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As filed with the Securities and Exchange Commission on July 9, 2004

Registration No. 333-115538

UNITED STATES SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Amendment No. 2 to
Form S-1

REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

Targacept, Inc.

(Exact name of registrant as specified in its charter)

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

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

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

Copies to:

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

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

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

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

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

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

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

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

PROSPECTUS (Subject to Completion)
Issued July 9, 2004

Shares

COMMON STOCK

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

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

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

PRICE $ A SHARE

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

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

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

Morgan Stanley & Co. Incorporated expects to deliver the shares to purchasers on , 2004.

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

, 2004

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

Until , 2004, 25 days after the commencement of this offering, all dealers that buy, sell or trade shares of our common stock, whether or not participating in this offering, may be required to deliver a prospectus. This delivery requirement is in addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

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

PROSPECTUS SUMMARY

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

TARGACEPT, INC.

We are a biopharmaceutical company engaged in the design, discovery and development of a new class of drugs to treat multiple diseases and disorders of the nervous system by selectively targeting neuronal nicotinic acetylcholine receptors, or NNRs. NNRs are found on nerve cells throughout the nervous system and serve as key regulators of nervous system activity. Our product candidates are designed to selectively target specific NNR subtypes to promote positive medical effects while limiting or eliminating adverse side effects. In addition to a marketed product, Inversine, we have four product candidates in clinical development and multiple ongoing preclinical programs. Our pipeline includes:

- TC-1734—in Phase II clinical trials for the treatment of cognitive impairment in elderly persons;
- TC-5231—in Phase II clinical trials for the treatment of attention deficit hyperactivity disorder, commonly referred to as ADHD;
- TC-2403—in a Phase II clinical trial for the treatment of a form of inflammatory bowel disease known as ulcerative colitis;
- TC-2696—in a Phase I clinical trial for the treatment of pain; and
- preclinical research programs in Alzheimer's disease, schizophrenia, depression and anxiety, smoking cessation and obesity.

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

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

We have entered into two collaboration agreements with Aventis Pharma SA relating to the development of treatments for Alzheimer's disease and other diseases of the central nervous system. In addition, we have entered into a collaboration agreement with Dr. Falk Pharma GmbH relating to the development of a treatment for ulcerative colitis.

Our Product Development Pipeline

TC-1734. TC-1734 is a novel small molecule that we are developing as an oral treatment for a range of cognitive impairment in the elderly that includes age associated memory impairment, commonly referred to as AAMI, and mild cognitive impairment, commonly referred to as MCI. In 2003, we evaluated TC-1734 in 84 healthy volunteers in four Phase I clinical trials. We are currently conducting a Phase II clinical trial of TC-1734 in 56 elderly persons classified with AAMI and have completed two arms of the trial. We are also currently conducting a Phase II clinical trial in 40 elderly persons classified with MCI. Subject to the results of discussions with the United States Food and Drug Administration, or the FDA, we anticipate commencing a separate Phase II clinical trial designed to evaluate the efficacy of TC-1734 in the fourth quarter of 2004. We are also evaluating TC-1734 for potential additional clinical development for indications marked by cognitive impairment that are not specific to the elderly, such as ADHD, schizophrenia and various forms of dementia.

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

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

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

Our Business Strategy

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

- *Develop and commercialize drugs that selectively target specific NNR subtypes.* Based on our understanding of the role of NNRs in the nervous system, we believe that drugs designed to selectively target specific NNR subtypes can have positive medical effects with limited or no adverse side effects. We believe that our four product candidates in clinical development may exhibit these attributes and we are aggressively pursuing their development.
- *Remain at the forefront of the commercialization of NNR research*. We have established ourselves as a leader in NNR research over the last 20 years. We intend to continue to invest significant resources to build upon our NNR expertise and to expand our intellectual property portfolio.

- *Identify and prioritize indications in which drugs that selectively target specific NNR subtypes can be exploited for medical benefit*. We have identified numerous indications in which NNRs have been implicated and for which we believe drugs that selectively target specific NNR subtypes can provide a medical benefit. We prioritize our product development in an effort to sustain our product pipeline.
- *Collaborate selectively to develop and commercialize product candidates.* We intend to selectively enter into collaboration agreements with leading pharmaceutical and biotechnology companies to assist us in furthering the development of our product candidates. In entering into these collaboration agreements, our goal will be to maintain co-promotion or co-commercialization rights in the United States and, in some cases, other markets.
- *Build a specialized sales and marketing organization.* We intend to build an internal sales and marketing organization for target indications in which specialists heavily influence the market, particularly neurology and psychiatry. We believe that we can effectively serve these markets with a specialized sales force, enabling us to retain greater value from our product candidates that receive marketing approval than if we relied on a third party's sales force.

