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Filed pursuant to Rule 424(b)(4)
Registration No. 333-131050

5,000,000 Shares
Common Stock

This is the initial public offering of Targacept, Inc. We are offering 5,000,000 shares of our common stock. Our common stock has been approved for listing on the NASDAQ National Market under the symbol “TRGT.”

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

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

	Price to Public	Underwriting Discounts and Commissions	Proceeds to Targacept
Per Share	$9.00	$0.63	$8.37
Total	$45,000,000	$3,150,000	$41,850,000

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

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

CIBC World Markets **Lazard Capital Markets**

The date of this prospectus is April 11, 2006

PROSPECTUS SUMMARY

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

Targacept, Inc.

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

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

Cognitive Impairment

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

Depression/Anxiety

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

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

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

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

Pain

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

Under our agreement with AstraZeneca relating to TC-1734, we and AstraZeneca have initiated a preclinical research collaboration designed to discover and develop additional compounds that, like TC-1734, act on the NNR known as a4ß2. AstraZeneca is responsible for funding the research collaboration, which has an initial term of four years and can be extended by mutual agreement. In addition to our a4ß2 research collaboration with AstraZeneca, we have a preclinical program focused on identifying and developing compounds that selectively target another NNR, known as a7, which we believe may have application in the treatment of conditions such as schizophrenia, cognitive impairment and inflammation. We have selected a lead compound that we refer to as TC-5619 that acts selectively on the a7 NNR. We are currently conducting additional preclinical studies to support the planned filing in 2007 of an IND for clinical trials of TC-5619. We have additional preclinical programs in areas in which we believe drugs that target specific NNR subtypes can be exploited for medical benefit, such as smoking cessation and obesity.

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

Strategic Collaboration with AstraZeneca AB

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

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

Our NNR Focus

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

Our Business Strategy

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

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

Risks Associated with Our Business

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

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

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

or before April 20, 2007 not to proceed with the further development of TC-1734 based on the results of the safety and product characterization studies that AstraZeneca is conducting at its expense for TC-1734 and all other available information with respect to TC-1734. In that event, we would have the financial obligations to AstraZeneca described above under "—Strategic Collaboration with AstraZeneca AB." In addition, we have the right to offer to AstraZeneca any compound that acts on any NNR other than the a4ß2 NNR that we may in the future seek to exploit for Alzheimer's disease, cognitive deficits in schizophrenia, other conditions marked by cognitive impairment or schizophrenia. However, if we do not offer the compound to AstraZeneca, we are generally not permitted to develop or commercialize the compound for any of these indications. As a result, our ability to work in these indications outside the collaboration is substantially limited during the term of the collaboration. Furthermore, the number of compounds that we are permitted to offer to AstraZeneca is limited under the agreement. We have also granted AstraZeneca rights of first negotiation for the development and commercialization of compounds for depression, anxiety and bipolar disorder.

Company History

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

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

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

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

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

Unless otherwise indicated, all information in this prospectus assumes:

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

Three of our principal stockholders or affiliated entities have indicated an interest in purchasing up to an aggregate of 500,000 shares of our common stock in this offering at the initial public offering price in the following amounts: New Enterprise Associates 10, Limited Partnership, 350,000 shares; Advent Private Equity Fund II, 75,000 shares; and Oxford Bioscience Partners IV L.P., 75,000 shares. However, because indications of interest are not binding agreements or commitments to purchase, these stockholders may elect not to purchase any shares in this offering.

Summary Financial Data

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

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

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

The pro forma balance sheet information gives effect to the conversion of all outstanding shares of our convertible preferred stock into 13,832,015 shares of common stock concurrently with the completion of this offering. The pro forma as adjusted balance sheet information gives further effect to our sale of 5,000,000 shares of common stock in this offering at the initial public offering price of $9.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	As of December 31, 2005		
	Actual	Pro forma	Pro forma as adjusted
		(unaudited) (in thousands)	
Balance Sheet Data:			
Cash and cash equivalents	$ 24,851	$ 24,851	$ 65,680
Working capital	20,531	20,531	61,261
Total assets	28,001	28,001	68,731
Long-term debt, net of current portion	1,409	1,409	1,409
Redeemable convertible preferred stock	183,628	—	—
Accumulated deficit	(174,983)	(138,486)	(138,258)
Total stockholders' equity (deficit)	(162,481)	21,147	61,877

RISK FACTORS

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

Risks Related to Our Financial Results and Need for Additional Financing

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Any of our product candidates could be unsuccessful if it:

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Dependence on Third Parties

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Our Intellectual Property

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Commercialization

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Risks Related to Employees and Managing Growth

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

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

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

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

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

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

Risks Related to Our Common Stock and this Offering

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

There has been no public market for our common stock prior to this offering, and it is possible that no active trading market for our common stock will develop or continue following this offering. You may not be able to sell your shares quickly or at the market price if trading in our common stock is not active. The initial public offering price for the shares was 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 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 is substantially higher than the net tangible book value of approximately $(602.73) per share, based on our existing capital stock as of December 31, 2005. As a result, based on the initial public offering price of $9.00 per share, purchasers of our common stock in this offering will incur immediate and substantial dilution of $5.79 per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the initial public offering price, and will incur $0.03 additional dilution if outstanding stock options and warrants with exercise prices below the public offering price are exercised. See “Dilution” for a more detailed discussion of the dilution new investors will incur in this offering.

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

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

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

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

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

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

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

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

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

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

Following the completion of this offering, our executive officers, directors and their affiliates will beneficially own or control approximately 39.0% of the outstanding shares of our common stock, excluding any shares that any of our directors or their affiliates may purchase in this offering. Accordingly, our current executive officers, directors and their affiliates will have substantial control over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transactions, as well as our management and affairs. The concentration of ownership may also delay or prevent a change of control of us at a premium price if these stockholders oppose it, even if it would benefit our other stockholders.

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

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

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

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

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

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

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

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

USE OF PROCEEDS

We estimate that our net proceeds from the sale of 5,000,000 shares of our common stock in this offering will be approximately $40.7 million, or approximately $47.0 million if the underwriters exercise their over-allotment option in full, based on the initial public offering price of $9.00 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

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

- approximately $10 million to complete our ongoing Phase I clinical trial, to conduct Phase II clinical trials and to conduct formulation activities for TC-2696, our product candidate for acute post-operative pain;
- approximately $9 million to conduct the additional preclinical safety studies necessary to support an IND for clinical trials, to conduct Phase I and Phase II clinical trials of TC-2216, our product candidate for depression and anxiety disorders;
- approximately $6 million to conduct the additional preclinical safety studies necessary to support an IND for clinical trials and, unless licensed by us to AstraZeneca under the terms of our collaboration agreement, to conduct Phase I clinical trials of TC-5619;
- approximately $4 million to fund preclinical testing and other research and development activities in one or more of the areas of smoking cessation, obesity and inflammation;
- approximately $2 million to complete our ongoing Phase II clinical trial of mecamylamine hydrochloride as an add-on therapy for depression; and
- the remaining $9.7 million to fund general and administrative expenses, other research and development expenses, working capital needs and other general corporate purposes.

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

The amounts and timing of our actual expenditures may vary significantly depending upon numerous factors, including the progress and status of our development and commercialization efforts, the amount of proceeds actually raised in this offering, the amount of cash generated through our existing strategic collaboration with AstraZeneca, any additional strategic collaborations into which we may enter and sales of Inversine, and our operating costs and capital expenditures. Accordingly, our management will have significant flexibility in applying the net proceeds of this offering. We may change the allocation of use of these proceeds as a result of contingencies such as the progress and results of our clinical trials and other research and development activities, product development timelines and the status of our intellectual property position, a decision by us to conduct a Phase III clinical trial of mecamylamine hydrochloride or to accelerate the development of TC-5214 as an add-on therapy for depression in lieu of further advancement of mecamylamine hydrochloride, any decision by us to offer TC-5619 or any other compound to AstraZeneca and by AstraZeneca to license the compound under the terms of our collaboration agreement, the establishment of collaborations, the results of our commercialization efforts, our manufacturing requirements and regulatory or competitive developments. In particular, if AstraZeneca terminates our collaboration agreement following the completion of the additional safety and product characterization studies of TC-1734 that

AstraZeneca is conducting and we choose to fund the clinical development of TC-1734 on our own, we would need to use a substantial portion of the net proceeds of this offering for that purpose or seek additional funds from external sources.

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

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

DIVIDEND POLICY

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

CAPITALIZATION

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

- on an actual basis;
- on a pro forma basis to give effect to the conversion of all outstanding shares of our convertible preferred stock into 13,832,015 shares of common stock concurrently with the completion of this offering; and
- on a pro forma as adjusted basis to give further effect to our sale of 5,000,000 shares of common stock in this offering at the initial public offering price of $9.00 per share, after deducting underwriting discounts and commissions and estimated offering expenses payable by us.

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

	As of December 31, 2005		
	Actual	Pro Forma	Pro Forma As Adjusted
		(in thousands, except share and per share data)	
Total long-term obligations	$ 2,193	$ 2,193	$ 2,193
Redeemable convertible preferred stock, $0.001 par value; 93,309,532 shares authorized, 88,505,565 shares issued and outstanding actual; no shares authorized, issued or outstanding pro forma and pro forma as adjusted	183,628	—	—
Stockholders' equity (deficit):			
Common stock, $0.001 par value; 16,666,666 shares authorized actual and pro forma; 100,000,000 shares authorized pro forma as adjusted; 270,427 issued and outstanding actual; 14,102,442 shares issued and outstanding pro forma; 19,102,442 shares issued and outstanding pro forma as adjusted	—	14	19
Preferred stock, $0.001 par value; no shares authorized, issued or outstanding actual and pro forma; 5,000,000 shares authorized and no shares issued and outstanding pro forma as adjusted	—	—	—
Capital in excess of par value	12,288	159,405	200,116
Common stock warrants	214	214	—
Accumulated deficit	(174,983)	(138,486)	(138,258)
Total stockholders' equity (deficit)	(162,481)	21,147	61,877
Total capitalization	$ 23,340	$ 23,340	$ 64,070

The table above does not include:

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

DILUTION

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

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

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

After giving effect to the sale of the 5,000,000 shares of our common stock offered by this prospectus at the initial public offering price of $9.00 per share and after deducting underwriting discounts and commissions and estimated offering expenses payable by us, our pro forma net tangible book value as of December 31, 2005 would have been $61.4 million, or $3.21 per share. This represents an immediate increase in pro forma net tangible book value of $1.75 per share to our existing stockholders and an immediate dilution in pro forma net tangible book value of $5.79 per share to investors purchasing in this offering at the initial public offering price. The following table illustrates this dilution on a per share basis:

Initial public offering price per share		$9.00
Historical net tangible book value per share	$(602.73)	
Increase attributable to the conversion of convertible preferred stock	604.19	
Pro forma net tangible book value per share before this offering	1.46	
Increase per share attributable to new investors	1.75	
Pro forma net tangible book value per share after this offering		3.21
Dilution per share to new investors		$5.79

The following table summarizes, on a pro forma basis as of December 31, 2005, the total number of shares of common stock purchased from us, the total consideration paid and the average price per share paid by existing stockholders and by investors purchasing shares in this offering at the initial public offering price of $9.00 per share, before deducting underwriting discounts and commissions and estimated offering expenses payable by us.

