Shares subject to the Award.
- (f) Compliance with Securities Laws. The Shares subject to the Award have not been registered with the Securities and Exchange Commission ("SEC") under the Securities Act and, notwithstanding any other provision of this Agreement or the Plan to the contrary, the right to acquire any shares subject to this Award is expressly conditioned upon compliance with the Securities Act and all applicable state

securities laws. The Participant agrees to cooperate with the Corporation to ensure compliance with such laws.

- (g) No Transfer Unless Registered or Exempt. None of the Corporation's securities is presently publicly traded, and the Corporation has made no representation, covenant or agreement as to whether there will be a public market for any of its securities. The Participant understands that he may not transfer any Shares subject to the Award unless such Shares are registered under the Securities Act and qualified under applicable state securities laws or unless, in the opinion of counsel to the Corporation, exemptions from such registration and qualification requirements are available. The Participant understands that only the Corporation may file a registration statement with the SEC and that the Corporation is under no obligation to do so with respect to the Shares subject to the Award. The Participant has also been advised that exemptions from registration and qualification may not be available or may not permit the Participant to transfer all or any of the Shares subject to the Award in the amounts or at the times proposed by him. The Participant also agrees in connection with any registration of the Corporation's securities that, upon the request of the Corporation or the underwriters managing any public offering of the Corporation's securities, the Participant will not sell or otherwise dispose of any shares without the prior written consent of the Corporation or such underwriters, as the case may be, for such period of time (not to exceed 180 days) after the effective date of such registration requested by such managing underwriters and subject to all restrictions as the Corporation or the underwriters may specify.
- (h) Income Tax Consequences. The Corporation has made no warranties or representations to the Participant with respect to the income tax consequences of the transactions contemplated by this Agreement, and the Participant is in no manner relying on the Corporation or its representatives for an assessment of such tax consequences.

10. Other Restrictions on Award and Shares.

- (a) As a condition to the issuance and delivery of shares subject to the Award, or the grant of any benefit pursuant to the terms of the Plan, the Corporation may require the Participant or other person to become a party to a stockholders agreement, buy-sell agreement, redemption agreement, repurchase agreement or other agreement between the Corporation and stockholders of the Corporation or among stockholders of the Corporation or such other agreements imposing such restrictions as may be required by the Corporation. Without in any way limiting the effect of the foregoing, the Participant hereby expressly acknowledges and agrees that the Corporation shall require, prior to the issuance of any shares pursuant to this Agreement, that the Participant become a party to that certain Second Amended and Restated Stockholders Agreement dated as of November 26, 2002, by and among Targacept, Inc. and the stockholders thereof, as amended.
- (b) The Corporation may impose such restrictions on the Award and any Shares issuable pursuant to the Award as it may deem advisable, including without limitation restrictions under the federal securities laws, or the requirements of any stock

exchange or similar organization or any blue sky or state securities laws applicable to such Shares. Notwithstanding any other provision in the Plan or the Agreement to the contrary, the Corporation shall not be obligated to issue, deliver or transfer shares of Common Stock, to make any other distribution of benefits, or to take any other action, unless such delivery, distribution or action is in compliance with all applicable laws, rules and regulations (including but not limited to the requirements of the Securities Act). The Corporation will be under no obligation to register the shares of Common Stock with the SEC or to effect compliance with the exemption, registration, qualification or listing requirements of any state securities laws, stock exchange or similar organization, and the Corporation will have no liability for any inability or failure to do so. The Corporation may cause a restrictive legend to be placed on any certificate issued pursuant to the Award in such form as may be prescribed from time to time by applicable laws and regulations or as may be advised by legal counsel.

11. Withholding. The Participant acknowledges that the Corporation shall require the Participant to pay the Corporation the amount of any federal, state, local or other tax or other amount required by any governmental authority to be withheld and paid over by the Corporation to such authority for the account of the Participant, and the Participant agrees, as a condition to the grant of the Award and delivery of the shares, to satisfy such obligations.

12. Administration. The authority to construe and interpret this Agreement and the Plan, and to administer all aspects of the Plan, shall be vested in the Administrator (as such term is defined in the Plan), and the Administrator shall have all powers with respect to this Agreement as are provided in the Plan. Any interpretation of the Agreement by the Administrator and any decision made by it with respect to the Agreement is final and binding.

13. Superseding Agreement; Binding Effect. This Agreement supersedes any statements, representations or agreements of the Corporation with respect to the grant of the Award or any related rights, and the Participant hereby waives any rights or claims related to any such statements, representations or agreements. This Agreement shall be binding upon and shall inure to the benefit of the parties hereto and their respective executors, administrators, next-of-kin, successors and assigns.

14. Governing Law. Except as otherwise provided in the Plan or herein, this Agreement shall be construed and enforced according to the laws of the State of Delaware, without regard to the principles of conflict of laws.

15. Amendment and Termination; Waiver. Subject to the terms of the Plan, this Agreement may be modified or amended only by the written agreement of the parties hereto. The waiver by the Corporation of a breach of any provision of the Agreement by the Participant shall not operate or be construed as a waiver of any subsequent breach by the Participant.

16. No Rights as Stockholder. Except as may be provided in Section 4 herein, the Participant and his legal representative, legatees or distributees shall not be deemed to be the holder of any shares subject to the Award and shall not have any rights of a stockholder unless and until certificates for such shares have been issued and delivered to him or them.

17. Notices. Except as may be otherwise provided by the Plan, any written notices provided for in this Agreement or the Plan shall be in writing and shall be deemed sufficiently given if either hand delivered or if sent by fax or overnight courier, or by postage paid first class mail. Notices sent by mail shall be deemed received three business days after mailed but in no event later than the date of actual receipt. Notices shall be directed, if to the Participant, at the Participant's address indicated by the Corporation's records, or if to the Corporation, at the Corporation's principal office.

18. Severability. The provisions of this Agreement are severable and if any one or more provisions may be determined to be illegal or otherwise unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

IN WITNESS WHEREOF, this Agreement has been executed in behalf of the Corporation and by the Participant on the day and year first above written.

TARGACEPT, INC.

By: _____
Name: _____
Title: _____

Attest:

Secretary

[Corporate Seal]

PARTICIPANT

**2000 EQUITY INCENTIVE PLAN
OF TARGACEPT, INC.**

**Restricted Stock Award Agreement
(Service-Based Award)**

SCHEDULE A

Grant Date: _____.

Number of Shares Subject to Award: _____ shares.

Restriction Period: The Shares subject to the Award shall vest and be earned in installments, as provided below, subject to Section 6 and such other terms and conditions as may be imposed by the Plan and this Agreement:

Date of Vesting	Percentage of Shares Vested
_____	_____
_____	100.00%

TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN

TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN

1. Definitions

In addition to other terms defined herein, the following terms shall have the meanings given below:

(a) Administrator means the Board, and, upon its delegation of all or part of its authority to administer the Plan to the Committee, the Committee.

(b) Affiliate means any Parent or Subsidiary of the Corporation, and also includes any other business entity which is controlled by, under common control with or controls the Corporation; provided, however, that the term "Affiliate" shall be construed in a manner in accordance with the registration provisions of applicable federal securities laws.

(c) Annual Option means an Option granted on an annual basis to a Nonemployee Director of the Corporation as provided in Section 8.

(d) Award means, individually or collectively, a grant under the Plan of an Option (including an Incentive Option, Nonqualified Option or a Director Option); a Stock Appreciation Right (including a Related SAR or a Freestanding SAR); a Restricted Award (including a Restricted Stock Award or a Restricted Unit Award); a Performance Award (including a Performance Share Award or a Performance Unit Award); a Phantom Stock Award; a Dividend Equivalent Award; or any other award granted under the Plan.

(e) Award Agreement means an agreement (which may be in written or electronic form, in the Administrator's discretion, and which includes any amendment or supplement thereto) between the Corporation and a Participant specifying the terms, conditions and restrictions of an Award granted to the Participant. An Agreement may also state such other terms, conditions and restrictions, including but not limited to terms, conditions and restrictions applicable to shares or any other benefit underlying an Award, as may be established by the Administrator.

(f) Board or Board of Directors means the Board of Directors of the Corporation.

(g) Cause shall mean, unless the Administrator determines otherwise, a Participant's termination of employment or service resulting from the Participant's (i) termination for "cause" as defined under the Participant's employment, consulting or other agreement with the Corporation or an Affiliate, if any, or (ii) if the Participant has not entered into any such employment, consulting or other agreement (or if any such agreement does not address the effect of a "cause" termination), then the Participant's termination shall be for "Cause" if termination results due to the Participant's (A) dishonesty; (B) refusal to perform his duties for the Corporation; (C) engaging in fraudulent conduct; or (D) engaging in any conduct that could be materially damaging to the Corporation without a reasonable good faith belief that such conduct

was in the best interest of the Corporation. The determination of “Cause” shall be made by the Administrator and its determination shall be final and conclusive.

(h) Change in Control:

(i) *General*: Except as may be otherwise provided in an individual Award Agreement or as may be otherwise required in order to comply with Code Section 409A, a Change in Control shall be deemed to have occurred on the earliest of the following dates:

(A) The date any entity or person shall have become the beneficial owner of, or shall have obtained voting control over, thirty percent (30%) or more of the outstanding Common Stock of the Corporation;

(B) The date the stockholders of the Corporation approve a definitive agreement (X) to merge or consolidate the Corporation with or into another corporation or other business entity (each, a “corporation”), in which the Corporation is not the continuing or surviving corporation or pursuant to which any shares of Common Stock of the Corporation would be converted into cash, securities or other property of another corporation, other than a merger or consolidation of the Corporation in which the holders of Common Stock immediately prior to the merger or consolidation continue to own at least 50% of Common Stock, or if the Corporation is not the surviving corporation, the common stock (or other voting securities) of the surviving corporation immediately after the merger as immediately before; provided, however, that if consummation of such merger or consolidation is subject to the approval of federal, state or other regulatory authorities, then, unless the Administrator determines otherwise, a “Change in Control” shall not be deemed to occur until the later of the date of stockholder approval of such merger or consolidation or the date of final regulatory approval of such merger or consolidation; or (Y) to sell or otherwise dispose of all or substantially all the assets of the Corporation; or

(C) The date there shall have been a change in a majority of the Board of Directors of the Corporation within a 12-month period unless the nomination for election by the Corporation’s stockholders of each new Director was approved by the vote of two-thirds of the members of the Board (or a committee of the Board, if nominations are approved by a Board committee rather than the Board) then still in office who were in office at the beginning of the 12-month period.

(For the purposes herein, the term “person” shall mean any individual, corporation, partnership, group, association or other person, as such term is defined in Section 13(d)(3) or Section 14(d)(2) of the Exchange Act, other than the Corporation, a subsidiary of the Corporation or any employee benefit plan(s) sponsored or maintained by the Corporation or any subsidiary thereof, and the term “beneficial owner” shall have the meaning given the term in Rule 13d-3 under the Exchange Act.)

(D) The Administrator shall have full and final authority, in its discretion, to determine whether a Change in Control of the Corporation has occurred pursuant to the above definition, the date of the occurrence of such Change in Control and any incidental matters relating thereto.

(ii) *Definition Applicable to Awards subject to Code Section 409A*: Notwithstanding the preceding provisions of Section 1(h)(i), in the event that any Awards granted under the Plan are deemed to be deferred compensation subject to the provisions of Code Section 409A, then distributions related to such Awards may be permitted, in the Administrator's discretion, upon the occurrence of one or more of the following events (as they are defined and interpreted under Code Section 409A, related regulations, or other guidance): (A) a change in the ownership of the Corporation, (B) a change in effective control of the Corporation, or (C) a change in the ownership of a substantial portion of the assets of the Corporation.

(i) Code means the Internal Revenue Code of 1986, as amended.

(j) Committee means the Compensation Committee of the Board appointed to administer the Plan.

(k) Common Stock means the common stock of Targacept, Inc., \$0.001 par value.

(l) Corporation means Targacept, Inc., a Delaware corporation, together with any successor thereto.

(m) Covered Employee shall have the meaning given the term in Section 162(m) of the Code and related regulations.

(n) Director means a member of the Board or of the board of directors of an Affiliate.

(o) Director Option means an Option granted to a Nonemployee Director of the Corporation as provided in Section 8. Director Options may be Initial Options or Annual Options as provided in Section 8.

(p) Disability shall, except as may be otherwise determined by the Administrator or required under Code Section 409A or related regulations or other guidance, have the meaning given in any employment agreement, consulting agreement or other similar agreement, if any, to which a Participant is a party, or, if there is no such agreement (or if any such agreement does not address the effect of termination due to disability), "Disability" shall mean the inability to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death, or which has lasted or can be expected to last for a continuous period of not less than 12 months. The Administrator shall have discretion to determine if a termination due to Disability has occurred.

(q) Displacement shall, as applied to any Participant, be as defined in any employment agreement, consulting agreement or other similar agreement, if any, to which the Participant is a party, or, if there is no such agreement (or if any such agreement does not address

the effect of a termination due to displacement), “Displacement” shall mean the termination of the Participant’s employment or service due to the elimination of the Participant’s job or position without fault on the part of the Participant (as determined by the Administrator).

(r) Dividend Equivalent Award means a right granted to a Participant pursuant to Section 13 to receive the equivalent value (in cash or shares of Common Stock) of dividends paid on Common Stock.

(s) Effective Date means the effective date of the Plan, as provided in Section 4.

(t) Employee means any person who is an employee of the Corporation or any Affiliate (including entities which become Affiliates after the Effective Date of the Plan). For this purpose, an individual shall be considered to be an Employee only if there exists between the individual and the Corporation or an Affiliate the legal and bona fide relationship of employer and Employee; provided, however, that, with respect to Incentive Options, “Employee” means any person who is considered an employee of the Corporation or any Parent or Subsidiary for purposes of Treas. Reg. Section 1.421-1(h) (or any successor provision related thereto).

(u) Exchange Act means the Securities Exchange Act of 1934, as amended.

(v) Fair Market Value per share of the Common Stock shall be established in good faith by the Administrator and, except as may otherwise be determined by the Administrator, the Fair Market Value shall be determined in accordance with the following provisions: (A) if the shares of Common Stock are listed for trading on the New York Stock Exchange or the American Stock Exchange, the Fair Market Value shall be the closing sales price per share of the shares on the New York Stock Exchange or the American Stock Exchange (as applicable) on the date immediately preceding the date an Option is granted or other determination is made (such date of determination being referred to herein as a “valuation date”), or, if there is no transaction on such date, then on the trading date nearest preceding the valuation date for which closing price information is available, and, provided further, if the shares are quoted on the Nasdaq National Market or the Nasdaq SmallCap Market of the Nasdaq Stock Market but are not listed for trading on the New York Stock Exchange or the American Stock Exchange, the Fair Market Value shall be the closing sales price for such stock (or the closing bid, if no sales were reported) as quoted on such system on the date immediately or nearest preceding the valuation date for which such information is available; or (B) if the shares of Common Stock are not listed or reported in any of the foregoing, then the Fair Market Value shall be determined by the Administrator based on such valuation measures or other factors as it deems appropriate (provided, however, that, (i) with respect to the grant of Incentive Options, the Fair Market Value shall be determined by the Administrator in accordance with the applicable provisions of Section 20.2031-2 of the Federal Estate Tax Regulations, or in any other manner consistent with the Code Section 422 and accompanying regulations; and (ii) to the extent, if any, required by Code Section 409A, Fair Market Value shall be determined in accordance with Section 409A, related regulations or other guidance).

(w) Freestanding SAR means an SAR that is granted without relation to an Option, as provided in Section 9.

(x) Incentive Option means an Option that is designated by the Administrator as an Incentive Option pursuant to Section 7 and intended to meet the requirements of incentive stock options under Code Section 422 and related regulations.

(y) Independent Contractor means an independent contractor, consultant or advisor providing services to the Corporation or an Affiliate.

(z) Initial Option means an Option granted to a Nonemployee Director of the Corporation upon initial election or appointment to the Board, as provided in Section 8.

(aa) Nonemployee Director means a Director of the Board who is not an Employee of the Corporation or an Affiliate and who is eligible to receive a Director Option pursuant to Section 8.

(bb) Nonqualified Option means an Option granted under Section 7 or Section 8 that is not intended to qualify as an incentive stock option under Code Section 422 and related regulations.

(cc) Option means a stock option granted under Section 7 or Section 8 that entitles the holder to purchase from the Corporation a stated number of shares of Common Stock at the price set forth in an Award Agreement.

(dd) Option Period means the term of an Option, as provided in Section 7(d) and Section 8(f).

(ee) Option Price means the price at which an Option may be exercised, as provided in Section 7(b) and Section 8(e).

(ff) Parent means a "parent corporation," whether now or hereafter existing, as defined in Section 424(e) of the Code.

(gg) Participant means an individual employed by, or providing services to, the Corporation or an Affiliate who satisfies the requirements of Section 6 and is selected by the Administrator to receive an Award under the Plan.

(hh) Performance Award means a Performance Share Award and/or a Performance Unit Award, as provided in Section 11.