Risks Associated with Our Business

Our business is subject to numerous risks, as more fully described in the section entitled "Risk Factors" immediately following this prospectus summary. We have a limited operating history and have incurred substantial net losses since our incorporation in 1997. We expect to continue to incur substantial losses for the foreseeable future. Inversine is the only product that we have available for commercial sale, and it generates limited revenues. All of our other product candidates are undergoing clinical trials or are in early stages of development, and failure is common and can occur at any stage of development. None of our product candidates, other than Inversine, has received regulatory approval for marketing and sale. Our ability to generate product revenue in the future will depend heavily on the successful development and commercialization of these product candidates. Even if we succeed in developing and commercializing one or more of our product candidates, we may never generate sufficient sales revenue to achieve and then sustain profitability.

Company History

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

THE OFFERING

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

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

- 73,739,905 shares of common stock issuable upon conversion of all currently outstanding shares of our series A, series B and series C convertible preferred stock concurrently with the completion of this offering; and
- shares of common stock issuable upon the exercise of an outstanding warrant that will expire if not exercised concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share. The cash exercise price of the warrant is $ per share.

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

- 8,024,394 shares of common stock issuable upon the exercise of options outstanding as of March 31, 2004, at a weighted average exercise price of $0.64 per share, of which options to purchase 4,078,011 shares were exercisable; and
- 448,274 shares of common stock reserved for future grant under our 2000 equity incentive plan as of March 31, 2004.

Unless otherwise indicated, all information in this prospectus assumes:

- no exercise by the underwriters of their over-allotment option to purchase up to shares of our common stock;
- the conversion of all outstanding shares of our convertible preferred stock into 73,739,905 shares of common stock concurrently with the completion of this offering; and
- the issuance of shares of common stock upon the exercise of an outstanding warrant that will expire if not exercised concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share.

In addition, unless otherwise noted, all information in this prospectus gives effect to the one-for- reverse stock split of our common stock that will be effective prior to the completion of this offering.

SUMMARY FINANCIAL DATA

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

The pro forma net loss attributable to common stockholders per share information is computed using the weighted average number of common shares outstanding, after giving pro forma effect to the conversion of all outstanding shares of our convertible preferred stock into 73,739,905 shares of common stock concurrently with the completion of this offering, as if the conversion had occurred at the date of the original issuance. This pro forma information does not give effect to the exercise of an outstanding warrant.

	Year ended December 31,			Three months ended March 31,	
	2001	2002	2003	2003	2004
					(unaudited)
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Net revenue	$ 1,703	$ 2,286	$ 2,458	$ 691	$ 497
Operating expenses:					
Research and development	8,152	16,244	18,179	4,069	6,050
General and administrative	2,302	4,135	3,600	697	1,109
Cost of product sales	—	244	743	200	182
Purchased in-process research and development	—	2,666	—	—	—
Total operating expenses	10,454	23,289	22,522	4,966	7,341
Loss from operations	(8,751)	(21,003)	(20,064)	(4,275)	(6,844)
Interest and dividend income	1,449	88	791	124	231
Interest expense	—	(103)	(122)	(34)	(25)
Loss on disposal of fixed assets	—	(54)	—	—	—
Net loss	(7,302)	(21,072)	(19,395)	(4,185)	(6,638)
Preferred stock accretion	(3,808)	(4,173)	(8,341)	(1,915)	(2,142)
Net loss attributable to common stockholders	$ (11,110)	$ (25,245)	$ (27,736)	$ (6,100)	$ (8,780)
Basic and diluted net loss per share applicable to common stockholders	$ (26.80)	$ (45.28)	$ (33.91)	$ (9.48)	$ (7.89)
Shares used to compute basic and diluted net loss per share	414,624	557,492	817,894	643,571	1,112,591
Pro forma basic and diluted net loss per share applicable to common stockholders (unaudited)			$ (0.27)		$ (0.09)
Shares used to compute pro forma basic and diluted net loss per share (unaudited)			71,118,629		74,852,496

The pro forma balance sheet information gives effect to the conversion of all outstanding shares of our convertible preferred stock into 73,739,905 shares of common stock concurrently with the completion of this offering. The pro forma as adjusted balance sheet information gives further effect to:

- our sale of shares of common stock in this offering at an assumed initial public offering price of $ per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us; and
- our issuance of shares of common stock upon the exercise of an outstanding warrant that will expire if not exercised concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share. The cash exercise price of the warrant is $ per share.