	Shares Purchased		Total Consideration		
	Number	Percent	Amount	Percent	Average Price per Share
Existing stockholders	14,102,442	73.8%	$149,092,000	76.8%	$ 10.57
New investors	5,000,000	26.2	45,000,000	23.2	9.00
Total	19,102,442	100.0%	$194,092,000	100.0%	

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

The share data in the table above excludes:

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

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

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

SELECTED FINANCIAL DATA

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

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

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

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

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

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

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

Overview

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

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

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

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

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

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

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

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

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

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

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

Critical Accounting Policies and Estimates

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

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

Revenue Recognition

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

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

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

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

Accrued Expenses

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

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

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

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

Stock-Based Compensation

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

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

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

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

Financial Operations Overview

Revenue

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

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

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

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

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

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

Research and Development Expense

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

Research and development expense includes expenses associated with:

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

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

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

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

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

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

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

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

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

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

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

General and Administrative Expense

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

Cost of Product Sales

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

Interest and Dividend Income

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

Interest Expense

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

Income Taxes

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

Results of Operations

Years ended December 31, 2005 and December 31, 2004

Revenue

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

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

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

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

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

Research and Development Expense

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

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

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

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

General and Administrative Expense

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

Cost of Product Sales

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

Interest and Dividend Income

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

Interest Expense

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

Years ended December 31, 2004 and December 31, 2003

Revenue

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

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

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

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

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

Research and Development Expense

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

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

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

General and Administrative Expense

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

Cost of Product Sales

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

Interest and Dividend Income

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

Interest Expense

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

Liquidity and Capital Resources

Sources of Liquidity

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

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

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

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

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

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

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

Cash Flows

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

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

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

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

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

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

Funding Requirements

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

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

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

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

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

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

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

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

Contractual Obligations

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

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

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

Quantitative and Qualitative Disclosures about Market Risk

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

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

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

Recent Accounting Pronouncements

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

BUSINESS

Overview

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

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

Cognitive Impairment

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

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

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

Depression/Anxiety

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

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

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

Pain

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

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

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

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

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

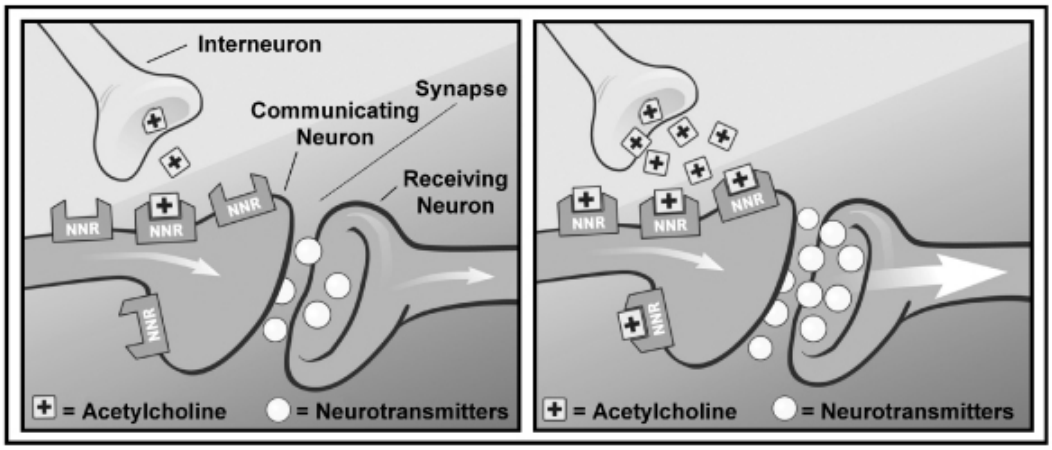
Role of NNRs in the Nervous System

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

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

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

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



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

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

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

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

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

Our Business Strategy

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

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

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

Opportunities in Our Target Indications

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

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

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

Alzheimer's Disease

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

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

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

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

Cognitive Deficits in Schizophrenia

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

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

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

AAMI

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

Depression/Anxiety

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

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

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

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

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

Pain

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

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

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

Our Product Development Pipeline

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

The following table summarizes our product development pipeline.

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

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

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

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

Cognitive Impairment

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

TC-1734

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

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

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

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

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

Clinical Development of TC-1734

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

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

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

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

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

Primary Endpoints

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

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

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

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

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

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

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

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

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

Secondary Endpoints

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

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

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

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

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

Tolerability

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Depression/Anxiety

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

Mecamylamine hydrochloride and TC-5214

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

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

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

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

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

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

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

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

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

TC-2216

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

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

Pain

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

TC-2696

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

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

Clinical Development of TC-2696

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

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

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

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

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

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

Discontinued Clinical Development

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

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

Our Preclinical Research Programs

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

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

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

a7

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

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

Smoking Cessation

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

Obesity

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

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

Our Drug Discovery Technologies—Pentad

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

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

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

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

Strategic Collaborations

AstraZeneca AB

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Aventis Pharma SA

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

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

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

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

The Stanley Medical Research Institute

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

Patents and Proprietary Rights

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

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

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

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

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

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

We also have an issued patent in the United States covering composition of matter for a family of compounds that includes TC-5619, our preclinical product candidate that acts selectively on the a7 NNR. This patent expires in August 2019.

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

License Agreements

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

University of South Florida Research Foundation

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

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

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

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

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

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

Virginia Commonwealth University Intellectual Property Foundation

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

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

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

Wake Forest University Health Sciences

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

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

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

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

University of Kentucky Research Foundation

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

Trade Secrets

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

Sales and Marketing

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

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

Manufacturing

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

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

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

Competition

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

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

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

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

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

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

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

Government Regulation

Drug Regulation in the United States

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Fast Track Designation

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

Drug Regulation Outside the United States

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

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

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

Third-Party Reimbursement

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

Price Controls

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

Employees

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

Property and Facilities

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

Legal Proceedings

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

MANAGEMENT

Executive Officers and Directors

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Board Composition

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

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

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

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

Board Committees

Audit Committee

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

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

Compensation Committee

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

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

Governance and Nominating Committee

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

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

Compensation Committee Interlocks and Insider Participation

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

Director Compensation

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

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

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

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

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

Executive Compensation

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

Summary Compensation Table

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

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

Stock Options

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

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

Option Grants in Last Fiscal Year

Name	Number of Securities Underlying Options Granted	Percentage of Total Options Granted to Employees in Fiscal Year	Exercise Price Per Share	Expiration Date	Potential Realizable Value at Assumed Annual Rates of Stock Price Appreciation for Option Terms (1)	
					5%	10%
J. Donald deBethizy, Ph.D.	174,000	26.9%	$ 1.75	3/29/2015	$ 2,246,340	$ 3,756,660
Merouane Bencherif, M.D., Ph.D.	50,000	7.7	1.75	3/29/2015	645,500	1,079,500
Jeffrey P. Brennan	40,000	6.2	1.75	3/29/2015	516,400	863,600
William S. Caldwell, Ph.D.	42,000	6.5	1.75	3/29/2015	542,220	906,780
Geoffrey C. Dunbar, M.D.	54,000	8.4	1.75	3/29/2015	697,140	1,165,860
Alan A. Musso	48,000	7.4	1.75	3/29/2015	619,680	1,036,320

(1) The dollar amounts under these columns are the result of rates set by the Securities and Exchange Commission and, therefore, are not intended to forecast possible future appreciation, if any, in the price of the underlying common stock. The potential realizable values at 5% and 10% appreciation are calculated using the initial public offering price of $9.00 per share and assuming that the market price appreciates from this price at the indicated rate for the entire term of each option and that each option is exercised at the exercise price and sold on the last day of its term at the assumed appreciated price.

Option Exercises and Year-End Option Values

The following table sets forth information regarding the number of shares of our common stock issued upon option exercises by our named executive officers during the year ended December 31, 2005 and the value realized by our named executive officers. The table also sets forth information regarding the number and value of unexercised stock options held by our named executive officers as of December 31, 2005. There was no public trading market for our common stock as of December 31, 2005. Accordingly, as permitted by the rules of the Securities and Exchange Commission, we have calculated the value of the unexercised in-the-money options at fiscal year end by determining the difference between the exercise price per share and an assumed fair market value of our common stock as of December 31, 2005 equal to the initial offering price of $9.00 per share.

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

Name	Number of Shares Acquired on Exercise	Value Realized	Number of Securities Underlying Unexercised Options Held at December 31, 2005		Value of Unexercised In-the-Money Options at December 31, 2005	
			Exercisable	Unexercisable	Exercisable	Unexercisable
J. Donald deBethizy, Ph.D.	—	—	242,293	183,698	$ 1,306,270	$ 1,331,811
Merouane Bencherif, M.D., Ph.D.	—	—	102,772	52,470	539,850	380,408
Jeffrey P. Brennan	—	—	32,755	29,778	194,115	215,891
William S. Caldwell, Ph.D.	—	—	96,063	44,363	496,859	321,632
Geoffrey C. Dunbar, M.D.	—	—	89,599	56,147	461,303	407,066
Alan A. Musso	399	$ 1,728	88,777	49,579	454,076	359,448

Employment Agreements

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

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

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

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

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

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

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

Stock Option and Other Compensation Plans

2000 Equity Incentive Plan

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

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

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

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

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

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

Significant Transactions. If:

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

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

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

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

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

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

2006 Stock Incentive Plan

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

Targacept Retirement Savings Plan—401(k) Plan

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

Limitation of Liability and Indemnification

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

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

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

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

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

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

Stock Issuances

Issuances of Series C Convertible Preferred Stock

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

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

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

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

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

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

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

Participation in Offering

Three of our principal stockholders or affiliated entities have indicated an interest in purchasing up to an aggregate of 500,000 shares of our common stock in this offering at the initial public offering price in the following amounts: New Enterprise Associates 10, Limited Partnership, 350,000 shares; Advent Private Equity Fund II, 75,000 shares; and Oxford Bioscience

Partners IV L.P., 75,000 shares. However, because indications of interest are not binding agreements or commitments to purchase, these stockholders may elect not to purchase any shares in this offering.

Registration Rights

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

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

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

Payments to R.J. Reynolds Tobacco Company

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

Director Compensation

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

Executive Compensation and Employment Agreements

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

PRINCIPAL STOCKHOLDERS

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

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

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

The following table does not include any shares that may be purchased in this offering by our principal stockholders or affiliated entities.