(ii) Performance Measures mean one or more performance factors which may be established by the Administrator with respect to an Award. Performance factors may be based on 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 shall be limited to one or more of the following (as determined by the Administrator in its discretion): (i) cash flow; (ii) return on equity; (iii) return on assets; (iv) earnings per share; (v) achievement of clinical development or regulatory milestones; (vi) operations expense efficiency milestones; (vii) consolidated earnings before or after taxes (including earnings before interest, taxes, depreciation and amortization); (viii) net income; (ix) operating income; (x) book value

per share; (xi) return on investment; (xii) return on capital; (xiii) improvements in capital structure; (xiv) expense management; (xv) profitability of an identifiable business unit or product; (xvi) maintenance or improvement of profit margins; (xvii) stock price or total stockholder return; (xviii) market share; (xix) revenues or sales; (xx) costs; (xxi) working capital; (xxii) economic wealth created; (xxiii) strategic business criteria; (xxiv) efficiency ratio(s); (xxv) achievement of division, group, function or corporate financial, strategic or operational goals; and (xxvi) comparisons with stock market indices or performances of metrics of peer companies. To the extent that Section 162(m) of the Code is applicable, the Administrator shall, within the time and in the manner prescribed by Section 162(m) of the 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. Such performance factors may be adjusted or modified due to extraordinary items, transactions, events or developments, or in recognition of, or in anticipation of, any other unusual or nonrecurring events affecting the Corporation or the financial statements of the Corporation, or in response to, or in anticipation of, changes in applicable laws, regulations, accounting principles or business conditions, in each case as determined by the Administrator.

(jj) Performance Share means an Award granted under Section 11, in an amount determined by the Administrator and specified in an Award Agreement, stated with reference to a specified number of shares of Common Stock, that entitles the holder to receive shares of Common Stock, a cash payment or a combination of Common Stock and cash (as determined by the Administrator), subject to the terms of the Plan and the terms and conditions established by the Administrator.

(kk) Performance Unit means an Award granted under Section 11, in an amount determined by the Administrator and specified in an Award Agreement, that entitles the holder to receive Shares of Common Stock, a cash payment or a combination of Common Stock and cash (as determined by the Administrator), subject to the terms of the Plan and the terms and conditions established by the Administrator.

(ll) Phantom Stock Award means an Award granted under Section 12, entitling a Participant to a payment in cash, shares of Common Stock or a combination of cash and Common Stock (as determined by the Administrator), following the completion of the applicable vesting period and compliance with the terms of the Plan and other terms and conditions established by the Administrator. The unit value of a Phantom Stock Award shall be based on the Fair Market Value of a share of Common Stock.

(mm) Plan means the Targacept, Inc. 2005 Stock Incentive Plan, as it may be hereafter amended and/or restated.

(nn) Prior Plan or Prior Plans means the 2000 Equity Incentive Plan of Targacept, Inc., as amended, and any other employee stock incentive plan maintained by the Corporation prior to the Effective Date of the Plan.

(oo) Public Offering Date means the date on which the Underwriting Agreement between the Corporation and the managing underwriters of the Corporation's initial public offering of its Common Stock is executed and delivered.

(pp) Related SAR means an SAR granted under Section 9 that is granted in relation to a particular Option and that can be exercised only upon the surrender to the Corporation, unexercised, of that portion of the Option to which the SAR relates.

(qq) Restricted Award means a Restricted Stock Award and/or a Restricted Stock Unit Award, as provided in Section 10.

(rr) Restricted Stock Award means shares of Common Stock awarded to a Participant under Section 10. Shares of Common Stock subject to a Restricted Stock Award shall cease to be restricted when, in accordance with the terms of the Plan and the terms and conditions established by the Administrator, the shares vest and become transferable and free of substantial risks of forfeiture.

(ss) Restricted Stock Unit means a Restricted Award granted to a Participant pursuant to Section 10 which is settled (i) by the delivery of one share of Common Stock for each Restricted Stock Unit, (ii) in cash in an amount equal to the Fair Market Value of one share of Common Stock for each Restricted Stock Unit, or (iii) in a combination of cash and Shares equal to the Fair Market Value of one share of Common Stock for each Restricted Stock Unit, as determined by the Administrator. A Restricted Stock Unit Award represents the promise of the Corporation to deliver shares, cash or a combination thereof, as applicable, at the end of the Restriction Period, subject to compliance with the terms of the Plan and the terms and conditions established by the Administrator.

(tt) Retirement shall, as applied to any Participant, be as defined in any employment agreement, consulting agreement or other similar agreement, if any, to which the Participant is a party, or, if there is no such agreement (or if any such agreement does address the effect of termination due to retirement), "Retirement" shall mean retirement in accordance with the retirement policies and procedures established by the Corporation, as determined by the Administrator.

(uu) SAR means a stock appreciation right granted under Section 9 entitling the Participant to receive, with respect to each share of Common Stock encompassed by the exercise of such SAR, the excess of the Fair Market Value on the date of exercise over the SAR base price, subject to the terms of the Plan and any other terms and conditions established by the Administrator. References to "SARs" include both Related SARs and Freestanding SARs, unless the context requires otherwise.

(vv) Securities Act means the Securities Act of 1933, as amended.

(ww) Subsidiary means a "subsidiary corporation," whether now or hereafter existing, as defined in Section 424(f) of the Code.

(xx) Termination Date means the date of termination of a Participant's employment or service for any reason, as determined by the Administrator in its discretion.

2. Purpose

The purpose of the Plan is to encourage and enable selected Employees, Directors and Independent Contractors of the Corporation and its Affiliates to acquire or to increase their holdings of Common Stock of the Corporation and other proprietary interests in the Corporation in order to promote a closer identification of their interests with those of the Corporation and its stockholders, thereby further stimulating their efforts to enhance the efficiency, soundness, profitability, growth and stockholder value of the Corporation. This purpose will be carried out through the granting of Awards to selected Employees, Independent Contractors and Directors, including the granting to selected Participants of Options in the form of Incentive Stock Options and Nonqualified Options; SARs in the form of Related SARs and Freestanding 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/or Dividend Equivalent Awards.

3. Administration of the Plan

(a) The Plan shall be administered by the Board of Directors of the Corporation or, upon its delegation, by the Committee. Unless the Board determines otherwise, the Committee shall be comprised solely of two or more "non-employee directors," as such term is defined in Rule 16b-3 under the Exchange Act, or as may otherwise be permitted under Rule 16b-3. Further, to the extent required by Section 162(m) of the Code and related regulations, the Plan shall be administered by a committee comprised of two or more "outside directors" (as such term is defined in Section 162(m) or related regulations) or as may otherwise be permitted under Section 162(m) and related regulations. For the purposes of the Plan, the term "Administrator" shall refer to the Board and, upon its delegation to the Committee of all or part of its authority to administer the Plan, to the Committee. Notwithstanding the foregoing, the Board shall have sole authority to grant discretionary Awards (that is, Awards other than Director Options) to Directors who are not employees of the Corporation or its Affiliates.

(b) Subject to the provisions of the Plan, the Administrator shall have full and final authority in its discretion to take any action with respect to the Plan including, without limitation, the authority (i) to determine all matters relating to Awards, including selection of individuals to be granted Awards, the types of Awards, the number of shares of the Common Stock, if any, subject to an Award, and all terms, conditions, restrictions and limitations of an Award; (ii) to prescribe the form or forms of Award Agreements evidencing any Awards granted under the Plan; (iii) to establish, amend and rescind rules and regulations for the administration of the Plan; and (iv) to construe and interpret the Plan, Awards and Award Agreements made under the Plan, to interpret rules and regulations for administering the Plan and to make all other determinations deemed necessary or advisable for administering the Plan. Except to the extent otherwise required under Code Section 409A or related regulations or other guidance, (i) the Administrator shall have the authority, in its sole discretion, to accelerate the date that any Award which was

not otherwise exercisable, vested or earned shall become exercisable, vested or earned in whole or in part without any obligation to accelerate such date with respect to any other Award granted to any recipient; and (ii) the Administrator also may in its sole discretion modify or extend the terms and conditions for exercise, vesting or earning of an Award. The Administrator may determine 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) shall 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. Such events may include, but shall not be limited to, termination of employment for cause, violation of policies of the Corporation or an Affiliate, breach of non-solicitation, noncompetition, confidentiality or other restrictive covenants that may apply to the Participant, or other conduct by the Participant that is determined by the Administrator to be detrimental to the business or reputation of the Corporation or any Affiliate. In addition, the Administrator shall have the authority and discretion to establish terms and conditions of Awards (including but not limited to the establishment of subplans) as the Administrator determines to be necessary or appropriate to conform to the applicable requirements or practices of jurisdictions outside of the United States. In addition to action by meeting in accordance with applicable laws, any action of the Administrator with respect to the Plan may be taken by a written instrument signed by all of the members of the Board or Committee, as appropriate, and any such action so taken by written consent shall be as fully effective as if it had been taken by a majority of the members at a meeting duly held and called. No member of the Board or Committee, as applicable, shall be liable while acting as Administrator for any action or determination made in good faith with respect to the Plan, an Award or an Award Agreement. The members of the Board or Committee, as applicable, shall be entitled to indemnification and reimbursement in the manner provided in the Corporation's certificate of incorporation and bylaws and/or under applicable law.

(c) Notwithstanding the other provisions of Section 3, the Administrator may delegate to one or more officers of the Corporation the authority to grant Awards, and to make any or all of the determinations reserved for the Administrator in the Plan and summarized in Section 3(b) with respect to such Awards (subject to any restrictions imposed by applicable laws, rules and regulations and such terms and conditions as may be established by the Administrator); provided, however, that, to the extent required by Section 16 of the Exchange Act or Section 162(m) of the Code, the Participant, at the time of said grant or other determination, (i) is not deemed to be an officer or director of the Corporation within the meaning of Section 16 of the Exchange Act; and (ii) is not deemed to be a Covered Employee as defined under Section 162(m) of the Code and related regulations. To the extent that the Administrator has delegated authority to grant Awards pursuant to this Section 3(c) to one or more officers of the Corporation, references to the Administrator shall include references to such officer or officers, subject, however, to the requirements of the Plan, Rule 16b-3, Section 162(m) of the Code and other applicable laws, rules and regulations.

4. *Effective Date*

The Effective Date of the Plan shall be the day prior to the Public Offering Date. Awards may be granted under the Plan on and after the Effective Date, but not after the date that

is the tenth anniversary less one day after the Effective Date. Awards that are outstanding at the end of the Plan term (or such earlier termination date as may be established by the Board pursuant to Section 15(a)) shall continue in accordance with their terms, unless otherwise provided in the Plan or an Award Agreement.

5. Shares of Stock Subject to the Plan; Award Limitations

(a) *Shares of Stock Subject to the Plan:* Subject to adjustments as provided in Section 5(d), the aggregate number of shares of Common Stock that may be issued pursuant to Awards granted under the Plan shall not exceed the sum of (i) 3,300,000 shares, plus (ii) no more than 40,286 shares of Common Stock remaining available for issuance as of the Effective Date of the Plan under any Prior Plan, plus (iii) no more than 986,073 shares of Common Stock if and to the extent that any of such shares are subject to an award granted under a Prior Plan, which award is forfeited, cancelled, terminated, expires or lapses for any reason without the issuance of shares pursuant to the award. Shares delivered under the Plan shall be authorized but unissued shares, treasury shares or shares purchased on the open market or by private purchase. The Corporation hereby reserves sufficient authorized shares of Common Stock to meet the grant of Awards hereunder.

(b) *Award Limitations:* Notwithstanding any provision in the Plan to the contrary, the following limitations shall apply to Awards granted under the Plan, in each case subject to adjustments pursuant to Section 5(d):

(i) The maximum number of shares of Common Stock that may be issued under the Plan pursuant to the grant of Incentive Options shall not exceed 4,326,359 shares, or such lesser number of shares as may be available under the Plan pursuant to Section 5(a) herein;

(ii) In any calendar year, no Participant may be granted Options and SARs that are not related to an Option for more than 500,000 shares of Common Stock;

(iii) No Participant may be granted Awards in any calendar year for more than 500,000 shares of Common Stock; and

(iv) No Participant may be paid more than \$1,000,000 with respect to any cash-settled award or awards which were granted during any single calendar year.

(For purposes of Section 5(b)(ii) and (iii), an Option and Related SAR shall be treated as a single Award.)

(c) *Shares Not Subject to Limitations:* The following will not be applied to the share limitations of Section 5(a) above: (i) dividends, including dividends paid in shares, 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 the Plan which Award is forfeited, cancelled, terminated, expires or lapses for any reason; and (iv) any shares surrendered by a Participant or withheld by the Corporation to pay the Option Price or purchase price for an Award or shares or used to satisfy any tax withholding requirement

in connection with the exercise, vesting or earning of an Award if, in accordance with the terms of the Plan, a Participant pays such Option Price or purchase price or satisfies such tax withholding by either tendering previously owned shares or having the Corporation withhold shares.

(d) *Adjustments*: If there is any change in the outstanding shares of Common Stock because of a merger, consolidation or reorganization involving the Corporation or an Affiliate, or if the Board of Directors of the Corporation declares a stock dividend, stock split distributable in shares of Common Stock, reverse stock split, combination or reclassification of the Common Stock, or if there is a similar change in the capital stock structure of the Corporation or an Affiliate affecting the Common Stock, the number of shares of Common Stock reserved for issuance under the Plan shall be correspondingly adjusted, and the Administrator shall make such adjustments to Awards and to any provisions of this Plan as the Administrator deems equitable to prevent dilution or enlargement of Awards or as may be otherwise advisable.

6. Eligibility

An Award may be granted only to an individual who satisfies all of the following eligibility requirements on the date the Award is granted:

(a) The individual is either (i) an Employee, (ii) a Director, or (iii) an Independent Contractor.

(b) With respect to the grant of Incentive Options, the individual is otherwise eligible to participate under Section 6, is an Employee of the Corporation or a Parent or Subsidiary and does not own, immediately before the time that the Incentive Option is granted, stock possessing more than 10% of the total combined voting power of all classes of stock of the Corporation or a Parent or Subsidiary. Notwithstanding the foregoing, an Employee who owns more than 10% of the total combined voting power of the Corporation or a Parent or Subsidiary may be granted an Incentive Option if the Option Price is at least 110% of the Fair Market Value of the Common Stock, and the Option Period does not exceed five years. For this purpose, an individual will be deemed to own stock which is attributable to him under Section 424(d) of the Code.

(c) With respect to the grant of substitute awards or assumption of awards in connection with a merger, consolidation, acquisition, reorganization or similar business combination involving the Corporation or an Affiliate, the recipient is otherwise eligible to receive the Award and the terms of the award are consistent with the Plan and applicable laws, rules and regulations (including, to the extent necessary, the federal securities laws registration provisions and Section 424(a) of the Code).

(d) The individual, being otherwise eligible under this Section 6, is selected by the Administrator as an individual to whom an Award shall be granted (as defined above, a "Participant").

7. Options

(a) *Grant of Options:* Subject to the limitations of the Plan, the Administrator may in its sole and absolute discretion grant Options to such eligible individuals in such numbers, subject to such terms and conditions, and at such times as the Administrator shall determine. Both Incentive Options and Nonqualified Options may be granted under the Plan, as determined by the Administrator; provided, however, that Incentive Options may only be granted to Employees of the Corporation or a Parent or Subsidiary. To the extent that an Option is designated as an Incentive Option but does not qualify as such under Section 422 of the Code, the Option (or portion thereof) shall be treated as a Nonqualified Option. An Option may be granted with or without a Related SAR.

(b) *Option Price:* The Option Price shall be established by the Administrator and stated in the Award Agreement evidencing the grant of the Option; provided, that (i) the Option Price of an Incentive Option shall be no less than 100% of the Fair Market Value per share of the Common Stock as determined on the date the Option is granted (or 110% of the Fair Market Value with respect to Incentive Options granted to an Employee who owns stock possessing more than 10% of the total voting power of all classes of stock of the Corporation or a Parent or Subsidiary, as provided in Section 6(b)); (ii) the Option Price of a Nonqualified Option shall be no less than 85% of the Fair Market Value per share of the Common Stock on the date the Option is granted; and (iii) in no event shall the Option Price per share of any Option be less than the par value per share of the Common Stock. Notwithstanding the foregoing, the Administrator may in its discretion authorize the grant of substitute or assumed options of an acquired entity with an Option Price not equal to at least 100% of the Fair Market Value on the date of grant, if such options are assumed or substituted in accordance with Section 424(a) and related regulations and if the option price of any such assumed or substituted option was at least equal to 100% of the fair market value of the underlying stock on the original date of grant.

(c) *Date of Grant:* An Incentive Option shall be considered to be granted on the date that the Administrator acts to grant the Option, or on any later date specified by the Administrator as the effective date of the Option. A Nonqualified Option shall be considered to be granted on the date the Administrator acts to grant the Option or any other date specified by the Administrator as the date of grant of the Option.