	As of March 31, 2004		
	Actual	Pro Forma	Pro Forma As Adjusted
		(unaudited) (in thousands)	
Balance Sheet Data:			
Cash, cash equivalents and short-term investments	$ 36,847	$ 36,847	
Working capital	33,663	33,663	
Total assets	40,806	40,806	
Long-term debt, net of current portion	1,298	1,298	
Redeemable convertible preferred stock	132,276	—	
Accumulated deficit	(82,818)	(82,818)	
Total stockholders' equity (deficit)	(99,510)	32,766	

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 March 31, 2004, we had an accumulated deficit of $82.8 million. Our net loss was $6.6 million for the three months ended March 31, 2004, $19.4 million for the year ended December 31, 2003 and $21.1 million for the year ended December 31, 2002. Our losses have resulted principally from costs incurred in connection with our research and development activities, including clinical trials, and from general and administrative expenses associated with our operations. We expect to continue to incur substantial losses for the foreseeable future. We expect our research and development expenses to increase substantially following completion of this offering as we expand our clinical trial activity and as our product candidates advance through the development cycle. We also expect our general and administrative costs to increase substantially as we expand our infrastructure. As a result, we will need to generate significant revenues to pay these costs and achieve profitability.

Inversine is our only current source of product revenue. We acquired the rights to Inversine in August 2002. Sales of Inversine generated revenues of only $188,000 for the three months ended March 31, 2004 and $815,000 for the year ended December 31, 2003. Inversine is approved in the United States for the treatment of moderately severe to severe essential hypertension, a high blood pressure disorder with an unknown cause. However, we believe that the substantial majority of Inversine sales are derived from prescriptions written by a very limited number of physicians for the treatment of Tourette's syndrome and other neuropsychiatric disorders. If any of these physicians were to change their prescribing habits, Inversine sales would suffer. We do not expect that sales of Inversine will increase substantially in the future.

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

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

We will require substantial future capital in order to continue to conduct the research and development and clinical and regulatory activities necessary to bring our product candidates to market and to establish marketing and sales capabilities. Our future capital requirements will depend on many factors, including:

- the scope, progress, results and cost of preclinical development and laboratory testing and clinical trials;
- the costs, timing and outcomes of regulatory reviews;
- the number and characteristics of product candidates that we pursue;

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

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

Our current operating plan provides for us to continue, either alone or with a collaborator, to advance our four product candidates currently in clinical development through the development process. It is also our objective to continue to invest in our preclinical programs and to file at least one investigational new drug application, or IND, or foreign equivalent each year beginning in 2005. We do not expect our existing capital resources and the net proceeds from this offering to be sufficient to enable us to fund the completion of the development of any of our product candidates. We expect that our existing capital resources and the net proceeds from this offering will enable us to maintain currently planned operations through June 2006. However, our operating plan may change as a result of many factors including those described above, and we may need additional funds sooner than planned to meet operational needs and capital requirements for product development and commercialization. Other than a modest amount of committed equipment financing, we currently have no credit facility or committed sources of capital. Additional funds may not be available when we need them on terms that are acceptable to us, or at all. If adequate funds are not available on a timely basis, we may:

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

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

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

Inversine is our only marketed product and generates limited revenues. Our most advanced product candidates are in Phase I or Phase II clinical trials. Our ability to generate product revenue in the future will depend heavily on the successful development and commercialization of these product candidates. Our other product candidates are in various stages of preclinical development. Any of our product candidates could be unsuccessful if it:

- does not demonstrate acceptable safety and efficacy in preclinical studies or clinical trials or otherwise does not meet applicable regulatory standards for approval;

- does not offer therapeutic or other improvements over existing or future drugs used to treat the same conditions;
- is not capable of being produced in commercial quantities at acceptable costs; or
- is not accepted in the medical community and by third-party payors.

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

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

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

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

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

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

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

In addition, we currently intend to pursue marketing approval for TC-1734 for cognitive impairment in the elderly. Cognitive impairment without dementia ranges in severity from AAMI to MCI. Neither the FDA nor, to our knowledge, any foreign regulatory authority has approved a drug indicated for use either for cognitive impairment in the elderly generally or for AAMI or MCI specifically. Furthermore, neither AAMI nor MCI is listed in the Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, or DSM-IV, the manual published by the American Psychiatric Association to establish diagnostic criteria. We do not know if the FDA or any other such regulatory authority will be willing to recognize AAMI or MCI as a defined condition or disease and grant approval of our product candidate for either of these indications.

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

If clinical trials for our product candidates are not successful, we will not be able to obtain regulatory approval for and commercialize them.