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

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

* Indicates less than one percent.

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

(2) Includes 2,913,512 shares owned of record by New Enterprise Associates 10, Limited Partnership, for which voting and investment power is shared by M. James Barrett, Peter J. Barris, C. Richard Kramlich, Peter T. Morris, Charles W. Newhall, III, Mark W. Perry, Scott D. Sandell and Eugene A. Trainor, III, each of whom is a general partner of NEA Partners 10, Limited Partnership, the general partner of New Enterprise Associates 10, Limited Partnership; 3,154 shares owned of record by NEA Ventures 2002, Limited Partnership, for which voting and investment power is held by its general partner, Pamela J. Clark; and 1,000 shares owned of record by, and 4,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006 held by, NEA Development Corp., for which voting and investment power is shared by Charles W. Newhall, III, Mark W. Perry, Peter J. Barris, C. Richard Kramlich and Peter T. Morris through their ownership of New Enterprise Associates, LLC. New Enterprise Associates, LLC is the sole owner of NEA Development Corp. Dr. Barrett, one of our directors, and each of the other general partners of NEA Partners 10, Limited Partnership and NEA Ventures 2002, Limited Partnership disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his or her pecuniary interest therein. New Enterprise Associates 10, Limited Partnership or its affiliated entities have indicated an interest in purchasing up to 350,000 shares in this offering. However, because indications of interest are not binding agreements or commitments to purchase, New Enterprise Associates 10, Limited Partnership and its affiliated entities may elect not to purchase any shares in this offering.

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

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

powers in his capacity as director of Nomura Phase4 Ventures Limited and as Head of Merchant Banking, Nomura International plc. Mr. Hashimoto and Dr. Pollard-Knight disclaim beneficial ownership of these shares.

(5) Includes 883,987 shares owned of record by Oxford Bioscience Partners IV L.P. and 8,869 shares owned of record by mRNA Fund II L.P., for which voting and investment power is shared by Alan G. Walton, Jonathan J. Fleming, Jeffrey T. Barnes, Mark P. Carthy and Michael Lytton, each of whom are general partners of OBP Management IV L.P., the sole general partner of Oxford Bioscience Partners IV L.P. and mRNA Fund II L.P. Each of Oxford Bioscience Partners IV L.P. and mRNA Fund II L.P. disclaim beneficial ownership of any shares held of record by the other. Each of the general partners of OBP Management IV L.P. disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his pecuniary interest therein. Oxford Bioscience Partners IV L.P. or its affiliated entities have indicated an interest in purchasing up to 75,000 shares in this offering. However, because indications of interest are not binding agreements or commitments to purchase, Oxford Bioscience Partners IV L.P. and its affiliated entities may elect not to purchase any shares in this offering.

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

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

(8) Includes 260,685 shares owned of record by Advent Private Equity Fund II 'A' Limited Partnership; 158,989 shares owned of record by Advent Private Equity Fund II 'B' Limited Partnership; 236,694 shares owned of record by Advent Private Equity Fund II 'C' Limited Partnership; and 56,218 shares owned of record by Advent Private Equity Fund II 'D' Limited Partnership. Voting and investment power over the shares held by each of the partnerships constituting Advent Private Equity Fund II is exercised by Advent Venture Partners LLP in its role as manager. The partners of Advent Venture Partners LLP are Sir David James Scott Cooksey (chairman), Jeryl Christine Andrew, Peter Anthony Baines, Jerry Christopher Benjamin, David Cheesman, Leslie Ian Gabb, Mohammed Shahzad Ahmed Malik, Patrick Pak-tin Lee, Martin Alexander McNair, William Harold Neil Pearce and Nicholas James Teasdale. Each partner disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein. Advent Private Equity Fund II or its affiliated entities have indicated an interest in purchasing up to 75,000 shares in this offering. However, because indications of interest are not binding agreements or commitments to purchase, Advent Private Equity Fund II and its affiliated entities may elect not to purchase any shares in this offering.

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

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

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

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

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

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

(15) Includes 2,913,512 shares owned of record by New Enterprise Associates 10, Limited Partnership, for which voting and investment power is shared by M. James Barrett, Peter J. Barris, C. Richard Kramlich, Peter T. Morris, Charles W. Newhall, III, Mark W. Perry, Scott D. Sandell and Eugene A. Trainor, III, each of whom is a general partner of NEA Partners 10, Limited Partnership, the general partner of New Enterprise Associates 10, Limited Partnership; 3,154 shares owned of record by NEA Ventures 2002, Limited Partnership, for which voting and investment power is held by its general partner, Pamela J. Clark; and 1,000 shares owned of record by, and 4,333 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006 held by, NEA Development Corp., for which voting and investment power is shared by Charles W. Newhall, III, Mark W. Perry, Peter J. Barris, C. Richard Kramlich and Peter T. Morris through their ownership of New Enterprise Associates, LLC. New Enterprise Associates, LLC is the sole owner of NEA Development Corp. Dr. Barrett, one of our directors, and each of the other general partners of NEA Partners 10, Limited Partnership and NEA Ventures 2002, Limited Partnership disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his or her pecuniary interest therein. New Enterprise Associates 10, Limited Partnership or its affiliated entities have indicated an interest in purchasing up to 350,000 shares in this offering. However, because indications of interest are not binding agreements or commitments to purchase, New Enterprise Associates 10, Limited Partnership and its affiliated entities may elect not to purchase any shares in this offering.

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

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

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

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

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

(21) Includes 770,890 shares of common stock issuable upon exercise of stock options exercisable within 60 days of February 28, 2006 and 215,054 shares issuable upon the exercise of an outstanding warrant, assuming that the warrant is exercised in full for cash. As described above, three of our principal stockholders or affiliated entities have indicated an interest in purchasing up to an aggregate of 500,000 shares of our common stock in this offering. However, because these indications of interest are not binding agreements or commitments to purchase, these stockholders may elect not to purchase any shares in this offering.

DESCRIPTION OF CAPITAL STOCK

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

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

As of February 28, 2006, we had outstanding:

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

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

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

Common Stock

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

Preferred Stock

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

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

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

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

Options

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

Registration Rights

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

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

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

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

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

Anti-Takeover Provisions

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

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

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

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

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

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

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

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

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

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

Transfer Agent and Registrar

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

NASDAQ National Market

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

SHARES ELIGIBLE FOR FUTURE SALE

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

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

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

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

Rule 144

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

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

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

Rule 144(k)

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

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

Rule 701

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

Lock-up Agreements

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

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

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

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

Stock Options

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

Registration Rights

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

UNDERWRITERS

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

Underwriters	Number of Shares
Deutsche Bank Securities Inc.	2,000,000
Pacific Growth Equities, LLC	1,350,000
CIBC World Markets Corp.	1,050,000
Lazard Capital Markets LLC	600,000
Total	5,000,000

The underwriters are offering the shares of common stock subject to their acceptance of the shares from us and subject to prior sale. The underwriting agreement provides that the obligations of the several underwriters to pay for and accept delivery of the shares of common stock offered by this prospectus are subject to the approval of specified legal matters by their counsel and to other conditions. The underwriters are obligated to take and pay for all of the shares of common stock offered by this prospectus if any such shares are taken. However, the underwriters are not required to take or pay for the shares covered by the underwriters' over-allotment option described below.

The underwriters initially propose to offer part of the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of $0.38 per share under the public offering price. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to an aggregate of 750,000 additional shares of common stock at the public offering price listed on the cover page of this prospectus, less underwriting discounts and commissions. The underwriters may exercise this option solely for the purpose of covering over-allotments, if any, made in connection with the offering of the shares of common stock offered by this prospectus. To the extent the option is exercised, each underwriter will become obligated, subject to certain conditions, to purchase approximately the same percentage of the additional shares of common stock as the number listed next to the underwriter's name in the preceding table bears to the total number of shares of common stock listed next to the names of all underwriters in the preceding table. If the underwriters' option is exercised in full, the total price to the public would be $51,750,000, the total underwriters' discounts and commissions would be $3,622,500 and the total proceeds to us would be $48,127,500.

The underwriters have informed us that they do not intend sales to discretionary accounts to exceed five percent of the total number of shares of common stock offered by them.

We and all of our directors and officers and holders of substantially all of our currently outstanding stock have agreed that, without the prior written consent of Deutsche Bank Securities on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus:

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

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

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

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

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

These restrictions do not apply to:

- the sale of shares to the underwriters;
- the issuance by us of shares of our common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus of which the underwriters have been advised in writing;
- the issuance by us of shares or options to purchase shares of our common stock pursuant to our 2000 plan or our 2006 plan, provided that the recipient of the shares agrees to be subject to the restrictions described above;
- transactions by any person other than us relating to shares of common stock or other securities acquired in open market transactions after the completion of the offering of the shares;
- transfers of shares as a gift or charitable contribution, or by will or intestacy;
- transfers of shares to any trust the sole beneficiaries of which are the transferee or a member of the immediate family of the transferee; or
- transfers to certain entities or persons affiliated with the stockholder;

provided that in the case of each of the last three transactions, each donee, distributee, transferee and recipient agrees to be subject to the restrictions described in the immediately preceding paragraph, no filing under Section 16 of the Securities Exchange Act of 1934, as amended, is required in connection with these transactions, other than a filing on a Form 5 made after the expiration of the 180-day period, and no transaction includes a disposition for value.

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of our common stock.

	Paid by Targacept	
	No Exercise	Full Exercise
Per share	$0.63	$0.63
Total	$3,150,000	$3,622,500

In addition, we estimate that the expenses of this offering payable by us, other than underwriting discounts and commissions, will be $1.1 million.

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

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

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

Directed Share Program

At our request, the underwriters have reserved for sale, at the initial public offering price, up to 150,000 shares offered by this prospectus to directors, officers, employees and other individuals associated with us and members of their respective families and friends through a directed share program. The number of shares of our common stock available for sale to the general public in the offering will be reduced to the extent these persons purchase these reserved shares. Any reserved shares not purchased by these persons will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus.

Pricing of the Offering

Prior to the offering, there has been no public market for our common stock. The initial public offering price was determined by negotiations between us and the representatives. Among the factors considered in determining the initial public offering price of the shares were 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.

LEGAL MATTERS

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

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, have audited our financial statements as of December 31, 2005 and 2004 and for each of the three years in the period ended December 31, 2005, as set forth in their report. We have included our financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock to be sold in this offering. This prospectus does not contain all of the information set forth in the registration statement. You should refer to the registration statement for additional information regarding us and the shares of our common stock to be sold in this offering. Whenever we reference any contract, agreement or other document in this prospectus, the reference is not necessarily complete and you should refer to the exhibits to the registration statement for the actual contract, agreement or other document. In each instance, reference is made to such exhibits and each such statement is qualified in all respects by such reference. In addition, when this offering is completed, we will become subject to the information and reporting requirements of the Exchange Act and, in accordance with the Exchange Act, will file periodic reports, proxy statements and other information with the Securities and Exchange Commission.