(d) *Option Period and Limitations on the Right to Exercise Options:*

(i) The Option Period shall be determined by the Administrator at the time the Option is granted and shall be stated in the Award Agreement. With respect to Incentive Options, the Option Period shall not extend more than 10 years from the date on which the Option is granted (or five years with respect to Incentive Options granted to an Employee who owns stock possessing more than 10% of the total combined voting power of all classes of stock of the Corporation or a Parent or Subsidiary, as provided in Section 6(b)). Any Option or portion thereof not exercised before expiration of the Option Period shall terminate. The period or periods during which, and conditions pursuant to which, an Option may become exercisable shall be determined by the Administrator in its discretion, subject to the terms of the Plan.

(ii) An Option may be exercised by giving written notice to the Corporation in form acceptable to the Administrator at such place and subject to such conditions as may be established by the Administrator or its designee. Such notice shall specify the number of shares to be purchased pursuant to an Option and the aggregate purchase price to be paid therefor and shall be accompanied by payment of such purchase price. The total number of shares that may be acquired upon exercise of an Option shall be rounded down to the nearest whole share. No fractional shares shall be issued. Unless an Award Agreement provides otherwise, such payment shall be in the form of cash or cash equivalent; provided that, where permitted by the Administrator and applicable laws, rules and regulations (and subject to such terms and conditions as may be established by the Administrator), payment may also be made:

(A) By delivery (by either actual delivery or attestation) of shares of Common Stock owned by the Participant for at least six months (or for such other time period determined by the Administrator) and otherwise acceptable to the Administrator;

(B) By shares of Common Stock withheld upon exercise;

(C) With respect only to purchases upon exercise of an Option after a public market for the Common Stock exists, by delivery of written notice of exercise to the Corporation and delivery to a broker of written notice of exercise and irrevocable instructions to promptly deliver to the Corporation the amount of sale or loan proceeds to pay the Option Price;

(D) By such other payment methods as may be approved by the Administrator and which are acceptable under applicable law; or

(E) By any combination of the foregoing methods.

Shares tendered or withheld in payment on the exercise of an Option shall be valued at their Fair Market Value on the date of exercise, as determined by the Administrator. For the purposes of the Plan, a "public market" for the Common Stock shall be deemed to exist (i) upon consummation of a firm commitment underwritten public offering of the Common Stock pursuant to an effective registration statement under the Securities Act, or (ii) if the Administrator otherwise determines that there is an established public market for the Common Stock.

(iii) Unless the Administrator determines otherwise, no Option granted to a Participant who was an Employee at the time of grant shall be exercised unless the Participant is, at the time of exercise, an Employee as described in Section 6(a), and has been an Employee continuously since the date the Option was granted, subject to the following:

(A) The employment relationship of a Participant shall be treated as continuing intact for any period that the Participant is on military or sick leave or

other bona fide leave of absence, provided that the period of such leave does not exceed 90 days, or, if longer, as long as the Participant's right to reemployment is guaranteed either by statute or by contract. The employment relationship of a Participant shall also be treated as continuing intact while the Participant is not in active service because of Disability. The Administrator shall have sole authority to determine whether a Participant is disabled and, if applicable, the Participant's Termination Date.

(B) Unless the Administrator determines otherwise, if the employment of a Participant is terminated because of Disability or death, the Option may be exercised only to the extent exercisable on the Participant's Termination Date, except that the Administrator may in its sole discretion accelerate the date for exercising all or any part of the Option which was not otherwise exercisable on the Termination Date. The Option must be exercised, if at all, prior to the first to occur of the following, whichever shall be applicable: (X) the close of the one-year period following the Termination Date (or such other period stated in the Award Agreement); or (Y) the close of the Option Period. In the event of the Participant's death, such Option shall be exercisable by such person or persons as shall have acquired the right to exercise the Option by will or by the laws of intestate succession.

(C) Unless the Administrator determines otherwise, if the employment of the Participant is terminated for any reason other than Disability, death or for "Cause," his Option may be exercised to the extent exercisable on his Termination Date, except that the Administrator may in its sole discretion accelerate the date for exercising all or any part of the Option which was not otherwise exercisable on the Termination Date. The Option must be exercised, if at all, prior to the first to occur of the following, whichever shall be applicable: (X) the close of the period of three months next succeeding the Termination Date (or such other period stated in the Award Agreement); or (Y) the close of the Option Period. If the Participant dies following such termination of employment and prior to the earlier of the dates specified in (X) or (Y) of this subparagraph (C), the Participant shall be treated as having died while employed under subparagraph (B) (treating for this purpose the Participant's date of termination of employment as the Termination Date). In the event of the Participant's death, such Option shall be exercisable by such person or persons as shall have acquired the right to exercise the Option by will or by the laws of intestate succession.

(D) Unless the Administrator determines otherwise, if the employment of the Participant is terminated for "Cause," his Option shall lapse and no longer be exercisable as of his Termination Date, as determined by the Administrator.

(E) Notwithstanding the foregoing, the Administrator may, in its sole discretion (subject to any requirements imposed under Code Section 409A, related regulations or other guidance), accelerate the date for exercising all or any part of an Option which was not otherwise exercisable on the Termination Date, extend

the period during which an Option may be exercised, modify the terms and conditions to exercise, or any combination of the foregoing.

(iv) Unless the Administrator determines otherwise, an Option granted to a Participant who was a Director but who was not an Employee at the time of grant may be exercised only to the extent exercisable on the Participant's Termination Date (unless the termination was for Cause), and must be exercised, if at all, prior to the first to occur of the following, as applicable: (X) the close of the period of six months next succeeding the Termination Date (or such other period stated in the Award Agreement); or (Y) the close of the Option Period. If the services of a Participant are terminated for Cause, his Option shall lapse and no longer be exercisable as of his Termination Date, as determined by the Administrator. Notwithstanding the foregoing, the Administrator may in its sole discretion (subject to any requirements imposed under Code Section 409A, related regulations or other guidance) accelerate the date for exercising all or any part of an Option which was not otherwise exercisable on the Termination Date, extend the period during which an Option may be exercised, modify the other terms and conditions to exercise, or any combination of the foregoing.

(v) Unless the Administrator determines otherwise, an Option granted to a Participant who was an Independent Contractor at the time of grant (and who does not thereafter become an Employee, in which case he shall be subject to the provisions of Section 7(d)(iii)) may be exercised only to the extent exercisable on the Participant's Termination Date (unless the termination was for Cause), and must be exercised, if at all, prior to the first to occur of the following, as applicable: (X) the close of the period of three months next succeeding the Termination Date (or such other period stated in the Award Agreement); or (Y) the close of the Option Period. If the services of a Participant are terminated for Cause, his Option shall lapse and no longer be exercisable as of his Termination Date, as determined by the Administrator. Notwithstanding the foregoing, the Administrator may in its sole discretion (subject to any requirements imposed under Code Section 409A, related regulations or other guidance) accelerate the date for exercising all or any part of an Option which was not otherwise exercisable on the Termination Date, extend the period during which an Option may be exercised, modify the other terms and conditions to exercise, or any combination of the foregoing.

(e) *Notice of Disposition*: If shares of Common Stock acquired upon exercise of an Incentive Option are disposed of within two years following the date of grant or one year following the transfer of such shares to a Participant upon exercise, the Participant shall, promptly following such disposition, notify the Corporation in writing of the date and terms of such disposition and provide such other information regarding the disposition as the Administrator may reasonably require.

(f) *Limitation on Incentive Options*: In no event shall there first become exercisable by an Employee in any one calendar year Incentive Options granted by the Corporation or any Parent or Subsidiary with respect to shares having an aggregate Fair Market Value (determined at the time an Incentive Option is granted) greater than \$100,000. To the extent that any Incentive

Options are first exercisable by a Participant in excess of such limitation, the excess shall be considered a Nonqualified Option.

(g) *Nontransferability*: Incentive Options shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession or, in the Administrator's discretion, as may otherwise be permitted in accordance with Treas. Reg. Section 1.421-1(b)(2) or any successor provision thereto. Nonqualified Options shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, except as may be permitted by the Administrator in a manner consistent with the registration provisions of the Securities Act. Except as may be permitted by the preceding sentence, an Option shall be exercisable during the Participant's lifetime only by him or by his guardian or legal representative. The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

8. Director Options

(a) *General*: Each Nonemployee Director who is otherwise eligible under this Section 8 shall be granted a Director Option or Director Options as provided in Section 8. Director Options shall be designated as Nonqualified Options. Director Options shall be subject to the other terms and conditions of the Plan except as otherwise provided in Section 8.

(b) *Eligibility*: A Director Option may be granted only to an individual who is a Nonemployee Director of the Corporation on the date the Director Option is granted. A Nonemployee Director may also be eligible for other Awards (including but not limited to Options granted pursuant to Section 7), subject to the terms of the Plan and the Administrator's discretion.

(c) *Grant of Initial Options Upon Initial Election or Appointment to the Board*: Each Nonemployee Director who is first elected or appointed to the Board after the Public Offering Date shall receive an Initial Option to purchase 25,000 shares of Common Stock. The date of grant of such an Initial Option shall be the fifth business day after the date of the annual meeting of stockholders as to those Nonemployee Directors who are first elected at an annual meeting of stockholders and the fifth business day after the date of election or appointment to the Board as to those Nonemployee Directors who are first elected or appointed to the Board other than at an annual meeting of stockholders. In addition, a Nonemployee Director who serves as chairman of the Board shall also receive an Initial Option for 10,000 shares when first elected or appointed as chairman. The date of grant of such Initial Option shall be the fifth business day after the date on which the Director is first elected or appointed as chairman of the Board.

(d) *Grant of Annual Options*: Each Nonemployee Director also shall be granted, on an annual basis commencing with the 2005 annual meeting of stockholders, a Director Option to purchase 7,500 shares of Common Stock (or, a Director Option for 12,500 shares, in the case of the chairman of the Board), provided that the Nonemployee Director continues to serve as a member of the Board as of the date of grant. The date of grant of such an Annual Option shall be the fifth business day after the date of the annual or other stockholders meeting at which directors are elected. For the avoidance of doubt, a Nonemployee Director elected for the first time to the

Board at an annual meeting of stockholders shall only receive an Initial Option in connection with such election, and shall not receive an Annual Option on the fifth business day following such meeting as well.

(e) *Option Price*: The price per share of Common Stock at which a Director Option may be exercised shall be 100% of the Fair Market Value per share of the Common Stock on the date the Option is granted.

(f) *Option Period and Limitations on the Right to Exercise Options*:

(i) The Option Period of a Director Option shall be 10 years from the date of grant. Initial Options shall become exercisable as provided in Section 8(f)(i)(A), and Annual Options shall become exercisable as provided in Section 8(f)(i)(B). To the extent that all or part of an Option becomes exercisable but is not exercised, such Option shall accumulate and be exercisable by the Director in whole or in part at any time before the expiration of the Option Period. The total number of shares that may be acquired upon the exercise of an Initial Option or Annual Option shall be rounded down to the nearest whole share. No fractional shares shall be issued. Any Director Option or portion thereof not exercised before expiration of the Option Period shall terminate.

(A) Initial Options. An Initial Option shall vest and become exercisable with respect to one-third of the shares subject to the Option on the first anniversary of the date of grant, provided that the Nonemployee Director remains in service on such anniversary date. An Initial Option shall vest and become exercisable with respect to the remaining two-thirds of the shares subject to the Option in pro rata quarterly installments over the second and third years following the date of grant so that an Initial Option will be vested and exercisable in full on the third anniversary of the date of grant, provided that the Nonemployee Director remains in service as a Director during such periods.

(B) Annual Options. An Annual Option granted shall vest and become exercisable on the first anniversary of the date of grant, provided that the Nonemployee Director remains in service as a Director on such anniversary date.

(ii) Unless the Administrator determines otherwise, a Director Option granted to a Nonemployee Director at the time of grant may be exercised only to the extent exercisable on the Nonemployee Director's Termination Date (unless the termination was for Cause), and must be exercised, if at all, prior to the first to occur of the following, as applicable: (X) the close of the period of six months next succeeding the Termination Date (or such other period stated in the Award Agreement); or (Y) the close of the Option Period. If the services of a Nonemployee Director are terminated for Cause, his Director Option shall lapse and no longer be exercisable as of his Termination Date, as determined by the Administrator.

(iii) A Director Option shall be exercised by giving written notice to the Administrator or its designee at such time and place as the Administrator shall direct.

Such notice shall specify the number of shares to be purchased pursuant to the Director Option and the aggregate purchase price to be paid therefor, and shall be accompanied by the payment of such purchase price. Payment shall be made in accordance with Section 7(d)(ii).

(g) *Nontransferability*: A Director Option shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, except as may be permitted by the Administrator in a manner consistent with the registration provisions of the Securities Act. Except as may be permitted by the preceding sentence, a Director Option shall be exercisable during the Nonemployee Director's lifetime only by him or by his guardian or legal representative. The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

9. Stock Appreciation Rights

(a) *Grant of SARs*: Subject to the limitations of the Plan, the Administrator may in its sole and absolute discretion grant SARs to such eligible individuals, in such numbers, upon such terms and at such times as the Administrator shall determine. SARs may be granted to the holder of an Option (a "Related Option") with respect to all or a portion of the shares of Common Stock subject to the Related Option (a "Related SAR") or may be granted separately to an eligible individual (a "Freestanding SAR"). The base price per share of an SAR shall be no less than 100% the Fair Market Value per share of the Common Stock on the date the SAR is granted.

(b) *Related SARs*: A Related SAR may be granted either concurrently with the grant of the Related Option or (if the Related Option is a Nonqualified Option) at any time thereafter prior to the complete exercise, termination, expiration or cancellation of such Related Option; provided, however, that Related SARs must be granted in accordance with Code Section 409A, related regulations and other guidance. The base price of a Related SAR shall be equal to the Option Price of the Related Option. Related SARs shall be exercisable only at the time and to the extent that the Related Option is exercisable (and may be subject to such additional limitations on exercisability as the Administrator may provide in the agreement), and in no event after the complete termination or full exercise of the Related Option. Notwithstanding the foregoing, a Related SAR that is related to an Incentive Option may be exercised only to the extent that the Related Option is exercisable and only when the Fair Market Value exceeds the Option Price of the Related Option. Upon the exercise of a Related SAR granted in connection with a Related Option, the Option shall be canceled to the extent of the number of shares as to which the SAR is exercised, and upon the exercise of a Related Option, the Related SAR shall be canceled to the extent of the number of shares as to which the Related Option is exercised or surrendered.

(c) *Freestanding SARs*: An SAR may be granted without relationship to an Option (as defined above, a "Freestanding SAR") and, in such case, will be exercisable upon such terms and subject to such conditions as may be determined by the Administrator, subject to the terms of the Plan.

(d) *Exercise of SARs:*

(i) Subject to the terms of the Plan, SARs shall be exercisable in whole or in part upon such terms and conditions as may be established by the Administrator and stated in the applicable Award Agreement. The period during which an SAR may be exercisable shall not exceed 10 years from the date of grant or, in the case of Related SARs, such shorter Option Period as may apply to the Related Option. Any SAR or portion thereof not exercised before expiration of the period established by the Administrator shall terminate.

(ii) SARs may be exercised by giving written notice to the Corporation in form acceptable to the Administrator at such place and subject to such terms and conditions as may be established by the Administrator or its designee. Unless the Administrator determines otherwise, the date of exercise of an SAR shall mean the date on which the Corporation shall have received proper notice from the Participant of the exercise of such SAR.

(iii) Each Participant's Award Agreement shall set forth the extent to which the Participant shall have the right to exercise an SAR following termination of the Participant's employment or service with the Corporation. Such provisions shall be determined in the sole discretion of the Administrator, need not be uniform among all SARs issued pursuant to this Section 9, and may reflect distinctions based on the reasons for termination of employment. Notwithstanding the foregoing, unless the Administrator determines otherwise, no SAR may be exercised unless the Participant is, at the time of exercise, an eligible Participant, as described in Section 6, and has been a Participant continuously since the date the SAR was granted, subject to the provisions of Sections 7(d)(iii), (iv) and (v).

(e) *Payment Upon Exercise:* Subject to the limitations of the Plan, upon the exercise of an SAR, a Participant shall be entitled to receive payment from the Corporation in an amount determined by multiplying (i) 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 (ii) the number of shares of Common Stock with respect to which the SAR is being exercised. Notwithstanding the foregoing, the Administrator in its discretion may limit in any manner the amount payable with respect to an SAR. The consideration payable upon exercise of an SAR shall be paid in cash, shares of Common Stock (valued at Fair Market Value on the date of exercise of the SAR) or a combination of cash and shares of Common Stock, as determined by the Administrator. Notwithstanding the foregoing, to the extent required to ensure that an SAR is not subject to, or complies with, Code Section 409A, related regulations, and other guidance, (i) an SAR shall be settled solely for shares of Common Stock of the Corporation, which Common Stock is traded on an established securities market, and which SAR does not include any feature for the deferral of compensation other than the deferral of recognition of income until the exercise of the SAR; or (ii) an SAR shall be structured in a manner designed to be exempt from, or to comply with, the requirements of Code Section 409A. No fractional shares of Common Stock will be issuable upon exercise of the SAR and, unless otherwise provided in the applicable Agreement, the Participant will receive cash in lieu of fractional shares.