To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate, through extensive preclinical studies and clinical trials, that the product candidate is safe and effective in humans. The number of clinical trials required to obtain approval varies depending on the particular product candidate, the disease or condition for which it is in development and the regulations applicable to it. Preclinical studies and clinical trials are lengthy and expensive, difficult to design and implement and subject to a historically high rate of failure. The development of each of our product candidates involves significant risks at each stage of testing. A failure of one or more of our clinical trials could occur at any stage of testing. If we experience difficulties or failures in our clinical trials, or if we are not able to design our clinical trials with clear criteria to determine the efficacy of our product candidates, our product candidates may never be approved for sale or become commercially available.

Success in preclinical studies of a product candidate may not be predictive of similar results in humans during clinical trials. In addition, successful results from early clinical trials of a product candidate may not be replicated in later clinical trials. In particular, in our Phase I and Phase II clinical trials of TC-1734, our product candidate in development for the treatment of cognitive impairment in the elderly, we have used a battery of tests developed by CDR Ltd. to assess each subject's cognitive function. The CDR test battery is different from the test battery that is most often used to assess the efficacy of drugs for the treatment of Alzheimer's disease, the most common form of dementia. We plan to meet with the FDA to discuss the use of the CDR test battery in our future clinical trials of TC-1734. If, based on the discussions with the FDA, we use an additional or a different test battery for our future clinical trials of TC-1734, there would be a greater risk that the results of our Phase I and Phase II clinical trials of TC-1734 will not be predictive of similar results of those future clinical trials.

We may not be able to obtain authority from the FDA, other applicable regulatory authorities or the institutional review boards at our intended investigational sites to commence or complete our clinical trials.

Before a clinical trial may commence in the United States, we must submit an IND containing preclinical studies, chemistry, manufacturing, control and other information and a study protocol to the FDA. If the FDA does not object within 30 days after submission of the IND, then the trial may commence. If commenced, we, the FDA, other applicable regulatory authorities or institutional review boards may delay, suspend or terminate clinical trials of a product candidate at any time if, among other reasons, we or they believe the subjects or patients participating in the clinical trials are being exposed to unacceptable health risks or for other reasons.

If we do not prove in clinical trials that our product candidates are safe and effective, we will not obtain marketing approvals from the FDA and other applicable regulatory authorities. In particular, one or more of our product candidates may not exhibit the expected medical benefits in humans, may cause harmful side effects or may have other unexpected characteristics that preclude regulatory approval for any or all indications of use or limit commercial use if approved. As of June 30, 2004, five of the 176 patients that had participated in the ongoing Phase II clinical trial of TC-2403, our product candidate for the treatment of ulcerative colitis, had experienced an elevation in liver enzymes in excess of three times the upper limit of normal. Four of these patients were withdrawn from the trial and their liver enzymes returned to within the normal range. The fifth patient continued in the trial. This patient's liver enzymes returned to the normal range during the last two weeks of the six-week dosing regimen and were within the normal range at the post-regimen follow-up visit. Because the trial is double blind, we do not know if these patients were administered TC-2403 or a placebo. If some or all of these patients were administered TC-2403 and if future clinical trials of TC-2403 show similar or more prevalent elevations of liver enzymes, the FDA or other regulatory authorities may not grant us approval to market TC-2403. Also, our product candidate TC-5231, in development for ADHD, is mecamylamine hydrochloride in a low dose. Mecamylamine hydrochloride is approved in a high dose as Inversine for the treatment of moderately severe to severe essential hypertension. If clinical trials show that TC-5231 has a similar effect on blood pressure as Inversine, the FDA or other regulatory authorities may not grant us approval to market TC-5231 for the treatment of ADHD in children or at all.

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

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

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

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

- negative or inconclusive results from clinical trials, or results that are inconsistent with earlier results, that necessitate additional clinical study;
- serious and unexpected drug-related side effects experienced by subjects and patients in clinical trials; or
- failure of our third-party contractors to comply with regulatory requirements or otherwise meet their contractual obligations to us in a timely manner.

Clinical trials require sufficient patient enrollment, which is a function of many factors, including the size of the patient population, the nature of the trial protocol, the proximity of patients to clinical sites, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial. Delays in patient enrollment can result in increased costs and longer development times. For example, we have not yet completed patient enrollment for our Phase II clinical trial of TC-5231 in children and adolescents with ADHD or our Phase II clinical trial of the enema formulation of TC-2403 for the treatment of ulcerative colitis. Our failure to enroll patients in our clinical trial could delay the completion of the clinical trial beyond our current expectations. In particular, patient enrollment rates for ulcerative colitis clinical trials are generally low. In addition, the FDA could require us to conduct clinical trials with a larger number of subjects than we have projected for any of our product candidates. We may not be able to enroll a sufficient number of patients in a timely or cost-effective manner. Furthermore, enrolled patients may drop out of our clinical trials, which could impair the validity or statistical significance of the clinical trials.