You can read the registration statement and our future filings with the Securities and Exchange Commission over the Internet at the Securities and Exchange Commission's website at http://www.sec.gov. You may also read and copy any document that we file with the Securities and Exchange Commission at its public reference room at 100 F Street, N.E., Room 1580, Washington, D.C. 20549.

You may obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the Securities and Exchange Commission at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. Please call the Securities and Exchange Commission at 1-800-SEC-0330 for further information on the operation of the public reference room. Such reports, proxy and information statements and other information may also be inspected at the offices of NASDAQ Operations, 1735 K Street, N.W., Washington, D.C. 20006.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors
Targacept, Inc.

We have audited the accompanying balance sheets of Targacept, Inc. as of December 31, 2004 and 2005, and the related statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2005. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Targacept, Inc. at December 31, 2004 and 2005, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2005, in conformity with U.S. generally accepted accounting principles.

As discussed in Notes 2 and 11 to the financial statements, effective January 1, 2005, the Company adopted the fair value method of accounting provisions of Statement of Financial Accounting Standards (SFAS) No. 123 (revised 2004), *Share-Based Payment*.

/s/ ERNST & YOUNG LLP

Greensboro, North Carolina
February 10, 2006

TARGACEPT, INC.

BALANCE SHEETS

	December 31, 2004	December 31, 2005
ASSETS		
Current assets:		
Cash and cash equivalents	$ 53,075,348	$ 24,851,302
Research fees and accounts receivable	484,565	118,163
Inventories	102,640	41,940
Prepaid expenses	1,727,836	729,241
Total current assets	55,390,389	25,740,646
Property and equipment, net	2,262,698	1,747,524
Intangible assets, net of accumulated amortization of $91,263 and $129,027 at December 31, 2004 and 2005, respectively	550,737	512,973
Total assets	$ 58,203,824	$ 28,001,143
LIABILITIES, REDEEMABLE CONVERTIBLE PREFERRED STOCK AND STOCKHOLDERS' EQUITY (DEFICIT)		
Current liabilities:		
Accounts payable	$ 1,854,138	$ 1,173,545
Accrued expenses	1,940,836	2,849,747
Current portion of long-term debt	1,113,350	783,895
Current portion of deferred rent incentive	402,647	402,647
Total current liabilities	5,310,971	5,209,834
Long-term debt, net of current portion	3,443,297	1,409,402
Deferred rent incentive, net of current portion	637,524	234,877
Total liabilities	9,391,792	6,854,113
Commitments		
Redeemable convertible preferred stock:		
Series A, $0.001 par value, 5,000,000 shares authorized, issued and outstanding, aggregate liquidation preference of $30,166,741 and $31,836,985 at December 31, 2004, and 2005, respectively, or $4.65 per share plus accreted redemption value	30,166,741	31,836,985
Series B, $0.001 par value, 6,567,567 shares authorized, issued and outstanding, aggregate liquidation preference of $39,622,161 and $41,759,905 at December 31, 2004, and 2005, respectively, or $4.65 per share, plus accreted redemption value	39,622,161	41,759,905
Series C, $0.001 par value, 76,441,866 and 81,741,965 shares authorized at December 31, 2004 and 2005, 76,441,866 and 76,937,998 shares issued and outstanding at December 31, 2004, and 2005, respectively, aggregate liquidation preference of $101,988,994 and $110,031,263 at December 31, 2004, and 2005, respectively, or $1.21 per share, plus accreted redemption value	101,988,994	110,031,263
Total redeemable convertible preferred stock	171,777,896	183,628,153
Stockholders' equity (deficit):		
Common stock, $0.001 par value, 16,666,666 shares authorized at December 31, 2004, and 2005, 256,816 and 270,427 shares issued and outstanding at December 31, 2004, and 2005, respectively	257	270
Capital in excess of par value	11,573,677	12,287,904
Common stock warrants	213,710	213,710
Accumulated deficit	(134,753,508)	(174,983,007)
Total stockholders' equity (deficit)	(122,965,864)	(162,481,123)
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 58,203,824	$ 28,001,143

See accompanying notes

TARGACEPT, INC.

STATEMENTS OF OPERATIONS

	Year ended December 31,		
	2003	2004	2005
Revenue:			
Research fee revenue	$ 1,302,500	$ 337,500	$ —
License fee revenue	269,532	1,917,224	—
Product sales	814,724	766,583	681,285
Grant revenue	71,529	717,067	498,632
Net revenue	2,458,285	3,738,374	1,179,917
Operating expenses:			
Research and development ($0, $0 and $457,670 stock-based compensation in 2003, 2004 and 2005, respectively)	18,179,542	22,770,881	24,251,463
General and administrative ($65,325, $50,623 and $232,784 stock-based compensation in 2003, 2004 and 2005, respectively)	3,599,673	5,162,474	6,388,437
Cost of product sales	742,941	198,446	480,933
Total operating expenses	22,522,156	28,131,801	31,120,833
Loss from operations	(20,063,871)	(24,393,427)	(29,940,916)
Other income (expense):			
Interest and dividend income	791,339	504,986	1,174,398
Interest expense	(122,789)	(132,749)	(225,005)
Loss on disposal of fixed assets	—	(4,199)	—
Total other income (expense)	668,550	368,038	949,393
Net loss	(19,395,321)	(24,025,389)	(28,991,523)
Deemed dividend—beneficial conversion feature for Series C redeemable convertible preferred stock issued December 2004	—	(10,312,499)	—
Preferred stock accretion	(8,340,628)	(8,743,559)	(11,237,976)
Net loss attributable to common stockholders	$ (27,735,949)	$ (43,081,447)	$ (40,229,499)
Basic and diluted net loss attributable to common stockholders per share	$ (254.33)	$ (196.53)	$ (153.54)
Weighted average common shares outstanding—basic and diluted	109,053	219,213	262,013
Unaudited pro forma basic and diluted net loss per share attributable to common stockholders assuming conversion of preferred stock and conversion of convertible debt			$ (2.06)
Unaudited pro forma weighted average shares outstanding—basic and diluted			14,068,182

See accompanying notes

TARGACEPT, INC.

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

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

See accompanying notes

TARGACEPT, INC.

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

	Redeemable Convertible Preferred Stock			Common Stock		Capital in Excess of Par Value	Common Stock Warrants	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Deficit
	Series A	Series B	Series C	Shares	Amount					
Balances as of December 31, 2004 (carried forward)	$30,166,741	$39,622,161	$101,988,994	256,816	$ 257	$11,573,677	$213,710	$ (134,753,508)	$ —	$ (122,965,864)
Issuance of 496,132 shares of Series C redeemable convertible preferred stock at $1.21 per share	—	—	612,281	—	—	—	—	—	—	—
Issuance of 13,611 shares of common stock at $0.001 per share par value, related to exercise of stock options	—	—	—	13,611	13	23,773	—	—	—	23,786
Stock-based compensation	—	—	—	—	—	690,454	—	—	—	690,454
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock	42,744	—	—	—	—	—	—	(42,744)	—	(42,744)
Accreted redemption value for Series A, Series B, and Series C redeemable convertible preferred stock	1,627,500	2,137,744	7,429,988	—	—	—	—	(11,195,232)	—	(11,195,232)
Net loss	—	—	—	—	—	—	—	(28,991,523)	—	(28,991,523)
Comprehensive loss										(28,991,523)
Balances at December 31, 2005	$31,836,985	$41,759,905	$110,031,263	270,427	$ 270	$12,287,904	$213,710	($ 174,983,007)	$ —	($ 162,481,123)

See accompanying notes

TARGACEPT, INC.

STATEMENTS OF CASH FLOWS

	Year ended December 31,		
	2003	2004	2005
Operating activities			
Net loss	$ (19,395,321)	$ (24,025,389)	$ (28,991,523)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization	672,927	766,335	803,185
Loss on disposal of equipment	—	4,199	—
Non-cash compensation expense	65,325	50,623	690,454
Recognition of deferred rent incentive	(402,647)	(402,647)	(402,647)
Realized loss on sale of investments	20,978	87,948	—
Changes in operating assets and liabilities:			
Research fees and accounts receivable	517,030	334,053	366,402
Inventories	51,016	15,880	60,700
Prepaid expenses	(205,054)	(1,091,627)	998,595
Accounts payable and accrued expenses	(326,451)	1,141,221	228,318
Deferred license fee revenue	(269,532)	(1,917,224)	—
Net cash used in operating activities	(19,271,729)	(25,036,628)	(26,246,516)
Investment activities			
Purchase of investments	(84,796,103)	(6,191,930)	(25,500,000)
Proceeds from sale of investments	58,500,000	37,379,107	25,500,000
Purchase of property and equipment	(545,254)	(660,624)	(250,247)
Proceeds from sale of property and equipment	—	38,191	—
Net cash (used in) provided by investing activities	(26,841,357)	30,564,744	(250,247)
Financing activities			
Proceeds from borrowing of long-term debt	—	3,250,000	—
Principal payments on long-term debt	(637,483)	(730,979)	(2,363,350)
Proceeds from issuance of redeemable convertible preferred stock, net of transaction costs	13,767,452	32,900,000	612,281
Proceeds from issuance of common stock	238,954	519,054	23,786
Net cash provided by (used in) financing activities	13,368,923	35,938,075	(1,727,283)
Net (decrease) increase in cash and cash equivalents	(32,744,163)	41,466,191	(28,224,046)
Cash and cash equivalents at beginning of period	44,353,320	11,609,157	53,075,348
Cash and cash equivalents at end of period	$ 11,609,157	$ 53,075,348	$ 24,851,302

See accompanying notes

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS
DECEMBER 31, 2005

1. The Company and Nature of Operations

Targacept, Inc., a Delaware corporation (the Company), was formed on March 7, 1997. The Company is a biopharmaceutical company engaged in the design, discovery and development of a new class of drugs to treat multiple diseases and disorders by selectively targeting a class of receptors known as neuronal nicotinic receptors, or NNRs. Its facilities are located in Winston-Salem, North Carolina.

The accompanying financial statements have been prepared on a going concern basis. The Company has incurred operating losses since its inception and expects to incur substantial additional losses for the foreseeable future. As a result, the Company will require substantial additional funds and plans to seek collaborative agreements, research funding, and private or public equity or debt financing to meet such needs. If such funds are not available, management may need to reassess its plans. Even if the Company does not have an immediate need for additional cash, it may seek access to the private or public equity markets if and when conditions are favorable. There is no assurance that such additional funds will be available for the Company to finance its operations on acceptable terms, if at all.