(f) *Nontransferability*: Unless the Administrator determines otherwise, (i) SARs shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, and (ii) SARs may be exercised during the Participant's lifetime only by him or by his guardian or legal representative. The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

10. Restricted Awards

(a) *Grant of Restricted Awards*: Subject to the limitations of the Plan, the Administrator may in its sole and absolute discretion grant Restricted Awards to such individuals in such numbers, upon such terms and at such times as the Administrator shall determine. Such 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 shall be payable in shares of Common Stock. Restricted Stock Units shall 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 the Plan and the discretion of the Administrator. The Administrator shall determine the nature, length and starting date of the period, if any, during which a Restricted Award may be earned (the "Restriction Period"), and shall determine the conditions which must be met in order for a Restricted Award to be granted or to vest or be earned (in whole or in part), which conditions may include, but are not limited to, 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. Notwithstanding the foregoing, Restricted Awards that vest based solely on continued service or the passage of time shall be subject to a minimum Restriction Period of one year (except in the case of (i) Restricted Awards assumed or substituted in connection with mergers, acquisitions or other business transactions, (ii) Restricted Awards granted in connection with the recruitment or hiring of a Participant, and/or (iii) Restricted Awards granted pursuant to any incentive compensation or bonus program established by the Corporation). In the case of Restricted Awards based upon performance criteria, or a combination of performance criteria and continued service, the Administrator shall determine the Performance Measures applicable to such Restricted Awards (subject to Section 1(ii)).

(b) *Vesting of Restricted Awards*: Subject to the terms of the Plan and Code Section 409A, related regulations or other guidance, the Administrator shall have sole authority to determine whether and to what degree Restricted Awards have vested and been earned and are payable and to establish and interpret the terms and conditions of Restricted Awards. The Administrator may (subject to any restrictions imposed under Code Section 409A, related regulations or other guidance) accelerate the date that any Restricted Award granted to a Participant shall be deemed to be vested or earned in whole or in part, without any obligation to accelerate such date with respect to other Restricted Awards granted to any Participant.

(c) *Forfeiture of Restricted Awards*: Unless the Administrator determines otherwise, if the employment or service of a Participant shall be terminated for any reason and all or any part of a Restricted Award has not vested or been earned pursuant to the terms of the Plan and the

individual Award, such Award, to the extent not then vested or earned, shall be forfeited immediately upon such termination and the Participant shall have no further rights with respect thereto.

(d) *Dividend and Voting Rights; Share Certificates:* The Administrator shall have sole discretion to determine whether a Participant shall have dividend rights, voting rights or other rights as a stockholder with respect to shares subject to a Restricted Award which has not yet vested or been earned. If the Administrator so determines, a certificate or certificates for shares of Common Stock subject to a Restricted Award may be issued in the name of the Participant as soon as practicable after the Award has been granted; provided, however, that, notwithstanding the foregoing, the Administrator shall have the right to retain custody of certificates evidencing the shares subject to a Restricted Award and to require the Participant to deliver to the Corporation a stock power, endorsed in blank, with respect to such Award, until such time as the Restricted Award vests (or is forfeited) and is no longer subject to a substantial risk of forfeiture.

(e) *Nontransferability:* Unless the Administrator determines otherwise, Restricted Awards that have not vested shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, and the recipient of a Restricted Award shall not sell, transfer, assign, pledge or otherwise encumber shares subject to the Award until the Restriction Period has expired and until all conditions to vesting have been met. The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

11. Performance Awards

(a) *Grant of Performance Awards:* Subject to the terms of the 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 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 Common Stock. An Award of a Performance Unit is a grant of a right to receive shares of Common Stock or a designated dollar value amount of Common Stock which is contingent upon the achievement of performance or other objectives during a specified period, and which has an initial value determined in a dollar amount established by the Administrator at the time of grant. Subject to Section 5(b), the Administrator shall have complete discretion in determining the number of Performance Units and/or Performance Shares granted to any Participant. The Administrator shall determine the nature, length and starting date of the period during which a Performance Award may be earned (the "Performance Period"), and shall determine the conditions which must be met in order for a Performance Award to be granted or to vest or be earned (in whole or in part), which conditions may include but are not limited to specified performance objectives, continued service or employment for a certain period of time, or a combination of such conditions. Subject to Section

1(ii), the Administrator shall determine the Performance Measures to be used in valuing Performance Awards.

(b) *Earning of Performance Awards*: Subject to the terms of the Plan and the requirements of Code Section 409A, related regulations or other guidance, the Administrator shall have sole authority to determine whether and to what degree Performance Awards have been earned and are payable and to interpret the terms and conditions of Performance Awards and the provisions of Section 11. The Administrator, in its sole and absolute discretion, may (subject to any restrictions imposed under Code Section 409A, related regulations or other guidance) accelerate the date that any Performance Award granted to a Participant shall be deemed to be earned in whole or in part, without any obligation to accelerate such date with respect to other Awards granted to any Participant.

(c) *Form of Payment*: Payment of the amount to which a Participant shall be entitled upon earning a Performance Award shall be made in cash, shares of Common Stock, or a combination of cash and shares of Common Stock, as determined by the Administrator in its sole discretion. Payment may be made in a lump sum or in installments upon such terms as may be established by the Administrator.

(d) *Forfeiture of Performance Awards*: Unless the Administrator determines otherwise, if the employment or service of a Participant shall terminate for any reason and the Participant has not earned all or part of a Performance Award pursuant to the terms of the Plan and individual Award, such Award, to the extent not then earned, shall be forfeited immediately upon such termination and the Participant shall have no further rights with respect thereto.

(e) *Nontransferability*: Unless the Administrator determines otherwise, Performance Awards that have not been earned shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, and the recipient of a Performance Award shall not sell, transfer, assign, pledge or otherwise encumber any shares subject to the Award until the Performance Period has expired and until the conditions to earning the Award have been met. The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

12. Phantom Stock Awards

(a) *Grant of Phantom Stock Awards*: Subject to the terms of the 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. A Phantom Stock Award is an Award to a Participant of a number of hypothetical share units with respect to shares of Common Stock, with a value based on the Fair Market Value of a share of Common Stock.

(b) *Vesting of Phantom Stock Awards*: Subject to the terms of the Plan and the requirements of Code Section 409A, related regulations or other guidance, the Administrator shall have sole authority to determine whether and to what degree Phantom Stock Awards have vested and are payable and to interpret the terms and conditions of Phantom Stock Awards.

(c) *Forfeiture of Phantom Stock Awards*: Unless the Administrator determines otherwise, if the employment or service of a Participant shall be 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 the Plan and the individual Award, such Award, to the extent not then vested or earned, shall be forfeited immediately upon such termination and the Participant shall have no further rights with respect thereto.

(d) *Payment of Phantom Stock Awards*: Upon vesting of all or a part of a Phantom Stock Award and satisfaction of such other terms and conditions as may be established by the Administrator, the Participant shall be entitled to a payment of an amount equal to the Fair Market Value of one share of Common Stock with respect to each such Phantom Stock unit which has vested. Payment may be made, in the discretion of the Administrator, in cash or in shares of Common Stock valued at their Fair Market Value on the applicable vesting date or dates (or other date or dates determined by the Administrator), or in a combination thereof. The Administrator may, however, establish a limitation on the amount payable in respect of each share of Phantom Stock. Payment may be made in a lump sum or upon such terms as may be established by the Administrator.

(e) *Nontransferability*: Unless the Administrator determines otherwise, (i) Phantom Stock Awards that have not vested shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, (ii) Phantom Stock Awards may be exercised during the Participant's lifetime only by him or by his guardian or legal representative, and (iii) shares of Common Stock (if any) subject to a Phantom Stock Award may not be sold, transferred, assigned, pledged or otherwise encumbered until the Phantom Stock Award has vested and all other conditions established by the Administrator have been met. The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

13. *Dividends and Dividend Equivalents*

The Administrator may, in its sole discretion, provide that Awards granted under the Plan earn dividends or dividend equivalents. Such dividends or dividend equivalents may be paid currently or may be credited to a Participant's account. Any crediting of dividends or dividend equivalents may be subject to such restrictions and conditions as the Administrator may establish, including reinvestment in additional shares of Common Stock or share equivalents.

14. *No Right or Obligation of Continued Employment or Service*

Neither the Plan, the grant of an Award nor any other action related to the Plan shall confer upon the Participant any right to continue in the service of the Corporation or an Affiliate as an Employee, Director or Independent Contractor or to interfere in any way with the right of the Corporation or an Affiliate to terminate the Participant's employment or service at any time.

15. *Amendment and Termination of the Plan*

(a) *Amendment and Termination of Plan*: The Plan may be amended, altered and/or terminated at any time by the Board; provided, that (i) approval of an amendment to the Plan by

the stockholders of the Corporation shall be required to the extent, if any, that stockholder approval of such amendment is required by applicable law, rule or regulation; and (ii) except for adjustments made pursuant to Section 5(d), 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 outstanding Option or SAR be surrendered to the Corporation as consideration for the grant of a new Option or SAR with a lower Option Price or base price than the original Option or SAR, as the case may be, without stockholder approval of any such action. No action to amend or terminate the Plan shall permit the acceleration of the time or schedule of any payment of amounts deemed to involve the deferral of compensation under Code Section 409A, except as may be otherwise permitted under Section 409A, related regulations or other guidance.

(b) *Amendment of Awards*: The Administrator may amend, alter or terminate any Award granted under the Plan, prospectively or retroactively, but such amendment, alteration or termination of an Award shall not, without the consent of the recipient of an outstanding Award, materially adversely affect the rights of the recipient with respect to the Award.

(c) *Unilateral Authority of Administrator to Modify Plan and Awards*: Notwithstanding Section 15(a) and Section 15(b) herein, the following provisions shall apply:

(i) The Administrator shall have unilateral authority to amend the Plan and any Award (without Participant consent and without stockholder approval, unless such stockholder approval is required by applicable laws, rules or regulations) to the extent necessary to comply with applicable laws, rules or regulations or changes to applicable laws, rules or regulations (including but not limited to Code Section 409A and Code Section 422 or related regulations or other guidance and federal securities laws).

(ii) The Administrator shall have unilateral authority to make adjustments to the terms and conditions of Awards in recognition of unusual or nonrecurring events affecting the Corporation or any Affiliate, or the financial statements of the Corporation or any Affiliate, or of changes in accounting principles, 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 the Plan or necessary or appropriate to comply with applicable accounting principles.

(d) *Cash Settlement*: Notwithstanding any provision of the Plan, an Award or an Award Agreement to the contrary, the Administrator may (subject to any requirements imposed under Code Section 409A, related regulations or other guidance) cause any Award (or portion thereof) granted under the Plan to be canceled in consideration of an alternative award or cash payment of an equivalent cash value, as determined by the Administrator in its sole discretion, made to the holder of such canceled Award.

16. Restrictions on Awards and Shares

The Corporation may impose such restrictions on Awards, shares and any other benefits underlying Awards hereunder as it may deem advisable, including without limitation restrictions under the federal securities laws, the requirements of any stock exchange or similar organization

and any blue sky, state or foreign securities laws applicable to such securities. Notwithstanding any other Plan provision to the contrary, the Corporation shall not be obligated to issue, deliver or transfer shares of Common Stock under the Plan, make any other distribution of benefits under the Plan, or take any other action, unless such delivery, distribution or action is in compliance with all applicable laws, rules and regulations (including but not limited to the requirements of the Securities Act). The Corporation may cause a restrictive legend to be placed on any certificate issued pursuant to an Award hereunder in such form as may be prescribed from time to time by applicable laws and regulations or as may be advised by legal counsel.

17. Change in Control

(a) Notwithstanding any other provision of the Plan to the contrary, and except as may be otherwise provided in an Award Agreement or required under Code Section 409A, related regulations or other guidance, in the event of a Change in Control:

(i) All Options and SARs outstanding as of the date of such Change in Control shall become fully exercisable, whether or not then otherwise exercisable.

(ii) Any restrictions, including but not limited to the Restriction Period, Performance Period, performance criteria and/or vesting conditions applicable to any Restricted Award, Performance Award and/or Phantom Stock Award, shall be deemed to have been met, and such Awards shall become fully vested, earned and payable to the fullest extent of the original grant of the applicable Award.

(b) Notwithstanding the foregoing, in the event of a merger, share exchange, reorganization, sale of all or substantially all of the assets of the Corporation or other similar transaction or event affecting the Corporation or its stockholders or an Affiliate, the Administrator may, in its sole and absolute discretion, determine that any or all Awards granted pursuant to the Plan shall not vest or become exercisable on an accelerated basis, if the Corporation or the surviving or acquiring corporation, as the case may be, shall have taken such action, including but not limited to the assumption of Awards granted under the Plan or the grant of substitute awards (in either case, with substantially similar terms or equivalent economic benefits as Awards granted under the Plan), as the Administrator determines to be equitable or appropriate to protect the rights and interests of Participants under the Plan. For the purposes herein, if the Committee is acting as the Administrator authorized to make the determinations provided for in this Section 17(b), the Committee shall be appointed by the Board of Directors, two-thirds of the members of which shall have been Directors of the Corporation prior to the merger, share exchange, reorganization or other business combination affecting the Corporation or an Affiliate.

18. Compliance with Code Section 409A

(a) *General:* Notwithstanding any other provision in the Plan or an Award to the contrary, if and to the extent that Section 409A of the Code is deemed to apply to the Plan or any Award granted under the Plan, it is the general intention of the Corporation that the Plan and all such Awards shall comply with Code Section 409A, related regulations or other guidance, and

the Plan and any such Award shall, to the extent practicable, be construed in accordance therewith. Deferrals of shares issuable pursuant to an Option, an SAR settled in shares of Common Stock, a Restricted Award or any other Award otherwise exempt from Code Section 409A in a manner that would cause Code Section 409A to apply shall not be permitted. Without in any way limiting the effect of the foregoing, in the event that Code Section 409A, related regulations or other guidance require that any special terms, provisions or conditions be included in the Plan or any Award, then such terms, provisions and conditions shall, to the extent practicable, be deemed to be made a part of the Plan or Award, as applicable. Further, in the event that the Plan or any Award shall be deemed not to comply with Code Section 409A or any related regulations or other guidance, then neither the Corporation, the Administrator nor its or their designees or agents shall be liable to any Participant or other person for actions, decisions or determinations made in good faith.

(b) *Specific Terms Applicable to Awards Subject to Code Section 409A:* Without limiting the effect of Section 18(a), above, and notwithstanding any other provision in the Plan to the contrary, the following provisions shall, to the extent required under Code Section 409A, related regulations or other guidance, apply with respect to Awards deemed to involve the deferral of compensation under Code Section 409A:

(i) Distributions: Distributions may be made with respect to Awards subject to Code Section 409A not earlier than upon the occurrence of one or more of the following events: (A) separation of service; (B) disability; (C) death; (D) a specified time or pursuant to a fixed schedule; (E) a change in the ownership or effective control of the Corporation, or in the ownership of a substantial portion of the assets of the Corporation; or (F) the occurrence of an unforeseeable emergency. Each of the preceding distribution events shall be defined and interpreted in accordance with Code Section 409A and related regulations or other guidance.

(ii) Key Employees: With respect to Participants who are “key employees” (as defined in Code Section 409A, related regulations or other guidance), a distribution due to separation of service may not be made before the date that is six months after the date of separation of service (or, if earlier, the date of death of the Participant), except as may be otherwise permitted pursuant to Code Section 409A, related regulations or other guidance. To the extent that a Participant is subject to this section and a distribution is to be paid in installments, through an annuity, or in some other manner where payment will be periodic, the Participant shall be paid, during the seventh month following separation from service, the aggregate amount of payments he would have received but for the application of this section; all remaining payments shall be made in their ordinary course. The previous sentence shall be applicable only if and to the extent that it complies with Code Section 409A, related regulations and other applicable guidance.

(iii) No Acceleration: Unless permissible under Code Section 409A, related regulations or other guidance, acceleration of the time or schedule of any payment under the Plan is prohibited, except that, to the extent permitted by the Administrator and to the extent such exceptions do not violate Code Section 409A, the following accelerations may be permitted in an Award:

(A) As necessary to fulfill a domestic relations order (as defined in Code Section 414(p)(1)(B));

(B) As necessary to comply with a certificate of divestiture (as defined in Code Section 1043(b)(2)); and

(C) To pay the Federal Insurance Contributions Act tax imposed under Code Sections 3101 and 3121(v)(2) on amounts deferred under the Plan (the "FICA Amount"), including the income tax at source on wages imposed under Code Section 3401 on the FICA Amount, and to pay the additional income tax at source of wages attributable to additional Code Section 3401 wages and taxes.