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

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

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

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

Even if we receive regulatory approval to market a particular product candidate, the approval could be conditioned on us conducting additional costly post-approval studies or could limit the indicated uses included in our labeling. Moreover, the product may later cause adverse effects that limit or prevent its widespread use, force us to withdraw it from the market or impede or delay our ability to obtain regulatory approvals in additional countries. In addition, the manufacturer of the product and its facilities will continue to be subject to FDA review and periodic inspections to ensure adherence to applicable regulations. After receiving marketing approval, the manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping

related to the product will remain subject to extensive regulatory requirements. We may be slow to adapt, or we may never adapt, to changes in existing regulatory requirements or adoption of new regulatory requirements.

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

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

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

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

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

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

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

- the research methodology used may not be successful in identifying potential product candidates; or

- potential product candidates may, on further study, be shown to have harmful side effects or other characteristics that indicate that they are unlikely to be effective products.

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

If we are unable to develop suitable product candidates through internal research programs, we will not be able to increase our revenues in future periods, which could result in significant harm to our financial position and adversely impact our stock price.

Risks Related to Our Dependence on Third Parties

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

We have granted worldwide exclusive commercialization rights to Aventis Pharma SA with respect to TC-4959 for the treatment or prevention of Alzheimer's disease. We also have granted exclusive commercialization rights to Dr. Falk Pharma GmbH with respect to TC-2403 for the treatment or prevention of ulcerative colitis and other gastrointestinal and liver diseases in specified European countries, Russia, the Commonwealth of Independent States countries, Egypt and Israel. We have limited control over the amount and timing of resources that our collaborators dedicate to the development of our licensed product candidates. Our ability to generate royalties from our collaborators depends on our collaborators' abilities to establish the safety and efficacy of our product candidates, to obtain regulatory approvals and to achieve market acceptance. If either Aventis or Dr. Falk Pharma does not perform as contemplated under our agreements with them, our potential for revenue from the related product candidates will be adversely impacted. Aventis has not elected to advance into clinical development any of the compounds subject to our collaboration agreement relating to our compounds. TC-4959 is the sole compound remaining under consideration for advancement into clinical development and potential commercialization under that agreement. Furthermore, our collaboration agreements with Aventis currently prohibit us from developing or commercializing product candidates for the treatment or prevention of Alzheimer's disease. As a result, we cannot currently seek to develop our product candidate TC-1734 for Alzheimer's disease.

Aventis and Dr. Falk Pharma may terminate our collaboration agreements under certain conditions on short notice and at their sole discretion. Our collaboration agreement with Aventis related to our compounds restricts Aventis from conducting clinical development or commercializing compounds that act upon specified NNR subtypes for the treatment or prevention of Alzheimer's disease other than under the agreement. In addition, our collaboration agreement with Dr. Falk Pharma restricts Dr. Falk Pharma from developing or commercializing compounds that act upon specified NNR subtypes. If our collaboration agreement with Aventis or Dr. Falk Pharma were to terminate, Aventis or Dr. Falk Pharma would not be subject to the development and commercialization restrictions contained in that collaboration agreement. Furthermore, if our collaboration agreement with either Aventis or Dr. Falk Pharma were to terminate, we may have to curtail the development of the applicable product candidate, reduce or delay its development program, increase our expenditures and undertake development or commercialization activities at our own expense or seek another collaborator.

In addition to our current collaboration agreements, we also intend to selectively enter into collaboration agreements with leading pharmaceutical and biotechnology companies where our potential collaborator has particular therapeutic expertise in a target indication or where the target indication represents a large, primary care market.

In general, strategic collaborations involving our product candidates pose the following risks to us:

- collaborators have significant discretion in determining the efforts and resources that they will apply to these collaborations;

- collaborators may not pursue further development and commercialization of our product candidates or may elect not to continue or renew research and development programs based on preclinical or clinical trial results, changes in their strategic focus or available funding, or external factors such as an acquisition that diverts resources or creates competing priorities;
- collaborators may delay clinical trials, provide insufficient funding for a clinical trial program, stop a clinical trial or abandon a product candidate, repeat or conduct new clinical trials or require a new formulation of a product candidate for clinical testing;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with our products or product candidates if the collaborators believe that competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive;
- a collaborator with marketing and distribution rights to one or more products may not commit enough resources to their marketing and distribution;
- collaborators may not properly maintain or defend our intellectual property rights or may use our proprietary information in such a way as to invite litigation that could jeopardize or invalidate our proprietary information or expose us to potential litigation;
- disputes may arise between us and the collaborators that result in the delay or termination of the research, development or commercialization of our product candidates or that result in costly litigation or arbitration that diverts management attention and resources; and
- collaborations may be terminated and, if terminated, may result in a need for additional capital to pursue further development of the applicable product candidates.