2. Summary of Significant Accounting Policies

Cash and Cash Equivalents

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

Investments

In accordance with the Company's investment policy, surplus cash is invested with high quality financial institutions in money market accounts, certificates of deposit, and certain other high credit quality financial investments including Government National Mortgage Association and other mortgage-backed securities, Student Loan Auction Rate Securities, United States Government debt and other asset-backed securities with AAA credit ratings. The Company determines the appropriate classification of marketable securities at the time of purchase and reevaluates such designation as of each balance sheet date. All marketable securities entered into during 2004 and 2005 were classified as available-for-sale. Interest and dividend income on investments, as well as realized gains and losses, are included in "Interest and dividend income." There were no unrealized holding gains or losses at December 31, 2004 or 2005. The cost of securities sold is based on the specific identification method.

Research Fees and Accounts Receivable

Substantially all of the Company's research fees and accounts receivable are related to the collaborative research and license agreements discussed in Note 14 and trade sales of Inversine, the Company's sole approved product. All of the Company's trade accounts receivable are due from customers located within the United States. The Company makes judgments with respect to the collectability of trade accounts receivable based on historical experience and current economic trends. Actual collections could differ from those estimates.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

During 2003, 2004 and 2005, the Company recognized revenues of $1,572,000, $2,255,000 and $0, respectively, or 64%, 60% and 0% of net revenues, respectively, from two collaborative research and license agreements discussed in Note 14.

Inventories

Inventories are stated at the lower of cost or market. Cost is determined by the weighted-average method.

Property and Equipment and Intangible Assets

Property and equipment consists primarily of lab equipment, office furniture and fixtures and leasehold improvements and is recorded at cost. Depreciation is computed using the straight-line method over the estimated useful lives of the assets ranging from three to ten years. Lab equipment is typically depreciated over 3-5 years, office furniture and fixtures are typically depreciated over 5-10 years, and leasehold improvements are amortized over the life of the applicable lease.

Intangible assets consist of patents acquired from Layton Bioscience, Inc. The intangible assets are being amortized to research and development expense on a straight-line basis over the remaining useful life of the patents, or a period of 17 years from the date of acquisition.

The Company assesses the net realizable value of its long-lived assets and evaluates such assets for impairment whenever events or changes in business circumstances indicate that the carrying amount of an asset may not be recoverable. An impairment would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. An impairment, if recognized, would be based on the excess of the carrying value of the impaired asset over its fair value. Through December 31, 2005, there has been no such impairment in the Company’s long-lived assets.

Patents

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

Research and Development Expense

Research and development costs are expensed as incurred and include related salaries of, and stock-based compensation for, personnel involved in research and development activities, contractor fees, administrative expenses and allocations of research-related overhead costs. Administrative expenses and research-related overhead costs included in research and development consist of allocations of facility and equipment lease charges, depreciation and amortization of assets, and insurance, legal and supply costs that are directly related to research and development activities.

The Company directly reduces research and development expenses for amounts reimbursed pursuant to cost-sharing agreements. During 2003, 2004 and 2005, research and development expenses were reduced by $131,000, $23,000 and $0, respectively, for costs reimbursed primarily by Dr. Falk Pharma, GmbH under the terms of the collaboration agreement described in Note 14.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

Clinical Trials Accruals

The Company records accruals based on estimates of the services received, efforts expended and amounts owed pursuant to contracts with numerous clinical trial centers and contract research organizations. In the normal course of business, the Company contracts with third parties to perform various clinical trial activities in the ongoing development of potential products. The financial terms of these agreements are subject to negotiation and variation from contract to contract and may result in uneven payment flows. Payments under the contracts depend on factors such as the achievement of certain events, the successful recruitment of patients, the completion of portions of the clinical trial or similar conditions. The objective of the Company's accrual policy is to match the recording of expenses in its financial statements to the actual services received and efforts expended. As such, expense accruals related to clinical trials are recognized based on the Company's estimate of the degree of completion of the event or events specified in the specific clinical study or trial contract.

Transaction Charges

In the first quarter of 2005, the Company recognized general and administrative expense of $1,635,000 for expenses incurred in connection with a terminated public offering, including $1,146,000 in prepaid expenses at December 31, 2004. As of December 31, 2005, the Company had $99,000 of IPO charges in prepaid expenses.

Deferred Rent Incentive

In August 2002, the Company received $2,013,000 as an incentive to lease its current office space. The incentive is being recognized monthly over the life of the lease on a straight-line basis as a reduction to the lease expense in general and administrative expenses. The Company recognized $403,000 of the incentive during each of 2003, 2004 and 2005.

Redeemable Convertible Preferred Stock

The carrying value of redeemable convertible preferred stock is increased by periodic accretions so that the carrying amount will equal the redemption amount at the earliest redemption date. These increases are affected through charges to accumulated deficit.

Fair Value of Financial Instruments

The carrying amounts of cash and cash equivalents, accounts receivable, accounts payable, accrued expenses and redeemable convertible preferred stock are considered to be representative of their respective fair values. The fair value of long-term debt was $4,504,000 and $2,162,000 at December 31, 2004 and 2005, respectively, as compared to the book value of $4,557,000 and $2,193,000 at December 31, 2004 and 2005, respectively. The difference between fair value and book value was attributable to the benefit of the interest grace period on the Company's loan from the City of Winston-Salem. The Company estimates the fair value of long-term debt using discounted cash flows based on its incremental borrowing rates for similar debt.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

Credit Risk

Financial instruments that potentially subject the Company to credit risk consist principally of cash and short-term investments. The Company places its cash and cash equivalents with high-credit quality financial institutions. The Company has established guidelines for investment of its excess cash designed to emphasize safety, liquidity and preservation of capital. At December 31, 2004 and 2005, the Company had deposits with a high credit quality major financial institution in excess of federally insured limits of approximately $53,000,000 and $24,800,000, respectively.

Revenue Recognition

The Company uses revenue recognition criteria in Staff Accounting Bulletin No. 101, *Revenue Recognition in Financial Statements,* as amended by Staff Accounting Bulletin No. 104, *Revenue Recognition (replacement of SAB 101)*. The Company considers a variety of factors in determining the appropriate method of revenue recognition under its collaboration agreements, such as whether the elements of the agreement are separable, whether there are determinable fair values and whether there is a unique earnings process associated with a particular element of an agreement. Research fee revenues are earned and recognized as research is performed and related expenses are incurred. License fees for access to the Company's intellectual property are recognized ratably over the contracted period in accordance with the provisions of the contract. Amounts received in advance of performance are recorded as deferred revenue and amortized in the statement of operations into revenue over the estimated life of the research and development period. Revenues based on the achievement of development and regulatory milestones that carry substantive performance risk are only recognized upon achievement of the milestone event. Product sales revenues are recorded when goods are shipped, at which point title has passed. Revenues from grants are recognized as the Company performs the work and incurs reimbursable costs in accordance with the objectives of the award.

Shipping and Handling Costs

During 2003, 2004 and 2005, $173,000, $174,000 and $175,000, respectively, of shipping and handling costs were included in cost of product sales.

Income Taxes

The liability method is used in accounting for income taxes as required by Statement of Financial Accounting Standards (SFAS) No. 109, *Accounting for Income Taxes*. Under this method, deferred tax assets and liabilities are recognized for operating loss and tax credit carryforwards and for the future tax consequences attributable to the differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the results of operations in the period that includes the enactment date. A

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

valuation allowance is recorded to reduce the carrying amounts of deferred tax assets unless it is more likely than not that such assets will be realized. Currently there is no provision for income taxes, as the Company has incurred net losses to date.

Comprehensive Loss

SFAS No. 130, *Reporting Comprehensive Income*, requires components of other comprehensive loss, including unrealized gains and losses on available-for-sale securities, to be included as part of total comprehensive loss. The components of comprehensive loss are included in the statements of redeemable convertible preferred stock and stockholders' equity (deficit).

Net Loss Per Share Attributable to Common Stockholders

The Company computes net loss per share attributable to common stockholders in accordance with SFAS No. 128, *Earnings Per Share* (SFAS 128). Under the provisions of SFAS 128, basic net loss per share attributable to common stockholders (Basic EPS) is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding. Diluted net loss per share attributable to common stockholders (Diluted EPS) is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares and dilutive common share equivalents then outstanding. Common share equivalents consist of the incremental common shares issuable upon the conversion of preferred stock, shares issuable upon the exercise of stock options and shares issuable upon the exercise of warrants. For the periods presented, Diluted EPS is identical to Basic EPS because common share equivalents are excluded from the calculation, as their effect is antidilutive.

Unaudited Pro Forma Stockholders' Equity and Pro Forma Net Loss Per Share

The Company's Board of Directors has authorized management of the Company to file a registration statement with the Securities and Exchange Commission permitting the Company to sell shares of its common stock to the public in an initial public offering (the IPO). If the IPO is closed at a price per share of at least $11.00 and gross proceeds to the Company are not less than $50,000,000, all of the redeemable convertible preferred stock outstanding at the time of the IPO will automatically convert into 13,832,015 shares of common stock. Unaudited pro forma basic and diluted net loss per share is computed using the weighted average number of common shares outstanding, including the pro forma effects of the conversion of outstanding redeemable convertible preferred stock into shares of the Company's common stock effective upon the completion of the Company's planned IPO as if such conversion had occurred at January 1, 2005, or the date of issuance, if later.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

The following table sets forth the computation of Basic EPS and Diluted EPS:

	Year ended December 31,		
	2003	2004	2005
Historical			
Numerator:			
Net loss attributable to common stockholders	$ (27,735,949)	$ (43,081,447)	$ (40,229,499)
Denominator:			
Weighted average common shares outstanding	109,053	219,213	262,013
Basic and diluted net loss per share attributable to common stockholders	$ (254.33)	$ (196.53)	$ (153.54)
Unaudited pro forma			
Numerator:			
Net loss attributable to common stockholders			$ (28,991,523)
Denominator:			
Shares used above			262,013
Pro forma adjustment to reflect assumed conversion of preferred stock, on a weighted average basis			13,806,169
Shares used to compute pro forma basic and diluted net loss per share attributable to common stockholders			14,068,182
Unaudited pro forma basic and diluted net loss per share attributable to common stockholders			$ (2.06)

The Company has excluded all outstanding stock options and warrants from the calculation of net loss per share attributable to common stockholders because such securities are antidilutive for all periods presented. Had the Company been in a net income position, these securities may have been included in the calculation. These potentially dilutive securities consist of the following on a weighted average basis:

	Year ended December 31,		
	2003	2004	2005
Outstanding common stock options	613,503	1,010,716	1,466,715
Redeemable convertible preferred stock	9,373,431	10,111,066	13,806,169
Outstanding warrants	215,054	215,054	215,054
Total	10,201,988	11,336,836	15,487,938

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

Stock-Based Compensation

The Company has an equity incentive plan, which is described more fully in Note 11. Prior to January 1, 2005, the Company accounted for the plan under the recognition and measurement provisions of APB Opinion No. 25, *Accounting for Stock Issued to Employees,* and related Interpretations, as permitted by FASB Statement No. 123, *Accounting for Stock-Based Compensation (SFAS 123)*. No stock-based employee compensation cost was recognized in the Statement of Operations for the years ended December 31, 2004 as all options granted under the plan to employees had an exercise price equal to the fair market value of the underlying common stock on the date of grant.