(iv) Short-Term Deferrals: Except to the extent otherwise required or permitted under Code Section 409A, related regulations or other guidance, the Administrator shall (unless an individual Award Agreement provides otherwise) provide that distributions pursuant to Awards must be made no later than the later of (A) the date that is 2-1/2 months from the end of the Participant's first taxable year in which the amount is no longer subject to a substantial risk of forfeiture; or (B) the date that is 2-1/2 months from the end of the Corporation's first taxable year in which the amount is no longer subject to a substantial risk of forfeiture.

(v) Deferral Elections:

(A) In the sole discretion of the Administrator, a Participant may be permitted to make an election as to the time and form of any distribution from an Award, provided that, except as specified in (B) and (C) below, such election is made not later than the close of the taxable year preceding the taxable year in which the services for which the Award is granted are to be performed, or at such other time or times as may be permitted under Code Section 409A, related regulations or other guidance.

(B) In the case of the first year in which the Participant becomes eligible to participate in the Plan, the election described in (A) may be made with respect to services to be performed subsequent to the election within 30 days after the date the Participant becomes eligible to participate in the Plan.

(C) In the case of any performance-based compensation (as that term is defined in Code Section 409A, related regulations or other guidance), where such compensation is based on services performed over a period of at least 12 months, the election described in (A) may be made no later than six months before the end of the period.

(vi) To the extent that the Administrator, in its sole discretion, permits a subsequent election to delay a payment or change the form of payment that has been specified under (A), (B) or (C) above, the following provisions shall apply:

(A) Such election may not take effect until 12 months after the date on which the election is made;

(B) Where the payment is to be made for reasons other than death, disability or unforeseen hardship, as those terms are defined in Section 18(b)(i), above, the first payment with respect to which such election is made must be deferred for a period of not less than five years from the date such payment would otherwise have been made; and

(C) Any election related to a payment based upon separation from service, as that term is defined in Section 18(b)(i), above, may not be made less than 12 months prior to the date of the first scheduled payment hereunder.

19. General Provisions

(a) *Stockholder Rights*: Except as otherwise determined by the Administrator (and subject to the provisions of Section 10(d) regarding Restricted Awards), a Participant and his legal representative, legatees or distributees shall not be deemed to be the holder of any shares subject to an Award and shall not have any rights of a stockholder unless and until certificates for such shares have been issued and delivered to him or them under the Plan. A certificate or certificates for shares of Common Stock acquired upon exercise of an Option or SAR shall be promptly issued in the name of the Participant (or his beneficiary) and distributed to the Participant (or his beneficiary) as soon as practicable following receipt of notice of exercise and, with respect to Options, payment of the Option Price (except as may otherwise be determined by the Corporation in the event of payment of the Option Price pursuant to Section 7(d)(ii)(C)). Except as otherwise provided in Section 10(d) regarding Restricted Awards, a certificate for any shares of Common Stock issuable pursuant to a Restricted Award, Performance Award or Phantom Stock Award shall be promptly issued in the name of the Participant (or his beneficiary) and distributed to the Participant (or his beneficiary) after the Award (or portion thereof) has vested or been earned. In no event will the issuance of certificates pursuant to the exercise of Options, settlement of SARs in shares of Common Stock, vesting of Restricted Awards or vesting of other Awards otherwise exempt from Code Section 409A be delayed in a manner that would cause the Award to be construed to involve the deferral of compensation under Code Section 409A.

(b) *Withholding*: The Corporation shall withhold all required local, state, federal, foreign and other taxes and any other amount required to be withheld by any governmental authority or law from any amount payable in cash with respect to an Award. Prior to the delivery or transfer of any certificate for shares or any other benefit conferred under the Plan, the Corporation shall require any recipient of an Award to pay to the Corporation in cash the amount of any tax or other amount required by any governmental authority to be withheld and paid over by the Corporation to such authority for the account of such recipient. Notwithstanding the foregoing, the Administrator may establish procedures to permit a recipient to satisfy such obligation in whole or in part, and any local, state, federal, foreign or other income tax obligations relating to such an Award, by electing (the "election") to have the Corporation withhold shares of Common Stock from the shares to which the recipient is entitled. The number

of shares to be withheld shall have a Fair Market Value as of the date that the amount of tax to be withheld is determined as nearly equal as possible to (but not exceeding) the amount of such obligations being satisfied. Each election must be made in writing to the Administrator in accordance with election procedures established by the Administrator.

(c) *Section 16(b) Compliance:* To the extent that any Participants in the Plan are subject to Section 16(b) of the Exchange Act, it is the general intention of the Corporation that transactions under the Plan shall comply with Rule 16b-3 under the Exchange Act and that the Plan shall be construed in favor of such Plan transactions meeting the requirements of Rule 16b-3 or any successor rules thereto. Notwithstanding anything in the Plan to the contrary, the Administrator, in its sole and absolute discretion, may bifurcate the Plan so as to restrict, limit or condition the use of any provision of the Plan to Participants who are officers or directors subject to Section 16 of the Exchange Act without so restricting, limiting or conditioning the Plan with respect to other Participants.

(d) *Code Section 162(m) Performance-Based Compensation.* To the extent to which Section 162(m) of the Code is applicable, the Corporation intends that compensation paid under the Plan to Covered Employees will, to the extent practicable, constitute “qualified performance-based compensation” within the meaning of Section 162(m) and related regulations, unless otherwise determined by the Administrator. Accordingly, Awards granted to Covered Employees which are intended to qualify for the performance-based exception under Code Section 162(m) and related regulations shall be deemed to include any such additional terms, conditions, limitations and provisions as are necessary to comply with the performance-based compensation exemption of Section 162(m), unless the Administrator, in its discretion, determines otherwise.

(e) *Unfunded Plan; No Effect on Other Plans:*

(i) The Plan shall be unfunded, and the Corporation shall not be required to create a trust or segregate any assets that may at any time be represented by Awards under the Plan. The Plan shall not establish any fiduciary relationship between the Corporation and any Participant or other person. Neither a Participant nor any other person shall, by reason of the Plan, acquire any right in or title to any assets, funds or property of the Corporation or any Affiliate, including, without limitation, any specific funds, assets or other property which the Corporation or any Affiliate, in their discretion, may set aside in anticipation of a liability under the Plan. A Participant shall have only a contractual right to the Common Stock or other amounts, if any, payable under the Plan, unsecured by any assets of the Corporation or any Affiliate. Nothing contained in the Plan shall constitute a guarantee that the assets of such entities shall be sufficient to pay any benefits to any person.

(ii) The amount of any compensation deemed to be received by a Participant pursuant to an Award shall not constitute compensation with respect to which any other employee benefits of such Participant are determined, including, without limitation, benefits under any bonus, pension, profit sharing, life insurance or salary continuation

plan, except as otherwise specifically provided by the terms of such plan or as may be determined by the Administrator.

(iii) The adoption of the Plan shall not affect any other stock incentive or other compensation plans in effect for the Corporation or any Affiliate, nor shall the Plan preclude the Corporation from establishing any other forms of stock incentive or other compensation for employees or service providers of the Corporation or any Affiliate.

(f) *Applicable Law*: The Plan shall be governed by and construed in accordance with the laws of the State of Delaware, without regard to the conflict of laws provisions of any state, and in accordance with applicable federal laws of the United States.

(g) *Beneficiary Designation*: The Administrator may permit a Participant to designate in writing a person or persons as beneficiary, which beneficiary shall be entitled to receive settlement of Awards (if any) to which the Participant is otherwise entitled in the event of death. In the absence of such designation by a Participant, and in the event of the Participant's death, the estate of the Participant shall be treated as beneficiary for purposes of the Plan, unless the Administrator determines otherwise. The Administrator shall have sole discretion to approve and interpret the form or forms of such beneficiary designation. A beneficiary, legal guardian, legal representative or other person claiming any rights pursuant to the Plan is subject to all terms and conditions of the Plan and any Award Agreement applicable to the Participant, except to the extent that the Plan and/or Award Agreement provide otherwise, and to any additional restrictions deemed necessary or appropriate by the Administrator.

(h) *Gender and Number*: Except where otherwise indicated by the context, words in any gender shall include any other gender, words in the singular shall include the plural and words in the plural shall include the singular.

(i) *Severability*: If any provision of the Plan shall be held illegal or invalid for any reason, such illegality or invalidity shall not affect the remaining parts of the Plan, and the Plan shall be construed and enforced as if the illegal or invalid provision had not been included.

(j) *Rules of Construction*: Headings are given to the sections of this Plan solely as a convenience to facilitate reference. The reference to any statute, regulation or other provision of law shall be construed to refer to any amendment to or successor of such provision of law.

(k) *Successors and Assigns*: The Plan shall be binding upon the Corporation, its successors and assigns, and Participants, their executors, administrators and permitted transferees and beneficiaries.

(l) *Right of Offset*: Notwithstanding any other provision of the Plan or an Award Agreement, the Corporation may reduce the amount of any payment or benefit otherwise payable to or on behalf of a Participant by the amount of any obligation of the Participant to the Corporation that is or becomes due and payable.

(m) *Effect of Changes in Status*: Unless an individual Award Agreement provides otherwise or the Administrator, in its sole discretion, determines otherwise, an Award shall not

be affected by any change in the terms, conditions or status of the Participant's employment or service, provided that the Participant continues to be in the employ of, or in service to, the Corporation or an Affiliate. Without limiting the foregoing, the Administrator has sole discretion to determine, at the time of grant of an Award or at any time thereafter, the effect, if any, on Awards granted to a Participant if the Participant's status as an Employee, Director or Independent Contractor changes, including but not limited to a change from full-time to part-time, or vice versa, or if other similar changes in the nature or scope of the Participant's employment or service occur.

IN WITNESS WHEREOF, this Targacept, Inc. 2005 Stock Incentive Plan, is, by the authority of the Board of Directors of the Corporation, executed in behalf of the Corporation, the _____ day of _____, 2005.

TARGACEPT, INC.

By: _____
Name: _____
Title: _____

ATTEST:

Secretary

[Corporate Seal]

TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN

Incentive Stock Option Agreement
(Employees)

THIS AGREEMENT (together with Schedule A, attached hereto, the "Agreement"), effective as of the date specified as the "Grant Date" on Schedule A attached hereto, between TARGACEPT, INC., a Delaware corporation (the "Corporation"), and the individual identified on Schedule A attached hereto, an Employee of the Corporation or an Affiliate (the "Participant");

R E C I T A L S :

In furtherance of the purposes of the Targacept, Inc. 2005 Stock Incentive Plan, as it may be hereafter amended (the "Plan"), the Corporation and the Participant hereby agree as follows:

1. Incorporation of Plan. The rights and duties of the Corporation and the Participant under this Agreement shall in all respects be subject to and governed by the provisions of the Plan, the terms of which are incorporated herein by reference. In the event of any conflict between the provisions in the Agreement and those of the Plan, the provisions of the Plan shall govern. Unless otherwise defined herein, capitalized terms in this Agreement shall have the same definitions as set forth in the Plan.

2. Grant of Option; Term of Option. The Corporation hereby grants to the Participant pursuant to the Plan, as a matter of separate inducement and agreement in connection with his or her employment or service to the Corporation, and not in lieu of any salary or other compensation for his or her services, the right and Option (the "Option") to purchase all or any part of such aggregate number of shares (the "Shares") of common stock of the Corporation (the "Common Stock") at a purchase price (the "Option Price") as specified on Schedule A, attached hereto, and subject to such other terms and conditions as may be stated herein or in the Plan or on Schedule A. The Participant expressly acknowledges that the terms of Schedule A shall be incorporated herein by reference and shall constitute part of this Agreement. The Corporation and the Participant further acknowledge and agree that the signatures of the Corporation and the Participant on the Grant Notice contained in Schedule A shall constitute their acceptance of all of the terms of this Agreement and their agreement to be bound by the terms of this Agreement. The Option (or any portion thereof) shall be designated as an Incentive Option, as stated on Schedule A. To the extent that the Option or any portion thereof is designated as an Incentive Option and such Option does not qualify as an Incentive Option, the Option or portion thereof shall be treated as a Nonqualified Option. Except as otherwise provided in the Plan or this Agreement, this Option will expire if not exercised in full by the Expiration Date specified on Schedule A.

3. Exercise of Option. Subject to the terms of the Plan and this Agreement, the Option shall become exercisable on the date or dates, and subject to such conditions, as are set forth on Schedule A attached hereto. To the extent that an Option which is exercisable is not exercised, such Option shall accumulate and be exercisable by the Participant in whole or in part at any time prior to expiration of the Option, subject to the terms of the Plan and this Agreement. The Participant expressly acknowledges that the Option may vest and be exercisable only upon such terms and conditions as are provided in this Agreement and the Plan. Upon the exercise of an Option in whole or in part and payment of the Option Price in accordance with the provisions of the Plan and this Agreement, the Corporation shall, as soon thereafter as practicable, deliver to the Participant a certificate or certificates for the Shares purchased. Payment of the Option Price may be made (i) in cash or by cash equivalent; and, where permitted by applicable law, payment may also be made (ii) by delivery (by either actual delivery or attestation) of shares of Common Stock owned by the Participant at the time of exercise for a period of at least six

months (or such other time period necessary to avoid variable accounting or other accounting consequences deemed unacceptable to the Corporation); (iii) by shares of Common Stock withheld upon exercise but only if and to the extent that payment by such method does not result in variable accounting or other accounting consequences deemed unacceptable to the Corporation; (iv) in the event that a Public Market (as defined in the Plan) for the Common Stock exists, by delivery of written notice of exercise to the Corporation and delivery to a broker of written notice of exercise and irrevocable instructions to promptly deliver to the Corporation the amount of sale or loan proceeds to pay the Option Price; (v) by such other payment methods as may be approved by the Administrator and which are acceptable under applicable law; or (vi) by any combination of the foregoing methods. Shares delivered or withheld in payment of the Option Price shall be valued at their Fair Market Value on the date of exercise, as determined by the Administrator by applying the provisions of the Plan.

4. No Right of Employment or Service; Forfeiture of Option. Neither the Plan, this Agreement nor any other action related to the Plan shall confer upon the Participant any right to continue in the employment or service of the Corporation or an Affiliate or interfere with the right of the Corporation or an Affiliate to terminate the Participant's employment or service at any time. Except as otherwise expressly provided in the Plan or this Agreement or as determined by the Administrator, all rights of the Participant with respect to the Option shall terminate upon termination of the employment of the Participant with the Corporation or an Affiliate.

5. Termination of Employment. Unless the Administrator determines otherwise, the Option shall not be exercised unless the Participant is, at the time of exercise, an Employee and has been an Employee continuously since the date the Option was granted, subject to the following:

(a) The employment relationship of the Participant shall be treated as continuing intact for any period that the Participant is on military or sick leave or other bona fide leave of absence, provided that the period of such leave does not exceed 90 days, or, if longer, as long as the Participant's right to reemployment is guaranteed either by statute or by contract. The employment relationship of the Participant shall also be treated as continuing intact while the Participant is not in active service because of Disability. The Administrator shall have sole authority to determine whether the Participant is disabled and, if applicable, the Participant's Termination Date.

(b) Unless the Administrator determines otherwise, if the employment of the Participant is terminated because of Disability or death, the Option may be exercised only to the extent vested and exercisable on the Participant's Termination Date. The Option must be exercised, if at all, prior to the first to occur of the following, whichever shall be applicable (X) the close of the period of 12 months next succeeding the Termination Date; or (Y) the close of the Option Period. In the event of the Participant's death, the Option shall be exercisable by such person or persons as shall have acquired the right to exercise the Option by will or by the laws of intestate succession.

(c) Unless the Administrator determines otherwise, if the employment of the Participant is terminated for any reason other than Disability, death or Cause, the Option may be exercised to the extent vested and exercisable on his or her Termination Date. The Option must be exercised, if at all, prior to the first to occur of the following, whichever shall be applicable: (X) the close of the period of three months next succeeding the Termination Date; or (Y) the close of the Option period. If the Participant dies following such termination of employment and prior to the date specified in (X) of this subparagraph (c), the Participant shall be treated as having died while employed under subparagraph (b) immediately preceding (treating for this purpose the Participant's date of termination of employment as the Termination Date). In the event of the Participant's death, the Option shall be exercisable by such person or persons as shall have acquired the right to exercise the Option by will or by the laws of intestate succession.

(d) Unless the Administrator determines otherwise, if the employment of the Participant is terminated for Cause, the Option shall lapse and no longer be exercisable as of his or her Termination Date, as determined by the Administrator.

6. Notice of Disposition. To the extent that this Option is designated as an Incentive Option, if Shares of Common Stock acquired upon exercise of the Option are disposed of within two years following the date of grant or one year following the transfer of such Shares to the Participant upon exercise, the Participant shall, promptly following such disposition, notify the Corporation in writing of the date and terms of such disposition and provide such other information regarding the disposition as the Administrator may reasonably require.

7. Limitation on Incentive Options. In no event shall there first become exercisable by the Participant in any one calendar year Incentive Options granted by the Corporation or any Parent or Subsidiary with respect to shares having an aggregate Fair Market Value (determined at the time an Incentive Option is granted) greater than \$100,000. To the extent that any Incentive Options are first exercisable by the Participant in excess of such limitation, the excess shall be considered a Nonqualified Option.