In addition, there have been a significant number of recent business combinations among large pharmaceutical companies that have resulted in a reduced number of potential future collaborators. If a present or future collaborator of ours were to be involved in a business combination, the continued pursuit and emphasis on our product development program could be delayed, diminished or terminated. For example, Aventis has announced an agreement to merge with Sanofi-Synthelabo. We do not know what effect, if any, this will have on our collaborations with Aventis.

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

Our drug development programs and potential commercialization of our product candidates will require substantial additional cash to fund expenses. Our strategy includes selectively collaborating with leading pharmaceutical and biotechnology companies to assist us in furthering development and potential commercialization of some of our product candidates. We intend to do so especially for target indications in which our potential collaborator has particular therapeutic expertise or that involve a large, primary care market that must be served by large sales and marketing organizations. We face significant competition in seeking appropriate collaborators and these collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate collaborations on acceptable terms, or at all. If that were to occur, we may have to curtail the development of a particular product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of our sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we will not be able to bring our product candidates to market and generate product revenue.

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

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

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

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

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

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

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

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

Risks Related to Our Intellectual Property

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

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

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

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

Because of the extensive time required for development, testing and regulatory review of a new drug, it is possible that any related patent may expire before any of our product candidates can be commercialized or remain in force for only a short period following commercialization. In either case, this would reduce any

advantages of the patent. The patent laws of various foreign countries in which we intend to compete may not protect our intellectual property to the same extent as the laws of the United States. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may diminish the value of our intellectual property or narrow the scope of our patent protection.

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

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

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

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

We are a party to various license agreements. In particular, we license patent rights for a method of use of TC-5231, our product candidate in development for ADHD, and TC-2696, our product candidate in development for pain. We may enter into additional licenses in the future. Our existing licenses impose, and we expect future licenses will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we might not be able to market any product that is covered by the licensed patents.

Our patent protection for any particular compound may be limited to a particular method of use or indication such that, if a third party were to obtain approval of the compound for use in another indication, we could be subject to competition arising from off-label use.

Although we generally seek the broadest patent protection available for our proprietary compounds, we may not be able to obtain patent protection for the actual composition of any particular compound and may be limited to protecting a new method of use for the compound or otherwise restricted in our ability to prevent others from exploiting the compound. For example, we have composition of matter patent coverage in the United States on only two of our four clinical stage compounds, TC-1734 and TC-2696. We rely on method of use patent coverage in the United States on our two other clinical stage compounds, TC-5231, for neuropsychiatric disorders, including ADHD, and TC-2403, for inflammatory bowel disease, including ulcerative colitis. Accordingly, we would likely be unable to prevent others from manufacturing TC-5231 or TC-2403 or from marketing either of them for any use that is not protected by our patent rights. If a third party were to receive marketing approval for either compound for another use, physicians could nevertheless prescribe it for indications that are not described in the product's labeling or approved by the FDA or other regulatory authorities. Even if we have patent protection for the prescribed indication, as a practical matter, we would have little recourse as a result of this off-label use. In that event, our revenues from the commercialization of the compound would likely be adversely affected.

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

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

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

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

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

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

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

Risks Related to Commercialization

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

The commercial success of any of our product candidates for which we may obtain marketing approval from the FDA or other regulatory authorities will depend upon their acceptance by the medical community and third-

party payors as clinically useful, cost-effective and safe. Many of the product candidates that we are developing are based upon technologies or methods of treatment that are relatively new and unproven. As a result, it may be more difficult for us to achieve market acceptance of our products.