Effective January 1, 2005, the Company adopted the fair value recognition provisions of FASB Statement No. 123 (revised 2004), *Share-Based Payment* (SFAS 123R), using the modified-prospective-transition method. Under that transition method, compensation cost recognized in 2005 includes: (a) compensation cost for all stock-based payments granted prior to, but not yet vested as of, January, 1, 2005, based on the grant date fair value estimated in accordance with the original provisions of Statement 123; (b) compensation cost for all stock-based payments granted subsequent to January 1, 2005, based on the grant date fair value estimated in accordance with the provisions of SFAS 123R; and (c) compensation cost for awards modified on April 7, 2005, based on the modification provisions in accordance with SFAS 123R. Results for prior periods have not been restated.

As a result of adopting SFAS 123R effective January 1, 2005, the Company's net loss for the year ended December 31, 2005, is $645,000 higher than if it had continued to account for stock-based compensation under APB Opinion 25.

SFAS 123R also requires the benefits of tax deductions in excess of recognized compensation cost to be reported as a financing cash flow, rather than as an operating cash flow as required under pre-existing literature. This requirement will reduce net operating cash flows and increase net financing cash flows in periods after adoption. While the Company cannot estimate what those amounts will be in the future (because they depend on, among other things, when employees exercise stock options and the tax deductions for the Company at those times), no amount of operating cash flows have been recognized in prior periods for such excess tax deductions because of net operating losses generated since inception.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

2. Summary of Significant Accounting Policies (continued)

The following table illustrates the effect on net income and earnings per share if the Company had applied the fair value recognition provisions of SFAS 123 to options granted under the Company's equity incentive plan in all periods presented. For purposes of this pro forma disclosure, the value of the options is estimated using a Black-Scholes-Merton option pricing formula and amortized to expense over the options' vesting periods.

	Year Ended December 31	
	2003	2004
Net loss attributable to common stockholders, as reported	$ (27,735,949)	$ (43,081,447)
Add: stock-based employee compensation expense included in reported net income, net of related tax effects of $0	65,325	50,623
Deduct: stock-based employee compensation expense determined under fair value based method for all awards, net of related tax effects	(515,405)	(916,988)
Pro forma net loss	$ (28,186,029)	$ (43,947,812)
Net loss per share:		
Basic and diluted, as reported	$ (254.33)	$ (196.53)
Basic and diluted, pro forma	$ (258.46)	$ (200.48)

Recent Accounting Pronouncements

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

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ materially from those estimates.

Reclassifications

Certain reclassifications have been made to the prior year financial statements to conform to the current year presentation. These reclassifications had no impact on net loss.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

3. Inventories

Inventories consisted of the following:

	December 31,	
	2004	2005
Raw materials	$ 53,388	$ 6,400
Finished goods	49,252	35,540
	$ 102,640	$ 41,940

4. Property and equipment

Property and equipment consists of the following:

	December 31,	
	2004	2005
Lab equipment	$ 4,795,050	$ 5,006,167
Office furniture and fixtures	1,438,329	1,474,655
Leasehold improvements	138,790	138,790
	6,372,169	6,619,612
Less: accumulated depreciation	4,109,471	4,872,088
Property and equipment, net	$ 2,262,698	$ 1,747,524

The Company recorded approximately $635,000, $729,000 and $765,000 of depreciation expense during 2003, 2004 and 2005, respectively.

5. Intangible Assets

Intangible assets consist of the following:

	December 31,	
	2004	2005
Patents	$642,000	$ 642,000
Less: accumulated amortization	(91,263)	(129,027)
Total	$550,737	$ 512,973

The Company recognized amortization expense of approximately $38,000 per year in 2003, 2004 and 2005. Based on the Company's current intangible assets, the Company expects to recognize $38,000 of amortization expense in each of the next five years.

6. Accrued Expenses

Accrued expenses consists of the following:

	December 31,	
	2004	2005
Clinical trials costs	$ 965,407	$ 1,688,277
Employee compensation	850,503	1.045.967
Other	124,926	115,503
	$ 1,940,836	$ 2,849,747

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

7. Long-term debt

During 2002, the Company entered into agreements to borrow $500,000 from the City of Winston-Salem and $2,500,000 from R.J. Reynolds Tobacco Company (RJRT). The note payable to the City of Winston-Salem matures on April 19, 2012, is non-interest bearing until April 2007 and, thereafter, bears interest between 5% and 7% depending on the gross revenues of the Company until maturity. No payments are due on the City of Winston-Salem note until the 5-year anniversary of the loan. At that time the Company will initiate monthly repayments of $9,000 over the five-year period until maturity, at which time any remaining principal and interest is then due. The note payable to RJRT accrues interest at 6.6%, and is repayable in monthly payments of $59,403 through the maturity date of May 1, 2006. In January 2004, the Company amended the note agreement with RJRT to allow additional borrowings for up to a total of $2,000,000. The Company was advanced an additional tranche on April 1, 2004 in the amount of $1,027,000. This additional tranche accrues interest at 5.87% and is repayable in monthly payments of $24,000 through the maturity date of April 1, 2008. The Company was advanced the final tranche on December 23, 2004 in the amount of $973,000. This tranche accrues interest at 6.89% and is repayable in monthly payments of $23,000 through the maturity date of January 1, 2009. The Company paid approximately $135,000, $133,000 and $146,000 for interest under the RJRT note during 2003, 2004 and 2005, respectively.

The notes with RJRT are secured by equipment owned by the Company with a book value of approximately $1,488,000, net of accumulated depreciation, at December 31, 2005.

On December 15, 2004, the Company entered into a development agreement with The Stanley Medical Research Institute (SMRI). In connection with the agreement, SMRI paid the Company $1,250,000 in return for the issuance by the Company of a convertible promissory note in an equal principal amount. The note bore interest at 10% per annum. The note's principal balance plus accrued interest of $84,000 was paid in full on August 18, 2005 and the development agreement with SMRI was terminated in December 2005.

Maturities of long-term debt are as follows at December 31, 2005:

2006	$ 783,895
2007	593,070
2008	455,813
2009	121,297
2010	103,182
Thereafter	136,040
	$ 2,193,297

8. Redeemable Preferred Stock

In August 2000, the Company issued 5,000,000 shares of its Series A redeemable convertible preferred stock (the Series A) to RJRT, and completed a private placement of 6,537,634 of its Series B redeemable convertible preferred stock (the Series B) generating cash of $29,073,000, net of offering costs.

In January 2001, the Company issued 29,933 shares of Series B to three consultants in partial payment of consulting fees owed by the Company.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

8. Redeemable Preferred Stock (continued)

In November 2002, the Company completed a private placement of 37,764,180 shares of its Series C redeemable convertible preferred stock (the Series C) and received cash of $45,488,000, net of offering costs.

In March 2003, the Company completed a private placement of an additional 11,404,958 shares of Series C and received cash of $13,767,000, net of offering costs.

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

In May 2005, the Company completed a private placement of an additional 496,132 shares of Series C and received cash of $612,000, net of offering costs.

The following is a summary of the rights, preferences and terms of the Company's outstanding series of redeemable convertible preferred stock:

Conversion

Each share of Series A, Series B and Series C is convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into fully paid and nonassessable shares of the Company's common stock. As of December 31, 2005, conversion of the Series A, Series B and Series C would result in the issuance of 666,667, 2,082,623 and 11,082,725 shares of common stock, respectively. Future sales of equity at prices below the respective conversion prices could result in adjustments to the number of shares of common stock into which each series of preferred stock is convertible.

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

Dividends

Dividends accrue daily on each share of Series C on a cumulative basis at the rate of 8% per annum and are recorded as an increase to Series C and an increase to accumulated deficit. Cumulative dividends may be declared and paid at any time and shall be payable upon

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

8. Redeemable Preferred Stock (continued)

liquidation or redemption. At December 31, 2004 and 2005, cumulative accrued dividends on the Series C stock totaled $9,834,000 and $17,264,000, respectively.

Dividends on the Series A, Series B and Series C are payable when and if declared by the Company's Board of Directors. No dividend may be paid on the common stock without the approval of the holders of a majority of the then outstanding shares of Series A and Series B, considered together on an as-converted basis, and the holders of 65% of the Series C. No dividend may be declared or paid on either the Series A or the Series B unless, simultaneously with such declaration or payment, the same dividend per share is declared or paid on both the Series A and the Series B, as well as the Series C, and any unpaid cumulative dividends on the Series C are declared and paid in full.

Voting

Each holder of the Series A, Series B and Series C is entitled to the number of votes equal to the number of shares of common stock into which such holder's shares are convertible on the applicable record date. In addition, certain actions by the Company require the approval of one or more of (i) the holders of a majority of the outstanding shares of Series A, (ii) the holders of at least two-thirds of the outstanding shares of Series B, (iii) the holders of a majority of the outstanding shares of Series A and Series B, considered together on an as-converted basis, and/or (iv) the holders of at least 65% of the outstanding shares of Series C.

Liquidation Preference

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

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

Mandatory Redemption

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

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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

8. Redeemable Preferred Stock (continued)

the holders of a majority of the outstanding shares of Series A (in the case of Series A) or a majority of the outstanding shares of Series B (in the case of Series B) shall be redeemed in an amount per share equal to $4.65 (subject to certain adjustments) plus (i) any previously declared but unpaid dividends on such share and (ii) an amount equal to $0.081375 per share (subject to certain adjustments) multiplied by the number of complete three-month periods that have elapsed from the date such share was originally issued to the redemption date. The Company may satisfy its redemption obligation with respect to the Series A and/or the Series B in cash or by paying a portion in cash and issuing a promissory note that meets certain prescribed conditions for the remaining amount.

9. Stockholders' Equity (Deficit)

On March 14, 2003, the Company amended its Certificate of Incorporation to increase the number of authorized shares of common stock to 11,333,333 and preferred stock to 60,736,705 and issued 11,404,958 shares of Series C.

On December 6, 2004, the Company amended its Certificate of Incorporation to increase the number of authorized shares of common stock to 16,666,666 and preferred stock to 93,309,532 and issued 27,272,728 shares of Series C.