8. Nontransferability of Option. To the extent that this Option is designated as an Incentive Option, the Option shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws or intestate succession, or, in the Administrator's discretion, as may otherwise be permitted in accordance with Section 422 of the Code and related regulations. To the extent that this Option is treated as a Nonqualified Option, the Option shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, except as may be permitted by the Administrator in a manner consistent with the registration provisions of the Securities Act of 1933, as amended (the "Securities Act"). Except as may be permitted by the preceding, the Option shall be exercisable during the Participant's lifetime only by him or her or by his or her guardian or legal representative. The designation of a beneficiary in accordance with the Plan does not constitute a transfer.

9. Superseding Agreement; Binding Effect. This Agreement supersedes any statements, representations or agreements of the Corporation with respect to the grant of the Option or any related rights, and the Participant hereby waives any rights or claims related to any such statements, representations or agreements. This Agreement does not supersede or amend any existing confidentiality agreement, nonsolicitation agreement, noncompetition agreement, employment agreement or any other similar agreement between the Participant and the Corporation, including, but not limited to, any restrictive covenants contained in such agreements. This Agreement shall be binding upon and shall inure to the benefit of the parties hereto and their respective executors, administrators, heirs, successors and assigns.

10. Governing Law. Except as otherwise provided in the Plan or herein, this Agreement shall be construed and enforced according to the laws of the State of Delaware, without regard to the conflict of laws provisions of any state, and in accordance with applicable federal laws of the United States.

11. Amendment and Termination; Waiver. Subject to the terms of the Plan, this Agreement may be modified or amended only by the written agreement of the parties hereto. The waiver by the Corporation of a breach of any provision of the Agreement by the Participant shall not operate or be construed as a waiver of any subsequent breach by the Participant. Notwithstanding the foregoing, the Administrator shall have unilateral authority to amend the Plan and this Agreement (without Participant consent) to the extent necessary to comply with applicable law or changes to applicable law (including but in no way limited to Code Section 409A and related regulations or other guidance and federal securities laws).

12. No Rights as Stockholder. The Participant and his or her legal representatives, legatees and distributees shall not be deemed to be the holder of any Shares subject to the Option and shall not have any rights of a stockholder unless and until certificates for such Shares have been issued and delivered to him or her or them.

13. Withholding; Tax Matters.

(a) The Participant acknowledges that the Corporation shall require the Participant to pay the Corporation in cash the amount of any tax or other amount required by any governmental authority to be withheld and paid over by the Corporation to such authority for the account of the Participant, and the Participant agrees, as a condition to the grant of the Option and delivery of the Shares or any other benefit, to satisfy such obligations. Notwithstanding the foregoing, the Corporation may establish procedures to permit the Participant to satisfy such obligations in whole or in part, and any other local, state, federal, foreign or other income tax obligations relating to the Option, by electing (the "election") to have the Corporation withhold shares of Common Stock from the Shares to which the Participant is entitled. The number of Shares to be withheld shall have a Fair Market Value as of the date that the amount of tax to be withheld is determined as nearly equal as possible to (but not exceeding) the amount of such obligations being satisfied. Each election must be made in writing to the Administrator in accordance with election procedures established by the Administrator.

(b) The Participant acknowledges that the Corporation has made no warranties or representations to the Participant with respect to the tax consequences (including, but not limited to, income tax consequences) related to the transactions contemplated by this Agreement, and the Participant is in no manner relying on the Corporation or its representatives for an assessment of such tax consequences. The Participant acknowledges that there may be adverse tax consequences upon acquisition or disposition of the Shares subject to the Option and that the Participant should consult a tax advisor prior to such exercise or disposition. The Participant acknowledges that he or she has been advised that he or she should consult with his own attorney, accountant, and/or tax advisor regarding the decision to enter into this Agreement and the consequences thereof. The Participant also acknowledges that the Corporation has no responsibility to take or refrain from taking any actions in order to achieve a certain tax result for the Participant.

14. Administration. The authority to construe and interpret this Agreement and the Plan, and to administer all aspects of the Plan, shall be vested in the Administrator, and the Administrator shall have all powers with respect to this Agreement as are provided in the Plan. Any interpretation of the Agreement by the Administrator and any decision made by it with respect to the Agreement is final and binding.

15. Notices. Except as may be otherwise provided by the Plan or determined by the Administrator, any written notices provided for in this Agreement or the Plan shall be in writing and shall be deemed sufficiently given if either hand delivered or if sent by fax or overnight courier, or by postage paid first class mail. Notices sent by mail shall be deemed received three business days after mailed but in no event later than the date of actual receipt. Notices shall be directed, if to the Participant, at the Participant's address indicated on Schedule A (or such other address as may be designated by the Participant in a manner acceptable to the Administrator), or, if to the Corporation, at the Corporation's principal office, attention Chief Financial Officer, Targacept, Inc. Notice may also be provided by electronic submission, if and to the extent permitted by the Administrator.

16. Severability. The provisions of this Agreement are severable and if any one or more provisions may be determined to be illegal or otherwise unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

17. Restrictions on Option and Shares. The Corporation may impose such restrictions on the Option and the Shares or other benefits underlying the Option as it may deem advisable, including without limitation restrictions under the federal securities laws, the requirements of any stock exchange or similar organization and any blue sky, state or foreign securities laws applicable to such Option or Shares. Notwithstanding any other provision in the Plan or the Agreement to the contrary, the Corporation shall not be obligated to issue, deliver or transfer shares of Common Stock, to make any other distribution of benefits, or to take any other action, unless such delivery, distribution or action is in compliance with all applicable laws, rules and regulations (including but not limited to the requirements of the Securities Act). The Corporation may cause a restrictive legend to be placed on any certificate for Shares issued pursuant to the exercise of the Option in such form as may be prescribed from time to time by applicable laws and regulations or as may be advised by legal counsel.

18. Cash Settlement. Notwithstanding any other provision of the Plan or this Agreement to the contrary, the Administrator may (subject to any requirements imposed under Code Section 409A, related regulations or other guidance) cause the Option or portion thereof to be cancelled in consideration of an alternative option or cash payment of an equivalent cash value, as determined by the Administrator in its sole discretion, made to the Participant.

19. Effect of Changes in Status. Unless the Administrator, in its sole discretion, determines otherwise, the Option shall not be affected by any change in the terms, conditions or status of the Participant's employment, provided that the Participant continues to be in the employ of the Corporation or an Affiliate. Without limiting the foregoing, the Administrator has sole discretion to determine, at the time of grant of the Option or at any time thereafter, the effect, if any, on the Option if the Participant's status as an Employee changes, including but not limited to a change from full-time to part-time, or vice versa, or if other similar changes in the nature or scope of the Participant's employment occur.

20. Right of Offset. Notwithstanding any other provision of the Plan or the Agreement, the Corporation may reduce the amount of any payment otherwise payable to or on behalf of the Participant by the amount of any obligation of the Participant to the Corporation that is then due and payable and the Participant shall be deemed to have consented to such reduction.

21. Counterparts; Further Instruments. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. The parties hereto agree to execute such further instruments and to take such further action as may be reasonably necessary to carry out the purposes and intent of this Agreement.

[Signatures of the Corporation and the Participant follow on Schedule A/Grant Notice.]

TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN

Incentive Stock Option Agreement
(Employees)

Schedule A/Grant Notice

1. Pursuant to the terms and conditions of the Corporation's 2005 Stock Incentive Plan (the "Plan"), you (the "Participant") have been granted an option (the "Option") to purchase _____ shares (the "Shares") of our Common Stock as outlined below.

Name of Participant:	_____
Address:	_____

Grant Date:	_____, 20__
Number of Shares Subject to Option:	_____
Option Price:	\$ _____
Type of Option:	Incentive Stock Option
Expiration Date (Last day of Option Period):	_____, 20__
Vesting Schedule/Conditions:	_____

2. By my signature below, I, the Participant, hereby acknowledge receipt of this Grant Notice and the Option Agreement (the "Agreement") dated _____, 200__, between the Participant and Targacept, Inc. (the "Corporation") which is attached to this Grant Notice. I understand that the Grant Notice and other provisions of Schedule A herein are incorporated by reference into the Agreement and constitute a part of the Agreement. By my signature below, I further agree to be bound by the terms of the Plan and the Agreement, including but not limited to the terms of this Grant Notice and the other provisions of Schedule A contained herein. The Corporation reserves the right to treat the Option and the Agreement as cancelled, void and of no effect if the Participant fails to return a signed copy of the Grant Notice within 30 days of grant date stated above.

Signature: _____

Date: _____

Agreed to by:

TARGACEPT, INC.

By: _____

J. Donald deBethizy
President & CEO

Attest:

Alan A. Musso
Vice President, Chief Financial Officer & Secretary

Note: If there are any discrepancies in the name or address shown above, please make the appropriate corrections on this form. Please retain a copy of the Agreement, including this Grant Notice, for your files.

TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN

Nonqualified Stock Option Agreement
(Employees)

THIS AGREEMENT (together with Schedule A, attached hereto, the "Agreement"), effective as of the date specified as the "Grant Date" on Schedule A attached hereto, between TARGACEPT, INC., a Delaware corporation (the "Corporation"), and the individual identified on Schedule A attached hereto, an Employee of the Corporation or an Affiliate (the "Participant");

R E C I T A L S :

In furtherance of the purposes of the Targacept, Inc. 2005 Stock Incentive Plan, as it may be hereafter amended (the "Plan"), the Corporation and the Participant hereby agree as follows:

1. Incorporation of Plan. The rights and duties of the Corporation and the Participant under this Agreement shall in all respects be subject to and governed by the provisions of the Plan, the terms of which are incorporated herein by reference. In the event of any conflict between the provisions in the Agreement and those of the Plan, the provisions of the Plan shall govern. Unless otherwise defined herein, capitalized terms in this Agreement shall have the same definitions as set forth in the Plan.

2. Grant of Option; Term of Option. The Corporation hereby grants to the Participant pursuant to the Plan, as a matter of separate inducement and agreement in connection with his or her employment or service to the Corporation, and not in lieu of any salary or other compensation for his or her services, the right and Option (the "Option") to purchase all or any part of such aggregate number of shares (the "Shares") of common stock of the Corporation (the "Common Stock") at a purchase price (the "Option Price") as specified on Schedule A, attached hereto, and subject to such other terms and conditions as may be stated herein or in the Plan or on Schedule A. The Participant expressly acknowledges that the terms of Schedule A shall be incorporated herein by reference and shall constitute part of this Agreement. The Corporation and the Participant further acknowledge and agree that the signatures of the Corporation and the Participant on the Grant Notice contained in Schedule A shall constitute their acceptance of all of the terms of this Agreement and their agreement to be bound by the terms of this Agreement. The Option (or any portion thereof) shall be designated as a Nonqualified Option, as stated on Schedule A. Except as otherwise provided in the Plan or this Agreement, this Option will expire if not exercised in full by the Expiration Date specified on Schedule A.

3. Exercise of Option. Subject to the terms of the Plan and this Agreement, the Option shall become exercisable on the date or dates, and subject to such conditions, as are set forth on Schedule A attached hereto. To the extent that an Option which is exercisable is not exercised, such Option shall accumulate and be exercisable by the Participant in whole or in part at any time prior to expiration of the Option, subject to the terms of the Plan and this Agreement. The Participant expressly acknowledges that the Option may vest and be exercisable only upon such terms and conditions as are provided in this Agreement and the Plan. Upon the exercise of an Option in whole or in part and payment of the Option Price in accordance with the provisions of the Plan and this Agreement, the Corporation shall, as soon thereafter as practicable, deliver to the Participant a certificate or certificates for the Shares purchased. Payment of the Option Price may be made (i) in cash or by cash equivalent; and, where permitted by applicable law, payment may also be made (ii) by delivery (by either actual delivery or attestation) of shares of Common Stock owned by the Participant at the time of exercise for a period of at least six months (or such other time period necessary to avoid variable accounting or other accounting consequences deemed unacceptable to the Corporation); (iii) by shares of Common Stock withheld upon exercise but only if and to the extent that

payment by such method does not result in variable accounting or other accounting consequences deemed unacceptable to the Corporation; (iv) in the event that a Public Market (as defined in the Plan) for the Common Stock exists, by delivery of written notice of exercise to the Corporation and delivery to a broker of written notice of exercise and irrevocable instructions to promptly deliver to the Corporation the amount of sale or loan proceeds to pay the Option Price; (v) by such other payment methods as may be approved by the Administrator and which are acceptable under applicable law; or (vi) by any combination of the foregoing methods. Shares delivered or withheld in payment of the Option Price shall be valued at their Fair Market Value on the date of exercise, as determined by the Administrator by applying the provisions of the Plan.

4. **No Right of Employment or Service; Forfeiture of Option.** Neither the Plan, this Agreement nor any other action related to the Plan shall confer upon the Participant any right to continue in the employment or service of the Corporation or an Affiliate or interfere with the right of the Corporation or an Affiliate to terminate the Participant's employment or service at any time. Except as otherwise expressly provided in the Plan or this Agreement or as determined by the Administrator, all rights of the Participant with respect to the Option shall terminate upon termination of the employment of the Participant with the Corporation or an Affiliate.

5. **Termination of Employment.** Unless the Administrator determines otherwise, the Option shall not be exercised unless the Participant is, at the time of exercise, an Employee and has been an Employee continuously since the date the Option was granted, subject to the following:

(a) The employment relationship of the Participant shall be treated as continuing intact for any period that the Participant is on military or sick leave or other bona fide leave of absence, provided that the period of such leave does not exceed 90 days, or, if longer, as long as the Participant's right to reemployment is guaranteed either by statute or by contract. The employment relationship of the Participant shall also be treated as continuing intact while the Participant is not in active service because of Disability. The Administrator shall have sole authority to determine whether the Participant is disabled and, if applicable, the Participant's Termination Date.

(b) Unless the Administrator determines otherwise, if the employment of the Participant is terminated because of Disability or death, the Option may be exercised only to the extent vested and exercisable on the Participant's Termination Date. The Option must be exercised, if at all, prior to the first to occur of the following, whichever shall be applicable (X) the close of the period of 12 months next succeeding the Termination Date; or (Y) the close of the Option Period. In the event of the Participant's death, the Option shall be exercisable by such person or persons as shall have acquired the right to exercise the Option by will or by the laws of intestate succession.

(c) Unless the Administrator determines otherwise, if the employment of the Participant is terminated for any reason other than Disability, death or Cause, the Option may be exercised to the extent vested and exercisable on his or her Termination Date. The Option must be exercised, if at all, prior to the first to occur of the following, whichever shall be applicable: (X) the close of the period of three months next succeeding the Termination Date; or (Y) the close of the Option period. If the Participant dies following such termination of employment and prior to the date specified in (X) of this subparagraph (c), the Participant shall be treated as having died while employed under subparagraph (b) immediately preceding (treating for this purpose the Participant's date of termination of employment as the Termination Date). In the event of the Participant's death, the Option shall be exercisable by such person or persons as shall have acquired the right to exercise the Option by will or by the laws of intestate succession.

(d) Unless the Administrator determines otherwise, if the employment of the Participant is terminated for Cause, the Option shall lapse and no longer be exercisable as of his or her Termination Date, as determined by the Administrator.

6. Nontransferability of Option. The Option shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, except as may be permitted by the Administrator in a manner consistent with the registration provisions of the Securities Act of 1933, as amended (the "Securities Act"). Except as may be permitted by the preceding sentence, the Option shall be exercisable during the Participant's lifetime only by him or her or by his or her guardian or legal representative. The designation of a beneficiary in accordance with the Plan does not constitute a transfer.

7. Superseding Agreement; Binding Effect. This Agreement supersedes any statements, representations or agreements of the Corporation with respect to the grant of the Option or any related rights, and the Participant hereby waives any rights or claims related to any such statements, representations or agreements. This Agreement does not supersede or amend any existing confidentiality agreement, nonsolicitation agreement, noncompetition agreement, employment agreement or any other similar agreement between the Participant and the Corporation, including, but not limited to, any restrictive covenants contained in such agreements. This Agreement shall be binding upon and shall inure to the benefit of the parties hereto and their respective executors, administrators, heirs, successors and assigns.

8. Governing Law. Except as otherwise provided in the Plan or herein, this Agreement shall be construed and enforced according to the laws of the State of Delaware, without regard to the conflict of laws provisions of any state, and in accordance with applicable federal laws of the United States.

9. Amendment and Termination; Waiver. Subject to the terms of the Plan, this Agreement may be modified or amended only by the written agreement of the parties hereto. The waiver by the Corporation of a breach of any provision of the Agreement by the Participant shall not operate or be construed as a waiver of any subsequent breach by the Participant. Notwithstanding the foregoing, the Administrator shall have unilateral authority to amend the Plan and this Agreement (without Participant consent) to the extent necessary to comply with applicable law or changes to applicable law (including but in no way limited to Code Section 409A and related regulations or other guidance and federal securities laws).

10. No Rights as Stockholder. The Participant and his or her legal representatives, legatees and distributees shall not be deemed to be the holder of any Shares subject to the Option and shall not have any rights of a stockholder unless and until certificates for such Shares have been issued and delivered to him or her or them.