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

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

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

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

We currently have limited sales, marketing and distribution experience. Our experience is limited to a contractual arrangement with a third party to distribute Inversine, which we acquired in 2002 and which generates only limited sales. We currently have no internal sales or distribution capabilities. Although we intend to build an internal sales force and expand our marketing capabilities in areas where specialists heavily influence our target markets, such as neurology and psychiatry, we also intend to seek to further augment our sales, marketing and distribution capabilities through arrangements with third parties. In particular, our strategy includes selectively entering into collaborations and other strategic alliances with respect to product candidates for disease indications with sales and distribution characteristics requiring a large sales force. There are risks involved with establishing our own sales force and marketing and distribution capabilities, as well as in entering into arrangements with third parties to perform these services. Developing our own sales force will be expensive and time-consuming and could delay any product launch. We may not be successful in entering into arrangements with third parties on terms that are favorable to us or at all. Also, we would have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell, market or distribute our products effectively. If we do not establish sales and distribution capabilities successfully, either on our own or in collaboration with third parties, we may not successfully commercialize our products.

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

The regulations governing drug pricing and reimbursement vary widely from country to country. Some countries require approval of the sale price of a drug before it can be marketed and, in many of these countries, the pricing review period begins only after approval is granted. In some countries, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. Although we monitor these regulations, our product candidates are currently in the development stage and we will not be able

to assess the impact of price regulations for at least several years. As a result, we may obtain regulatory approval for a product in a particular country, but then be subject to price regulations that delay the commercial launch of the product and may negatively impact the revenues we are able to derive from sales in that country.

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

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory proposals to change the healthcare system in the United States and other major healthcare markets have been proposed and adopted in recent years. For example, the U.S. Congress recently enacted a limited prescription drug benefit for Medicare recipients as part of the Medicare Prescription Drug, Improvement and Modernization Act of 2003. While the program established by this statute may increase demand for any products that we are able to successfully develop, if we participate in this program, our prices will be negotiated with drug procurement organizations for Medicare beneficiaries and are likely to be lower than prices we might otherwise obtain. If successfully developed, our product candidate for cognitive impairment in the elderly, TC-1734, could be particularly affected by this law because of its elderly target patient population. Non-Medicare third-party drug procurement organizations may also base the price they are willing to pay on the rate paid by drug procurement organizations for Medicare beneficiaries. In addition, ongoing initiatives in the United States have and will continue to increase pressure on drug pricing. The announcement or adoption of any such initiative could have an adverse effect on potential revenues from any product candidate that we may successfully develop.

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

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

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

- negotiate third-party licensing and collaboration arrangements more effectively than we do; and
- take advantage of acquisition or other opportunities more readily than we do.

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

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

Any products that we are able to successfully develop and commercialize in the future could be subject to competition from lower priced generic drugs. In particular, if mecamylamine hydrochloride is effective and receives regulatory approval for the treatment of ADHD at the low doses that we are currently developing as TC-5231, physicians could prescribe partial tablets of a generic version of Inversine for the off-label treatment of ADHD. We are currently evaluating mecamylamine hydrochloride at doses ranging from 0.2mg and 1.0mg. If we determine that the higher dose is more effective or otherwise more desirable for use in treating ADHD, physicians may view the higher dose as more similar to Inversine and be even more likely to prescribe partial tablets of Inversine for the off-label treatment of ADHD. In addition, the manufacturer of a generic product could challenge our patents as invalid or not infringed and subject us to expensive litigation. We do not know if we would prevail in litigation and succeed in keeping the generic product out of the market until our patent protection expires.

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

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

- for ADHD, stimulants such as Concerta from Johnson & Johnson, Ritalin from Novartis and Adderall from Shire Laboratories and the non-stimulant Strattera from Eli Lilly;
- for ulcerative colitis, 5-ASAs such as Asacol from Proctor & Gamble;
- for pain, non-steroidal anti-inflammatory drugs such as Celebrex from Pfizer and Vioxx from Merck and opioids such as OxyContin from Purdue Pharma;
- for Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer, Reminyl from Johnson & Johnson and Exelon from Novartis and an NMDA-receptor antagonist for moderate to late stage Alzheimer's disease, Namenda from Forest Laboratories;
- for schizophrenia, anti-psychotics such as Zyprexa from Eli Lilly, Risperdal from Johnson & Johnson and Abilify from Bristol-Myers Squibb;
- for depression, selective serotonin reuptake inhibitors such as Prozac from Eli Lilly, Paxil from GlaxoSmithKline, Zoloft from Pfizer, Celexa and Lexapro from Forest Laboratories and the dual uptake inhibitor Effexor from Wyeth; and
- for smoking cessation, Zyban from GlaxoSmithKline.

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

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

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

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

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

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

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

Risks Related to Employees and Managing Growth

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

Our performance depends substantially on the performance of our senior management and key scientific, technical and managerial personnel, including our Chief Executive Officer and President, J. Donald deBethizy,

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

Our ability to operate successfully and manage our potential future growth will depend on our ability to identify, recruit and retain additional qualified scientific, technical, financial and managerial personnel. There is currently a shortage of skilled executives in our industry, and we face intense competition for such personnel. We may not be able to continue to attract and retain personnel with the advanced qualifications necessary for the growth of our business.