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

In conjunction with the issuance of Series A, the Company issued a warrant to purchase 215,054 shares of the Company's common stock at an original exercise price of $34.88 per share (subject to certain adjustments). In connection with the Company's issuance of Series C and price adjustment provisions of the warrant, the conversion price of the warrant was adjusted to $14.63. The warrant is exercisable only upon the earlier of an initial public offering or a change in control. The fair value of the warrant is a direct cost of obtaining capital. As such, the fair value has been recorded in stockholders' equity, with the offset recorded as a decrease in the redemption value of the Series A. The Company will accrete to the redemption value of the Series A at the earliest date of redemption, or until November 2008, through an increase in redemption value to Series A and an increase to retained deficit. The fair value of the warrant to purchase 215,054 shares of the Company's common stock was estimated at the grant date to be $213,710 or $0.99 per share. The Company considered the anti-dilution features, the contingencies surrounding the limited opportunities for exercise, and the warrant's priorities over common stock options in relation to the fair value of the Company's common stock at the date of issuance when estimating the fair value of the warrant.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

9. Stockholders' Equity (Deficit) (continued)

At December 31, 2004 and 2005, the Company had reserved shares of common stock for future issuance as follows:

	December 31,	
	2004	2005
Convertible preferred stock	13,760,548	13,832,015
Warrant	215,054	215,054
Options	1,028,086	1,664,474
	15,003,688	15,711,543

10. Income Taxes

There is no income tax provision (benefit) for federal or state income taxes as the Company has incurred operating losses since inception.

The Company's effective tax rate differs from the federal income tax rate for the following reasons:

	Year Ended December 31,		
	2003	2004	2005
Expected federal income tax benefit at statutory rate	(34)%	(34)%	(34)%
Increase (decrease) resulting from:			
Research and development credits	(6)	(3)	(3)
State income tax expense, net of federal benefit	(5)	(5)	(4)
Net operating loss and credit limitations	3	—	—
Change in valuation allowance	41	42	41
Other	1	—	—
	— %	— %	— %

At December 31, 2003, 2004 and 2005, the Company had net operating loss carryforwards for federal income tax purposes of approximately $45,606,000, $70,866,000 and $98,333,000, respectively, and for state income tax purposes of approximately $45,627,000, $70,887,000 and $98,349,000, respectively, and research and development federal income tax credits of approximately $638,000, $1,357,000 and $2,131,000, respectively. The federal net operating loss carryforwards begin to expire in 2020. State net operating loss carryforwards begin to expire in 2015. The research and development tax credits begin to expire in 2021.

Utilization of the net operating loss carryforwards and credits may be subject to a substantial annual limitation due to ownership change limitations provided by Section 382 of the Internal Revenue Code of 1986, as amended, and similar state provisions. As a result of a series of stock issuances, the Company had such an ownership change on November 30, 2002. Consequently, an annual limitation is imposed on the Company's use of net operating loss and credit carryforwards attributable to periods before the change.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

10. Income Taxes (continued)

for income tax purposes. The Company's net deferred tax assets relate primarily to its net operating loss carryforwards. A valuation allowance has been recognized to offset the deferred tax assets related primarily to its net operating loss carryforward. If and when recognized, the tax benefit for those items will be reflected in current operations of the period in which the benefit is recorded as a reduction of income tax expense. The utilization of the loss carryforwards to reduce future income taxes will depend on the Company's ability to generate sufficient taxable income prior to the expiration of the net operating loss carryforwards. For the years ended December 31, 2003, 2004 and 2005, the valuation allowance increased approximately $8,050,000, $9,600,000 and $11,750,000, respectively.

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

	December 31,	
	2004	2005
Deferred tax assets:		
Net operating loss carryforward	$ 24,787,121	$ 35,299,808
Research and development tax credit	1,357,135	2,130,640
Patents	577,974	914,069
Stock based compensation	—	88,129
Total gross deferred tax assets	26,722,230	38,432,646
Valuation allowance	(26,599,098)	(38,347,057)
Net deferred tax asset	123,132	85,589
Deferred tax liabilities:		
Equipment and other	(123,132)	(85,589)
Net deferred tax asset	$ —	$ —

11. Equity Incentive Plan

On August 22, 2000, the Company established an equity incentive plan (the Plan) and authorized the issuance of up to 268,168 shares under the Plan to attract and retain employees, directors and certain independent contractors, consultants and advisors and to allow them to participate in the growth of the Company. During 2001, the number of shares authorized for issuance under the Plan was increased to 348,168. In conjunction with the November 2002 Series C financing, the Company authorized the issuance of an additional 400,000 shares, increasing the number of authorized shares to 748,168. Upon the issuance of the additional Series C shares in March 2003, the number of authorized shares was increased to 1,228,888. In March 2005, the number of authorized shares was increased to 1,878,888. Awards may be made to participants under the Plan in the form of incentive and nonqualified stock options, restricted stock, stock appreciation rights, stock awards, and performance awards. Eligible participants under the Plan include employees, directors and certain independent contractors, consultants or advisors of the Company or a related corporation. The vesting periods for awards made under the Plan are determined at the discretion of the Plan administrator and range from 0 to 5 years. Awards made under the Plan have 10-year contractual terms or, in some cases, shorter terms designed to comply with Section 409A of the Internal Revenue Code. The exercise price of incentive options granted under the Plan may not be less than 100% of the fair market value of the common stock on the date of grant, as determined by the Plan administrator.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

11. Equity Incentive Plan (continued)

On April 7, 2005 the Company's Board of Directors authorized an amendment to each stock option agreement held by current employees that changed the exercise price per share for each unvested portion as of March 31, 2005 to $1.75. As of March 31, 2005, there were 354,672 shares issued to 75 employees subject to the unvested portions of employee options ranging from an original option price of $5.10 to $5.63 that were affected by the amendments. Each affected option is required to be accounted for as a modification of an award under SFAS 123R. The fair market value was calculated immediately prior to the modification and immediately after the modification to determine the incremental fair market value. This incremental value of $147,000 and the fair market value of each modified option will be expensed as compensation on a quarterly basis, until the date that the option is exercised or forfeited or expires unexercised.

The Company uses the Black-Scholes-Merton formula to estimate the fair value of its stock-based payments. The volatility assumption used in the Black-Scholes-Merton formula is based on the calculated historical volatility of twelve benchmark biotechnology companies that have been identified as comparable public entities. The expected term of options granted is derived from the simplified method allowable under SEC Staff Accounting Bulletin No. 107. Under this approach, the expected term would be the mid-point between the weighted average of vesting period and the contractual term. The risk-free rate for periods within the contractual life of the option is based on the U.S. Treasury yield curve in effect at the time of grant.

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

	Year Ended December 31,	
	2004	2005
Dividend yield	—	—
Risk-free interest rate	3.0%	4.1%
Volatility	0.8	0.7
Expected life	4 years	6.25-6.5 years

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

11. Equity Incentive Plan (continued)

A summary of option activity under the Plan and changes during the periods are presented below:

	Options Granted	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at January 1, 2003	307,548	$ 4.43		
Granted	799,479	5.03		
Forfeited	(4,797)	1.95		
Exercised	(61,092)	3.90		
Outstanding at December 31, 2003	1,041,138	4.88		
Granted	65,200	5.33		
Forfeited	(6,066)	21.53		
Exercised	(112,472)	4.73		
Outstanding at December 31, 2004	987,800	4.88		
Granted	653,743	1.76		
Forfeited	(17,923)	5.00		
Exercised	(13,611)	1.75		
Outstanding at December 31, 2005	1,610,009	$ 2.88	8.0	$ 46,764
Vested and exercisable at December 31, 2005	979,784	$ 3.61	7.6	$ 37,614

The weighted average grant date fair value for an option granted during 2003, 2004 and 2005 was $3.08, $5.33 and $1.20, respectively. The total intrinsic value of options exercised during the year ended December 31, 2005 was $13,047.

A summary of the status of the Company's non-vested shares as of December 31, 2005, and changes during year ended December 31, 2005, is presented below:

Non-vested Options	Options Granted	Weighted-Average Grant-Date Fair Value
Non-vested at January 1, 2005	401,148	$ 3.00
Granted	653,743	1.20
Vested	(418,913)	2.93
Forfeited	(5,753)	3.06
Non-vested at December 31, 2005	630,225	1.18(a)

(a) Reflects the April 7, 2005 amendment that decreased the weighted average fair value of 354,672 shares subject to unvested options from $3.08 to $1.02 per option.

As of December 31, 2005, there was $989,000 of total unrecognized compensation cost related to non-vested stock-based compensation arrangements granted under the Plan. That cost is expected to be recognized over a weighted-average period of 3.3 years. The total fair value of shares vested during the twelve months ended December 31, 2005 was $1,016,000.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

11. Equity Incentive Plan (continued)

During 2004, the Company granted options to purchase 10,333 shares of common stock at an exercise price of $0.08, below the fair value of $5.63 per share of common stock. During 2005, the Company granted options to purchase 6,000 shares of common stock at an exercise price of $0.08, below the fair value of $1.75 per share of common stock. The fair value of these shares was recorded as compensation expense in the amounts of $51,000 and $46,000 during the twelve months ended December 31, 2004 and 2005, respectively.

12. Leases

On March 1, 2002, the Company entered into an agreement with Wake Forest University to lease an office and research facility in Winston-Salem, North Carolina with an initial term that extends through July 31, 2007. The lease contains a renewal option for up to one additional five-year term, with a lease rate similar to the original agreement. In December 2004, the Company amended the terms of the lease to include 1,000 square feet and an option on additional space in this facility. The lease amendment increased annual rent by $15,000 per year and included a $37,000 hold fee in the first year. Rent expense incurred by the Company under this lease was approximately $1,456,000, $1,456,000 and $1,500,000 for the years ended December 31, 2003, 2004 and 2005, respectively. Rent expense is offset by the monthly recognition of the deferred rent incentive discussed in Note 2. At December 31, 2005, the Company has the following future minimum lease payments in relation to this lease:

2006	$ 1,470,552
2007	857,822
2008 and thereafter	—
	$ 2,328,374

13. Retirement Savings Plan

The Company has a 401(k) retirement plan that covers substantially all of its employees. This plan provides for the Company to make 100% matching contributions up to a maximum of 6% of employees' eligible compensation. The Company contributed approximately $298,000, $368,000 and $412,000 to the plan for the years ended December 31, 2003, 2004 and 2005, respectively.