11. Withholding; Tax Matters.

(a) The Participant acknowledges that the Corporation shall require the Participant to pay the Corporation in cash the amount of any tax or other amount required by any governmental authority to be withheld and paid over by the Corporation to such authority for the account of the Participant, and the Participant agrees, as a condition to the grant of the Option and delivery of the Shares or any other benefit, to satisfy such obligations. Notwithstanding the foregoing, the Corporation may establish procedures to permit the Participant to satisfy such obligations in whole or in part, and any other local, state, federal, foreign or other income tax obligations relating to the Option, by electing (the "election") to have the Corporation withhold shares of Common Stock from the Shares to which the Participant is entitled. The number of Shares to be withheld shall have a Fair Market Value as of the date that the amount of tax to be withheld is determined as nearly equal as possible to (but not exceeding) the amount of such obligations being satisfied. Each election must be made in writing to the Administrator in accordance with election procedures established by the Administrator.

(b) The Participant acknowledges that the Corporation has made no warranties or representations to the Participant with respect to the tax consequences (including, but not limited to, income tax consequences) related to the transactions contemplated by this Agreement, and the

Participant is in no manner relying on the Corporation or its representatives for an assessment of such tax consequences. The Participant acknowledges that there may be adverse tax consequences upon acquisition or disposition of the Shares subject to the Option and that the Participant should consult a tax advisor prior to such exercise or disposition. The Participant acknowledges that he or she has been advised that he or she should consult with his own attorney, accountant, and/or tax advisor regarding the decision to enter into this Agreement and the consequences thereof. The Participant also acknowledges that the Corporation has no responsibility to take or refrain from taking any actions in order to achieve a certain tax result for the Participant.

12. Administration. The authority to construe and interpret this Agreement and the Plan, and to administer all aspects of the Plan, shall be vested in the Administrator, and the Administrator shall have all powers with respect to this Agreement as are provided in the Plan. Any interpretation of the Agreement by the Administrator and any decision made by it with respect to the Agreement is final and binding.

13. Notices. Except as may be otherwise provided by the Plan or determined by the Administrator, any written notices provided for in this Agreement or the Plan shall be in writing and shall be deemed sufficiently given if either hand delivered or if sent by fax or overnight courier, or by postage paid first class mail. Notices sent by mail shall be deemed received three business days after mailed but in no event later than the date of actual receipt. Notices shall be directed, if to the Participant, at the Participant's address indicated on Schedule A (or such other address as may be designated by the Participant in a manner acceptable to the Administrator), or, if to the Corporation, at the Corporation's principal office, attention Chief Financial Officer, Targacept, Inc. Notice may also be provided by electronic submission, if and to the extent permitted by the Administrator.

14. Severability. The provisions of this Agreement are severable and if any one or more provisions may be determined to be illegal or otherwise unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

15. Restrictions on Option and Shares. The Corporation may impose such restrictions on the Option and the Shares or other benefits underlying the Option as it may deem advisable, including without limitation restrictions under the federal securities laws, the requirements of any stock exchange or similar organization and any blue sky, state or foreign securities laws applicable to such Option or Shares. Notwithstanding any other provision in the Plan or the Agreement to the contrary, the Corporation shall not be obligated to issue, deliver or transfer shares of Common Stock, to make any other distribution of benefits, or to take any other action, unless such delivery, distribution or action is in compliance with all applicable laws, rules and regulations (including but not limited to the requirements of the Securities Act). The Corporation may cause a restrictive legend to be placed on any certificate for Shares issued pursuant to the exercise of the Option in such form as may be prescribed from time to time by applicable laws and regulations or as may be advised by legal counsel.

16. Cash Settlement. Notwithstanding any other provision of the Plan or this Agreement to the contrary, the Administrator may (subject to any requirements imposed under Code Section 409A, related regulations or other guidance) cause the Option or portion thereof to be cancelled in consideration of an alternative option or cash payment of an equivalent cash value, as determined by the Administrator in its sole discretion, made to the Participant.

17. Effect of Changes in Status. Unless the Administrator, in its sole discretion, determines otherwise, the Option shall not be affected by any change in the terms, conditions or status of the Participant's employment, provided that the Participant continues to be in the employ of the Corporation or an Affiliate. Without limiting the foregoing, the Administrator has sole discretion to determine, at the time of grant of the Option or at any time thereafter, the effect, if any, on the Option if the Participant's status as an Employee changes, including but not limited to a change from full-time to part-time, or vice versa, or if other similar changes in the nature or scope of the Participant's employment occur.

18. Right of Offset. Notwithstanding any other provision of the Plan or the Agreement, the Corporation may reduce the amount of any payment otherwise payable to or on behalf of the Participant by the amount of any obligation of the Participant to the Corporation that is then due and payable and the Participant shall be deemed to have consented to such reduction.

19. Counterparts; Further Instruments. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. The parties hereto agree to execute such further instruments and to take such further action as may be reasonably necessary to carry out the purposes and intent of this Agreement.

[Signatures of the Corporation and the Participant follow on Schedule A/Grant Notice.]

**TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN**

**Nonqualified Stock Option Agreement
(Employees)**

Schedule A/Grant Notice

1. Pursuant to the terms and conditions of the Corporation's 2005 Stock Incentive Plan (the "Plan"), you (the "Participant") have been granted an option (the "Option") to purchase _____ shares (the "Shares") of our Common Stock as outlined below.

Name of Participant:	_____
Address:	_____

Grant Date:	_____, 20__
Number of Shares Subject to Option:	_____
Option Price:	\$ _____
Type of Option:	Nonqualified Stock Option
Expiration Date (Last day of Option Period):	_____, 20__
Vesting Schedule/Conditions:	_____

2. By my signature below, I, the Participant, hereby acknowledge receipt of this Grant Notice and the Option Agreement (the "Agreement") dated _____, 200__, between the Participant and Targacept, Inc. (the "Corporation") which is attached to this Grant Notice. I understand that the Grant Notice and other provisions of Schedule A herein are incorporated by reference into the Agreement and constitute a part of the Agreement. By my signature below, I further agree to be bound by the terms of the Plan and the Agreement, including but not limited to the terms of this Grant Notice and the other provisions of Schedule A contained herein. The Corporation reserves the right to treat the Option and the Agreement as cancelled, void and of no effect if the Participant fails to return a signed copy of the Grant Notice within 30 days of grant date stated above.

Signature: _____

Date: _____

Agreed to by:

TARGACEPT, INC.

By: _____
J. Donald deBethizy
President & CEO

Attest:

Alan A. Musso
Vice President, Chief Financial Officer & Secretary

Note: If there are any discrepancies in the name or address shown above, please make the appropriate corrections on this form. Please retain a copy of the Agreement, including this Grant Notice, for your files.

TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN

Nonqualified Stock Option Agreement
(Nonemployee Directors)

THIS AGREEMENT (together with Schedule A, attached hereto, the "Agreement"), effective as of the date specified as the "Grant Date" on Schedule A attached hereto, between TARGACEPT, INC., a Delaware corporation (the "Corporation"), and the individual identified on Schedule A attached hereto, a Nonemployee Director of the Corporation or an Affiliate (the "Participant");

R E C I T A L S :

In furtherance of the purposes of the Targacept, Inc. 2005 Stock Incentive Plan, as it may be hereafter amended (the "Plan"), the Corporation and the Participant hereby agree as follows:

1. Incorporation of Plan. The rights and duties of the Corporation and the Participant under this Agreement shall in all respects be subject to and governed by the provisions of the Plan, the terms of which are incorporated herein by reference. In the event of any conflict between the provisions in the Agreement and those of the Plan, the provisions of the Plan shall govern. Unless otherwise defined herein, capitalized terms in this Agreement shall have the same definitions as set forth in the Plan.

2. Grant of Option; Term of Option. The Corporation hereby grants to the Participant pursuant to the Plan, as a matter of separate inducement and agreement in connection with his or her service to the Corporation, and not in lieu of any salary or other compensation for his or her services, the right and Option (the "Option") to purchase all or any part of such aggregate number of shares (the "Shares") of common stock of the Corporation (the "Common Stock") at a purchase price (the "Option Price") as specified on Schedule A, attached hereto, and subject to such other terms and conditions as may be stated herein or in the Plan or on Schedule A. The Participant expressly acknowledges that the terms of Schedule A shall be incorporated herein by reference and shall constitute part of this Agreement. The Corporation and the Participant further acknowledge and agree that the signatures of the Corporation and the Participant on the Grant Notice contained in Schedule A shall constitute their acceptance of all of the terms of this Agreement and their agreement to be bound by the terms of this Agreement. The Option shall be designated as a Nonqualified Option, as stated on Schedule A. Except as otherwise provided in the Plan or this Agreement, this Option will expire if not exercised in full by the Expiration Date specified on Schedule A.

3. Exercise of Option. Subject to the terms of the Plan and this Agreement, the Option shall become exercisable on the date or dates, and subject to such conditions, as are set forth on Schedule A attached hereto. To the extent that an Option which is exercisable is not exercised, such Option shall accumulate and be exercisable by the Participant in whole or in part at any time prior to expiration of the Option, subject to the terms of the Plan and this Agreement. The Participant expressly acknowledges that the Option may vest and be exercisable only upon such terms and conditions as are provided in this Agreement and the Plan. Upon the exercise of an Option in whole or in part and payment of the Option Price in accordance with the provisions of the Plan and this Agreement, the Corporation shall, as soon thereafter as practicable, deliver to the Participant a certificate or certificates for the Shares purchased. Payment of the Option Price may be made (i) in cash or by cash equivalent; and, where permitted by applicable law, payment may also be made (ii) by delivery (by either actual delivery or attestation) of shares of Common Stock owned by the Participant at the time of exercise for a period of at least six months (or such other time period necessary to avoid variable accounting or other accounting consequences deemed unacceptable to the Corporation); (iii) by shares of Common Stock withheld upon exercise but only if and to the extent that payment by such method does not result in variable accounting or other accounting consequences deemed

unacceptable to the Corporation; (iv) in the event that a Public Market (as defined in the Plan) for the Common Stock exists, by delivery of written notice of exercise to the Corporation and delivery to a broker of written notice of exercise and irrevocable instructions to promptly deliver to the Corporation the amount of sale or loan proceeds to pay the Option Price; (v) by such other payment methods as may be approved by the Administrator and which are acceptable under applicable law; or (vi) by any combination of the foregoing methods. Shares delivered or withheld in payment of the Option Price shall be valued at their Fair Market Value on the date of exercise, as determined by the Administrator by applying the provisions of the Plan.

4. No Right of Employment or Service; Forfeiture of Option. Neither the Plan, this Agreement nor any other action related to the Plan shall confer upon the Participant any right to continue in the employment or service of the Corporation or an Affiliate or interfere with the right of the Corporation or an Affiliate to terminate the Participant's employment or service at any time. Except as otherwise expressly provided in the Plan or this Agreement or as determined by the Administrator, all rights of the Participant with respect to the Option shall terminate upon termination of the employment of the Participant with the Corporation or an Affiliate.

5. Termination of Service. Unless the Administrator determines otherwise, the Option may be exercised only to the extent vested and exercisable on the Participant's Termination Date (unless the termination was for Cause), and must be exercised, if at all, prior to the first to occur of the following, as applicable: (a) the close of the period of six months next succeeding the Termination Date; or (b) the close of the Option Period. If the services of a Participant are terminated for Cause, his or her Option shall lapse and no longer be exercisable as of his or her Termination Date, as determined by the Administrator.

6. Nontransferability of Option. The Option shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, except as may be permitted by the Administrator in a manner consistent with the registration provisions of the Securities Act of 1933, as amended (the "Securities Act"). Except as may be permitted by the preceding sentence, the Option shall be exercisable during the Participant's lifetime only by him or her or by his or her guardian or legal representative. The designation of a beneficiary in accordance with the Plan does not constitute a transfer.

7. Superseding Agreement; Binding Effect. This Agreement supersedes any statements, representations or agreements of the Corporation with respect to the grant of the Option or any related rights, and the Participant hereby waives any rights or claims related to any such statements, representations or agreements. This Agreement does not supersede or amend any existing confidentiality agreement, nonsolicitation agreement, noncompetition agreement, employment agreement or any other similar agreement between the Participant and the Corporation, including, but not limited to, any restrictive covenants contained in such agreements. This Agreement shall be binding upon and shall inure to the benefit of the parties hereto and their respective executors, administrators, heirs, successors and assigns.

8. Governing Law. Except as otherwise provided in the Plan or herein, this Agreement shall be construed and enforced according to the laws of the State of Delaware, without regard to the conflict of laws provisions of any state, and in accordance with applicable federal laws of the United States.

9. Amendment and Termination; Waiver. Subject to the terms of the Plan, this Agreement may be modified or amended only by the written agreement of the parties hereto. The waiver by the Corporation of a breach of any provision of the Agreement by the Participant shall not operate or be construed as a waiver of any subsequent breach by the Participant. Notwithstanding the foregoing, the Administrator shall have unilateral authority to amend the Plan and this Agreement (without Participant consent) to the extent necessary to comply with applicable law or changes to applicable law (including but in no way limited to Code Section 409A and related regulations or other guidance and federal securities laws).

10. No Rights as Stockholder. The Participant and his or her legal representatives, legatees and distributees shall not be deemed to be the holder of any Shares subject to the Option and shall not have any rights of a stockholder unless and until certificates for such Shares have been issued and delivered to him or her or them.

11. Withholding; Tax Matters.

(a) The Participant acknowledges that the Corporation shall require the Participant to pay the Corporation in cash the amount of any tax or other amount required by any governmental authority to be withheld and paid over by the Corporation to such authority for the account of the Participant, and the Participant agrees, as a condition to the grant of the Option and delivery of the Shares or any other benefit, to satisfy such obligations. Notwithstanding the foregoing, the Corporation may establish procedures to permit the Participant to satisfy such obligations in whole or in part, and any other local, state, federal, foreign or other income tax obligations relating to the Option, by electing (the "election") to have the Corporation withhold shares of Common Stock from the Shares to which the Participant is entitled. The number of Shares to be withheld shall have a Fair Market Value as of the date that the amount of tax to be withheld is determined as nearly equal as possible to (but not exceeding) the amount of such obligations being satisfied. Each election must be made in writing to the Administrator in accordance with election procedures established by the Administrator.

(b) The Participant acknowledges that the Corporation has made no warranties or representations to the Participant with respect to the tax consequences (including, but not limited to, income tax consequences) related to the transactions contemplated by this Agreement, and the Participant is in no manner relying on the Corporation or its representatives for an assessment of such tax consequences. The Participant acknowledges that there may be adverse tax consequences upon acquisition or disposition of the Shares subject to the Option and that the Participant should consult a tax advisor prior to such exercise or disposition. The Participant acknowledges that he or she has been advised that he or she should consult with his own attorney, accountant, and/or tax advisor regarding the decision to enter into this Agreement and the consequences thereof. The Participant also acknowledges that the Corporation has no responsibility to take or refrain from taking any actions in order to achieve a certain tax result for the Participant.

12. Administration. The authority to construe and interpret this Agreement and the Plan, and to administer all aspects of the Plan, shall be vested in the Administrator, and the Administrator shall have all powers with respect to this Agreement as are provided in the Plan. Any interpretation of the Agreement by the Administrator and any decision made by it with respect to the Agreement is final and binding.

13. Notices. Except as may be otherwise provided by the Plan or determined by the Administrator, any written notices provided for in this Agreement or the Plan shall be in writing and shall be deemed sufficiently given if either hand delivered or if sent by fax or overnight courier, or by postage paid first class mail. Notices sent by mail shall be deemed received three business days after mailed but in no event later than the date of actual receipt. Notices shall be directed, if to the Participant, at the Participant's address indicated on Schedule A (or such other address as may be designated by the Participant in a manner acceptable to the Administrator), or, if to the Corporation, at the Corporation's principal office, attention Chief Financial Officer, Targacept, Inc. Notice may also be provided by electronic submission, if and to the extent permitted by the Administrator.

14. Severability. The provisions of this Agreement are severable and if any one or more provisions may be determined to be illegal or otherwise unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

15. Restrictions on Option and Shares. The Corporation may impose such restrictions on the Option and the Shares or other benefits underlying the Option as it may deem advisable, including without limitation restrictions under the federal securities laws, the requirements of any stock exchange or similar organization and any blue sky, state or foreign securities laws applicable to such Option or Shares. Notwithstanding any other provision in the Plan or the Agreement to the contrary, the Corporation shall not be obligated to issue, deliver or transfer shares of Common Stock, to make any other distribution of benefits, or to take any other action, unless such delivery, distribution or action is in compliance with all applicable laws, rules and regulations (including but not limited to the requirements of the Securities Act). The Corporation may cause a restrictive legend to be placed on any certificate for Shares issued pursuant to the exercise of the Option in such form as may be prescribed from time to time by applicable laws and regulations or as may be advised by legal counsel.

16. Cash Settlement. Notwithstanding any other provision of the Plan or this Agreement to the contrary, the Administrator may (subject to any requirements imposed under Code Section 409A, related regulations or other guidance) cause the Option or portion thereof to be cancelled in consideration of an alternative option or cash payment of an equivalent cash value, as determined by the Administrator in its sole discretion, made to the Participant.

17. Effect of Changes in Status. Unless the Administrator, in its sole discretion, determines otherwise, the Option shall not be affected by any change in the terms, conditions or status of the Participant's service, provided that the Participant continues to be in the service to the Corporation or an Affiliate. Without limiting the foregoing, the Administrator has sole discretion to determine, at the time of grant of the Option or at any time thereafter, the effect, if any, on the Option if the Participant's status as a Director changes.

18. Right of Offset. Notwithstanding any other provision of the Plan or the Agreement, the Corporation may reduce the amount of any payment otherwise payable to or on behalf of the Participant by the amount of any obligation of the Participant to the Corporation that is then due and payable and the Participant shall be deemed to have consented to such reduction.

19. Counterparts; Further Instruments. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. The parties hereto agree to execute such further instruments and to take such further action as may be reasonably necessary to carry out the purposes and intent of this Agreement.

[Signatures of the Corporation and the Participant follow on Schedule A/Grant Notice.]

TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN

Nonqualified Stock Option Agreement
(Nonemployee Directors)

Schedule A/Grant Notice

1. Pursuant to the terms and conditions of the Corporation's 2005 Stock Incentive Plan (the "Plan"), you (the "Participant") have been granted an option (the "Option") to purchase _____ shares (the "Shares") of our Common Stock as outlined below.

Name of Participant:	_____
Address:	_____ _____ _____
Grant Date:	_____, 20__
Number of Shares Subject to Option:	_____
Option Price:	_____
Type of Option:	Nonqualified Stock Option
Expiration Date (Last day of Option Period):	_____, 20__
Vesting Schedule/Conditions:	_____ _____ _____

2. By my signature below, I, the Participant, hereby acknowledge receipt of this Grant Notice and the Option Agreement (the "Agreement") dated _____, 200__, between the Participant and Targacept, Inc. (the "Corporation") which is attached to this Grant Notice. I understand that the Grant Notice and other provisions of Schedule A herein are incorporated by reference into the Agreement and constitute a part of the Agreement. By my signature below, I further agree to be bound by the terms of the Plan and the Agreement, including but not limited to the terms of this Grant Notice and the other provisions of Schedule A contained herein. The Corporation reserves the right to treat the Option and the Agreement as cancelled, void and of no effect if the Participant fails to return a signed copy of the Grant Notice within 30 days of grant date stated above.

Signature: _____

Date: _____

Agreed to by:

TARGACEPT, INC.

By: _____

J. Donald deBethizy
President & CEO

Attest:

Alan A. Musso
Vice President, Chief Financial Officer & Secretary

Note: If there are any discrepancies in the name or address shown above, please make the appropriate corrections on this form. Please retain a copy of the Agreement, including this Grant Notice, for your files.

TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN
Restricted Stock Award Agreement

THIS AGREEMENT (together with Schedule A, attached hereto, the "Agreement"), made the ___ day of _____, ____ (as defined below, the "Grant Date"), between TARGACEPT, INC. a Delaware corporation (the "Corporation"), and _____, an Employee of, or individual in service to, the Corporation or an Affiliate (the "Participant");

RECITALS:

In furtherance of the purposes of the Targacept, Inc. 2005 Stock Incentive Plan, as it may be hereafter amended (the "Plan"), the Corporation and the Participant hereby agree as follows:

1. Incorporation of Plan. The rights and duties of the Corporation and the Participant under this Agreement shall in all respects be subject to and governed by the provisions of the Plan, the terms of which are incorporated herein by reference. In the event of any conflict between the provisions in the Agreement and those of the Plan, the provisions of the Plan shall govern. Unless otherwise defined herein, capitalized terms in this Agreement shall have the same definitions as set forth with the Plan.

2. Terms of Award. The following terms used in this Agreement shall have the meanings set forth in this Section 2:

- (a) The "Participant" is _____.
- (b) The "Grant Date" is _____.
- (c) The "Restriction Period" is the period beginning on the Grant Date and ending on such date or dates and satisfaction of such conditions as described in Schedule A, which is attached hereto and expressly made a part of this Agreement.
- (d) The number of shares of Common Stock subject to the Restricted Stock Award granted under this Agreement shall be _____ shares (the "Shares").

3. Grant of Restricted Stock Award. Subject to the terms of this Agreement and the Plan, the Corporation hereby grants the Participant a Restricted Stock Award (the "Award") for that number of Shares of Common Stock as is set forth in Section 2.

4. Vesting and Earning of Award.

- (a) Subject to the terms of the Plan, the Award shall be deemed vested and earned upon such date or dates, and subject to such conditions, as are described in this Agreement, including but not limited to the terms of Schedule A, attached hereto.
- (b) The Administrator has sole authority to determine whether and to what degree the Award has vested and been earned and is payable and to interpret the terms and conditions of this Agreement and the Plan.

5. Forfeiture of Award. Except as may be otherwise provided in the Plan, in the event that the employment or service of the Participant is terminated for any reason and the Participant has not yet earned all or part of the Award pursuant to Section 4 and Schedule A herein, then the Award, to the extent not earned as of the Participant's Termination Date, shall be forfeited immediately upon such termination, and the Participant shall have no further rights with respect to the Award or the Shares underlying that portion of the Award that has not yet been earned and vested. The Participant expressly acknowledges and agrees that the termination of his or her employment or service shall result in forfeiture of the Award and the Shares to the extent the Award has not been earned and vested as of his or her Termination Date.

6. Settlement of Award. The Award shall be payable in whole shares of Common Stock (except to the extent otherwise provided pursuant to Section 18 herein).

7. No Right of Employment or Service; Forfeiture of Award. Neither the Plan, this Agreement nor any other action related to the Plan shall confer upon the Participant any right to continue in the employment or service of the Corporation or an Affiliate or interfere with the right of the Corporation or an Affiliate to terminate the Participant's employment or service at any time. Except as otherwise expressly provided in the Plan or this Agreement or as determined by the Administrator, all rights of the Participant with respect to the Award shall terminate upon termination of the employment of the Participant with the Corporation or an Affiliate.

8. Nontransferability of Award and Shares. The Award shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession. The designation of a beneficiary does not constitute a transfer. The Participant shall not sell, transfer, assign, pledge or otherwise encumber the Shares subject to the Award (except as provided in Section 12 herein) until the Restriction Period has expired and all conditions to vesting and transfer have been met.

9. Superseding Agreement; Binding Effect. This Agreement supersedes any statements, representations or agreements of the Corporation with respect to the grant of the Award or any related rights, and the Participant hereby waives any rights or claims related to any such statements, representations or agreements. This Agreement does not supersede or amend any existing confidentiality agreement, nonsolicitation agreement, noncompetition agreement, employment agreement or any other similar agreement between the Participant and the Corporation, including, but not limited to, any restrictive covenants contained in such agreements. This Agreement shall be binding upon and shall inure to the benefit of the parties hereto and their respective executors, administrators, next-of-kin, successors and assigns.

10. Governing Law. Except as otherwise provided in the Plan or herein, this Agreement shall be construed and enforced according to the laws of the State of Delaware, without regard to the conflict of laws provisions of any state, and in accordance with applicable federal laws of the United States.

11. Amendment and Termination; Waiver. Subject to the terms of the Plan, this Agreement may be modified or amended only by the written agreement of the parties hereto. The waiver by the Corporation of a breach of any provision of the Agreement by the Participant shall not operate or be construed as a waiver of any subsequent breach by the Participant. Notwithstanding the foregoing, the Administrator shall have unilateral authority to amend the Plan and this Agreement (without Participant consent) to the extent necessary to comply with applicable law or changes to applicable law (including but in no way limited to Code Section 409A and related regulations or other guidance and federal securities laws).

12. Certificates for Shares; Rights as Stockholder. The Participant and his or her legal representatives, legatees or distributees shall not be deemed to be the holder of any shares subject to the

Award and shall not have any rights of a stockholder unless and until certificates for such shares have been issued to him or her or them. A certificate or certificates for Shares subject to the Award shall be issued in the name of the Participant as soon as practicable after the Award has been granted. Notwithstanding the foregoing, the Administrator may require that (a) the Participant deliver the certificate(s) for the Shares to the Administrator or its designee to be held in escrow until the Award vests (in which case the Shares will be released to the Participant) or is forfeited (in which case the Shares shall be returned to the Corporation); and/or (b) the Participant deliver to the Corporation a stock power, endorsed in blank, relating to the Shares subject to the Award which are subject to forfeiture. Except as otherwise provided in the Plan or the Agreement, the Participant will have all voting, dividend and other rights of a stockholder with respect to the Shares following issuance of the certificate or certificates for the Shares; provided, however, that if any dividend is declared and paid by the Corporation in any form other than cash, such non-cash dividend shall be subject to the same vesting schedule, forfeiture terms and other restrictions as are applicable to the Shares upon which such dividends are paid.

13. Withholding; Tax Matters.

(a) The Participant acknowledges that the Corporation shall require the Participant to pay the Corporation in cash the amount of any tax or other amount required by any governmental authority to be withheld and paid over by the Corporation to such authority for the account of the Participant, and the Participant agrees, as a condition to the grant of the Award and delivery of the Shares or any other benefit, to satisfy such obligations. Notwithstanding the foregoing, the Corporation may establish procedures to permit the Participant to satisfy such obligations in whole or in part, and any other local, state, federal, foreign or other income tax obligations relating to the Award, by electing (the "election") to have the Corporation withhold shares of Common Stock from the Shares to which the Participant is entitled. The number of Shares to be withheld shall have a Fair Market Value as of the date that the amount of tax to be withheld is determined as nearly equal as possible to (but not exceeding) the amount of such obligations being satisfied. Each election must be made in writing to the Administrator in accordance with election procedures established by the Administrator.

(b) The Participant acknowledges that the Corporation has made no warranties or representations to the Participant with respect to the tax consequences (including, but not limited to, income tax consequences) related to the transactions contemplated by this Agreement, and the Participant is in no manner relying on the Corporation or its representatives for an assessment of such tax consequences. The Participant acknowledges that there may be adverse tax consequences upon acquisition or disposition of the Shares subject to the Award and that the Participant should consult a tax advisor prior to such exercise or disposition. The Participant acknowledges that he or she has been advised that he or she should consult with his own attorney, accountant, and/or tax advisor regarding the decision to enter into this Agreement and the consequences thereof. The Participant also acknowledges that the Corporation has no responsibility to take or refrain from taking any actions in order to achieve a certain tax result for the Participant.

14. Administration. The authority to construe and interpret this Agreement and the Plan, and to administer all aspects of the Plan, shall be vested in the Administrator, and the Administrator shall have all powers with respect to this Agreement as are provided in the Plan. Any interpretation of the Agreement by the Administrator and any decision made by it with respect to the Agreement is final and binding.

15. Notices. Except as may be otherwise provided by the Plan or determined by the Administrator, any written notices provided for in this Agreement or the Plan shall be in writing and shall

be deemed sufficiently given if either hand delivered or if sent by fax or overnight courier, or by postage paid first class mail. Notices sent by mail shall be deemed received three business days after mailed but in no event later than the date of actual receipt. Notices shall be directed, if to the Participant, at the Participant's address indicated by the Corporation's records (or at such other address as may be designated by the Participant in a manner acceptable to the Administrator), or if to the Corporation, at the Corporation's principal office, attention Chief Financial Officer, Targacept, Inc. Notice may also be provided by electronic submission, if and to the extent permitted by the Administrator.

16. Severability. The provisions of this Agreement are severable and if any one or more provisions may be determined to be illegal or otherwise unenforceable, in whole or in part, the remaining provisions shall nevertheless be binding and enforceable.

17. Restrictions on Award and Shares. The Corporation may impose such restrictions on the Award and the Shares or other benefits underlying the Award as it may deem advisable, including without limitation restrictions under the federal securities laws, the requirements of any stock exchange or similar organization and any blue sky, state or foreign securities laws applicable to such Award or Shares. Notwithstanding any other provision in the Plan or the Agreement to the contrary, the Corporation shall not be obligated to issue, deliver or transfer shares of Common Stock, to make any other distribution of benefits, or to take any other action, unless such delivery, distribution or action is in compliance with all applicable laws, rules and regulations (including but not limited to the requirements of the Securities Act). The Corporation may cause a restrictive legend or legends (including but in no way limited to any legends which may be necessary or appropriate pursuant to Section 12 herein) to be placed on any certificate issued pursuant to the Award in such form as may be prescribed from time to time by applicable laws and regulations or as may be advised by legal counsel.

18. Cash Settlement. Notwithstanding any other provision of the Plan or this Agreement to the contrary, the Administrator may (subject to any requirements imposed under Code Section 409A, related regulations or other guidance) cause this Award or portion thereof to be canceled in consideration of an alternative award or cash payment of an equivalent cash value, as determined by the Administrator in its sole discretion, made to the Participant.

19. Effect of Changes in Status. Unless the Administrator, in its sole discretion, determines otherwise, the Award shall not be affected by any change in the terms, conditions or status of the Participant's employment or service, provided that the Participant continues to be in the employ of, or in service to, the Corporation or an Affiliate. Without limiting the foregoing, the Administrator has sole discretion to determine, at the time of grant of the Award or at any time thereafter, the effect, if any, on the Award if the Participant's status as an Employee, Director or Independent Contractor changes, including but not limited to a change from full-time to part-time, or vice versa, or if other similar changes in the nature or scope of the Participant's employment or service occur.

20. Right of Offset. Notwithstanding any other provision of the Plan or the Agreement, the Corporation may reduce the amount of any payment otherwise payable to or on behalf of the Participant by the amount of any obligation of the Participant to the Corporation that is then due and payable and the Participant shall be deemed to have consented to such reduction.

21. Counterparts; Further Instruments. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument. The parties hereto agree to execute such further instruments and to take such further action as may be reasonably necessary to carry out the purposes and intent of this Agreement.

IN WITNESS WHEREOF, this Agreement has been executed in behalf of the Corporation and by the Participant on the day and year first above written.

TARGACEPT, INC.

By: _____
J. Donald deBethizy
President & CEO

Attest:

Alan A. Musso
Vice President, Chief Financial Officer & Secretary

[Corporate Seal]

PARTICIPANT

Printed Name: _____ (SEAL)

**TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN**

Restricted Stock Award Agreement

SCHEDULE A

PERFORMANCE MEASURES

1. Purpose. The purpose of this Schedule A is to set forth the Performance Measures that will be applied to determine the amount of the Award to be made under the terms of the attached Restricted Stock Award Agreement (the "Agreement"). This Schedule A is incorporated into and forms a part of the Agreement.
2. Revision of Performance Measures. The Performance Measures set forth in this Schedule A may be modified by the Administrator during, and after the end of, the Restriction Period to reflect significant events that occur during the Restriction Period.
3. Performance Goals. The Performance Goals shall be as follows:

[Insert Schedule]

4. Amount of Award. The amount distributable to the Participant under the Agreement shall be determined in accordance with the following schedule:

[Insert Schedule]

**TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN**

Restricted Stock Award Agreement

SCHEDULE A

SERVICE MEASURES

Grant Date: _____, _____.

Number of Shares Subject to Award: _____ shares.

Restriction Period: The Shares subject to the Award shall vest and be earned, as provided below, subject to the terms and conditions as may be imposed by the Plan and the Agreement:

Date of Vesting

Percentage of Shares Vested

[Insert Schedule]

TARGACEPT, INC.
2005 STOCK INCENTIVE PLAN

Restricted Stock Award Agreement

SCHEDULE A

COMBINATION OF PERFORMANCE AND SERVICE MEASURES

A. Performance Measures

1. Purpose. The purpose of this portion of Schedule A is to set forth the Performance Measures that will be applied to determine the amount of the Award to be made under the terms of the attached Restricted Stock Award Agreement (the "Agreement"). This Schedule A is incorporated into and forms a part of the Agreement.
2. Revision of Performance Measures. The Performance Measures set forth in this Schedule A may be modified by the Administrator during, and after the end of, the Restriction Period to reflect significant events that occur during the Restriction Period.
3. Performance Goals. The Performance Goals shall be as follows:

[Insert Schedule]

4. Amount of Award. The amount distributable to the Participant under the Agreement shall be determined in accordance with the following schedule:

[Insert Schedule]

B. Service Measures

Grant Date: _____, _____.

Number of Shares Subject to Award: _____ shares.

Restriction Period: The Shares subject to the Award shall vest and be earned, as provided below, subject to the terms and conditions as may be imposed by the Plan and the Agreement:

Date of Vesting

Percentage of Shares Vested

[Insert Schedule]

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated February 4, 2005, in Amendment No. 6 to the Registration Statement (Form S-1 No. 333-115538) and related Prospectus of Targacept, Inc. dated February 22, 2005.

/s/ Ernst & Young LLP

Greensboro, North Carolina
February 22, 2005