14. Collaborative Research and License Agreements

Aventis Pharma

In December 1998, the Company entered into a collaborative research and license agreement with Aventis Pharma whereby the Company and Aventis agreed to collaborate on the discovery, development and commercialization of nicotinic agonists for use in prevention of certain human diseases. Under the agreement, as restated in January 2002, Aventis was granted a license under certain patent rights and knowledge to develop, manufacture and commercialize certain compounds. The agreement provided for the payment of research fees on a "fee for service" basis for development work that the Company agreed to perform. For the years ended December 31, 2003, 2004 and 2005, these fees were approximately $1,303,000, $338,000 and $0, respectively. The Company was entitled to receive milestone payments under the contract at

14. Collaborative Research and License Agreements (continued)

specified dates during the development period. The Company did not receive milestone payments under the agreement during 2003, 2004 or 2005. In addition, Aventis agreed to make royalty payments based on net sales of products developed and sold. In general, either party could terminate the agreement in the event of a material breach by the other party, including a material breach of research obligations or the issuance of third-party patent rights to a competitor. Additionally, Aventis could terminate the agreement without cause by providing the Company with 30 days, written notice at any time after the research term, in which case all rights to the product candidate would revert to the Company. All royalty and other payment obligations of the parties survive any termination of the agreement.

During 1999, the Company received a one-time non-refundable license fee payment of $2,000,000 to enter into this agreement. During 2003 and 2004, the product candidate subject to the agreement had not completed the research and clinical development process. Accordingly, the Company has deferred recognition of the license fee and was amortizing it over the expected term of the research and development period. On December 3, 2004, Aventis provided the Company with 30 days advance written notice of Aventis' plans to terminate the collaborative research and license agreement. The agreement was terminated effective January 2, 2005 and was within the provisions of termination clauses of the agreement. As a result of the termination of the agreement, the Company recognized the remaining deferred revenue of $825,000 related to the agreement during the fourth quarter of 2004, as there were no further responsibilities or duties to be performed under the agreement as of December 31, 2004.

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

Dr. Falk Pharma

On January 26, 2001, the Company entered into a collaborative research development and license agreement with Dr. Falk Pharma GmbH, a German corporation, pursuant to which the parties agreed to collaborate to research, develop and commercialize nicotinic therapeutics for use in the prevention or treatment of ulcerative colitis and other gastrointestinal and liver diseases. Upon execution of the agreement, Dr. Falk Pharma paid the Company a $1,000,000 upfront license fee and purchased 14,815 shares of the Company's common stock for $1,000,000. The Company deferred recognition of the upfront license fee payment and was amortizing it over the expected term of the research and development period. To account for the $1,000,000 in proceeds for the common stock, the Company used the estimated fair value of the common stock to value the shares issued to arrive at a total equity value of $76,000, with the remaining proceeds of $924,000 allocated to deferred revenue. This deferred revenue was also being amortized over the expected term of the research and development period.

The Company and Dr. Falk Pharma mutually agreed to discontinue the development of the lead compound subject to the collaboration agreement, resulting in the recognition of the

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

14. Collaborative Research and License Agreements (continued)

remaining deferred revenue of $890,000 during the fourth quarter of 2004, and terminated the collaboration agreement in November 2005. The Company recognized $170,000 and $1,017,000 of deferred revenue under this agreement during 2003 and 2004, respectively.

Stanley Medical Research Institute

On December 15, 2004, the Company entered into a development agreement with The Stanley Medical Research Institute (SMRI). In connection with the agreement, SMRI paid the Company $1,250,000 in return for the issuance by the Company of a convertible promissory note in an equal principal amount. The note bore interest at 10% per annum. In August 2005, the Company re-paid the promissory note in full. The Company and SMRI terminated the development agreement in December 2005.

AstraZeneca AB

In December 2005, the Company entered into a collaborative research and license agreement with AstraZeneca AB under which the Company granted AstraZeneca exclusive development and worldwide commercialization rights to the Company's product candidate known as TC-1734 as a treatment for Alzheimer's disease, cognitive deficits in schizophrenia and potentially other conditions marked by cognitive impairment such as attention deficit hyperactivity disorder, age associated memory impairment and mild cognitive impairment. The collaboration agreement also provides for a multi-year preclinical research collaboration to be conducted by the Company and AstraZeneca.

The Company is eligible to receive future research fees, license fees and milestone payments under its collaboration agreement with AstraZeneca. The amount of research fees, license fees and milestone payments will depend on the extent of the Company's research activities and the timing and achievement of development, regulatory and first commercial sale milestone events. AstraZeneca paid the Company an initial fee of $10 million in February 2006. Based on the collaboration agreement terms, the Company allocated $5 million of the initial fee to the research collaboration, which the Company expects to recognize as revenue over the four-year term of the research collaboration. The Company deferred recognition of the remaining $5 million of the initial fee, which was allocated to the TC-1734 license grants, until AstraZeneca makes a determination whether to conduct Phase II clinical development of TC-1734 following the completion of additional safety and product characterization studies that AstraZeneca is conducting. If AstraZeneca decides to conduct a Phase II clinical trial of TC-1734 following the completion of the safety and product characterization studies, the Company would recognize the deferred $5 million of the initial fee as revenue over the expected development period for TC-1734. The Company expects to recognize any revenue based on the achievement of milestones under the collaboration agreement upon achievement of the milestone event, if the Company determines that the revenue satisfies the revenue recognition requirements of SEC Staff Accounting Bulletin, or SAB, No. 101, *Revenue Recognition Financial Statements*, as amended by SAB No. 104. SAB No. 101 requires that four basic criteria must be met before revenue can be recognized: persuasive evidence of an arrangement exists; delivery has occurred or services have been rendered; the fee is fixed and determinable; and collectability is reasonably assured. The Company will record research fees that the Company receives from

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NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

14. Collaborative Research and License Agreements (continued)

AstraZeneca while it is conducting the safety and product characterization studies on TC-1734 as deferred revenue. The Company expects to receive approximately $2.5 million (unaudited) in research fees from AstraZeneca while AstraZeneca is conducting the safety and product characterization studies of TC-1734. If the agreement continues in effect following the completion of the additional safety and product characterization studies that AstraZeneca is conducting, the Company will recognize all research fees previously recorded as deferred revenue and recognize future research fee revenues as the research is performed and related expenses are incurred. In that event, the Company would be entitled to receive at least an additional $21.2 million (unaudited) in research fees. Based on the current research budget, the Company would expect to receive an additional $23.9 million (unaudited) in research fees.

If AstraZeneca terminates the collaboration agreement upon completion of any or all of the additional safety and product characterization studies, the Company would be required to reimburse AstraZeneca for the amount of all research fees that it paid to the Company under the research collaboration under the agreement while AstraZeneca conducted the studies. In addition, the Company would be required to pay AstraZeneca an additional $5 million as compensation for assigning to it the data and any intellectual property generated in the studies. In that event, upon final termination by AstraZeneca in accordance with the terms of the Agreement, the Company would reduce deferred revenue by $5 million.

The Company's collaboration agreement with AstraZeneca became effective on January 20, 2006. AstraZeneca paid the Company an initial fee of $10 million in February 2006.

15. Related Party Transactions

RJRT is the holder of 5,000,000 shares of Series A redeemable preferred stock convertible to 666,667 shares of common stock, 1,652,893 shares of Series C redeemable preferred stock convertible to 238,095 shares of common stock, a warrant to purchase 215,054 shares of common stock, 3,333 shares of common stock, and options to purchase 5,230 shares of common stock. The Company has entered into the following transactions and agreements with RJRT in the ordinary course of business.

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

The Company was advanced the final tranche on December 23, 2004 in the amount of $973,000. This tranche accrues interest at 6.89% and is repayable in monthly payments of $23,000 through the maturity date of January 1, 2009. Under this related party note payable, the Company paid RJRT $772,000, $846,000 and $1,259,000 during 2003, 2004 and 2005, respectively.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

15. Related Party Transactions (continued)

The notes are secured by equipment owned by the Company with a book value of approximately $1,488,000 net of accumulated depreciation, at December 31, 2005.

A member of the Company's board of directors serves as an officer of RJRT. Equity compensation for such director's service has been made, at the director's request, directly to RJRT. The numbers of shares subject to stock options granted to RJRT during the years ended December 31, 2003, 2004 and 2005 in connection with the director's services are 1,000 shares per year. In connection with the issuance of the stock options, the Company recognized compensation expense of $2,512, $4,247 and $4,656 during 2003, 2004 and 2005, respectively.

Prior to December 31, 2003, the Company used the services of a RJRT employee for toxicology studies and purchased materials used for research and development and copy and print services through RJRT. The Company paid RJRT $201,000 for these services during 2003. During 2004 and 2005 the Company continued to use copy and print services totaling $79,000 and $71,000, respectively.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(CONTINUED)

16. Selected Quarterly Financial Data (unaudited)

	2004 Quarter			
	First	Second	Third	Fourth
Net revenue	$ 496,939	$ 528,026	$ 555,583	$ 2,157,826
Gross profit on product sales	6,060	494,780	55,697	11,600
Operating loss	(6,843,593)	(6,485,006)	(6,664,381)	(4,400,447)
Net loss	(6,637,935)	(6,481,318)	(6,617,687)	(4,288,449)
Net loss attributable to common stockholders	(8,779,826)	(8,623,208)	(8,759,577)	(16,918,836)
Basic and diluted net loss per share attributable to common stockholders(1)	$ (59.18)	$ (38.76)	$ (34.94)	$ (66.46)
Weighted average common shares outstanding—basic and diluted	148,345	222,504	250,710	254,556

	2005 Quarter			
	First	Second	Third	Fourth
Net revenue	$ 303,233	$ 299,646	$ 338,310	$ 238,728
Gross profit (loss) on product sales	157,518	62,477	39,768	(59,411)
Operating loss(2)	(7,656,423)	(8,339,228)	(7,170,082)	(6,775,183)
Net loss	(7,437,771)	(8,105,493)	(6,920,200)	(6,528,059)
Net loss attributable to common stockholders	(10,239,660)	(10,913,785)	(9,734,099)	(9,341,955)
Basic and diluted net loss per share attributable to common stockholders(1)	$ (39.51)	$ (41.95)	$ (37.28)	$ (35.29)
Weighted average common shares outstanding—basic and diluted	259,173	260,140	261,094	264,739

Diluted EPS is identical to Basic EPS since common stock equivalent shares are excluded from the calculation, as their effect is anti-dilutive.

(1) Per common share amounts for the quarters and full years have been calculated separately. Accordingly, quarterly amounts do not add to the annual amount because of differences in the weighted average common shares outstanding during each period principally due to the effect of the Company's issuing shares of its common stock during the year.

(2) Net loss for the first quarter of 2005 includes $1,635,000 of expenses incurred in connection with a public offering that was terminated.

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

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Until May 6, 2006 (25 days after the date of this prospectus), all dealers that effect transactions in these securities, whether or not participating in this offering, may be required to deliver a prospectus. This is in addition to the dealer's obligation to deliver a prospectus when acting as an underwriter and with respect to unsold allotments or subscriptions.

5,000,000 Shares

Common Stock

Deutsche Bank Securities

Pacific Growth Equities, LLC

CIBC World Markets

Lazard Capital Markets

Prospectus

April 11, 2006