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

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

Risks Related to Our Common Stock and this Offering

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

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

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

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

The offering price of our common stock will be substantially higher than the net tangible book value of $(85.95) per share of our existing capital stock as of March 31, 2004. As a result, based on an assumed initial

public offering price of , purchasers of our common stock in this offering will incur immediate and substantial dilution of $ per share, representing the difference between our pro forma net tangible book value per share after giving effect to this offering and the assumed initial public offering price, and will incur additional dilution if outstanding stock options and warrants with exercise prices below the public offering price are exercised. See "Dilution" for a more detailed discussion of the dilution new investors will incur in this offering.

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

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

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

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

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

Sales of a substantial number of shares of our common stock in the public market following this offering could cause the market price to decline. Such sales also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. After this offering, we will have shares of common stock outstanding based on the number of shares outstanding as of , 2004. If there are more shares of our common stock offered for sale than buyers are willing to purchase, the market price of our common stock may decline to a market price at which buyers are willing to purchase the offered shares and sellers remain willing to sell the shares. The number of shares of our common stock available for sale in the public market is limited by restrictions under federal securities laws and under lock-up agreements that substantially all of our stockholders have entered into with the underwriters. Except in limited circumstances, these lock-up agreements restrict our stockholders from selling or otherwise disposing of their shares for a period of 180 days after the date of this prospectus, subject to a possible extension, without the prior written consent of Morgan Stanley & Co. Incorporated on behalf of the underwriters. However, Morgan Stanley may, in its sole discretion, release all or any portion of the common stock from the restrictions of the lock-up agreements. Morgan Stanley does not have any pre-established conditions to waiving the terms of the lock-up agreements. Any determination to release any shares subject to the lock-up agreements would be based on a number of factors at the time of determination, including but not necessarily limited to the market price of the common stock, the liquidity of the trading market for the common stock, general market conditions, the number of shares proposed to be sold and the timing, purpose and terms of the proposed sale.

Additionally, of the shares of our common stock that may be issued upon the exercise of options outstanding as of , 2004, approximately shares will be vested and eligible for sale 180 days after the date of this prospectus. For a further description of the eligibility of shares for sale into the public market following the offering, see "Shares Eligible for Future Sale." In the future, we may issue additional shares to our

employees, directors or consultants, in connection with corporate alliances or acquisitions or to raise capital. Accordingly, sales of a substantial number of shares of our common stock in the public market could occur at any time.

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

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

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

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

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

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

- allow the authorized number of directors to be changed only by resolution of our board of directors;
- establish a classified board of directors, providing that not all members of the board be elected at one time;
- authorize our board of directors to issue without stockholder approval blank check preferred stock that, if issued, could operate as a "poison pill" to dilute the stock ownership of a potential hostile acquirer to prevent an acquisition that is not approved by our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit stockholder action by written consent;
- establish advance notice requirements for stockholder nominations to our board of directors or for stockholder proposals that can be acted on at stockholder meetings;
- limit who may call stockholder meetings; and
- require the approval of the holders of 66 2/3% of the outstanding shares of our capital stock entitled to vote in order to amend certain provisions of our certificate of incorporation and bylaws.

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

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

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

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

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

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

USE OF PROCEEDS

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

We expect that we will use:

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

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

The amounts and timing of our actual expenditures will depend upon numerous factors, including the status of our development and commercialization efforts, the amount of proceeds actually raised in this offering, the amount of cash generated through our existing strategic collaborations, any additional strategic collaborations into which we may enter and sales of Inversine. Accordingly, our management will have significant flexibility in applying the net proceeds of this offering.

We do not expect our existing capital resources and the net proceeds from this offering to be sufficient to enable us to fund the completion of the development of any of our product candidates. We believe that our existing capital resources and the net proceeds from this offering will be sufficient to enable us to complete our ongoing clinical trials and to:

- complete a Phase II clinical trial of TC-1734 that we currently plan to initiate in the fourth quarter of 2004;
- initiate a Phase III clinical trial of TC-1734;
- initiate a Phase III clinical trial of TC-5231;
- initiate and complete a Phase I clinical trial, and potentially initiate a Phase II clinical trial, of the oral formulation of TC-2403; and
- initiate and complete an additional Phase I clinical trial, and potentially initiate a Phase II clinical trial, of TC-2696.

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

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

DIVIDEND POLICY

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

CAPITALIZATION

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

- on an actual basis;
- on a pro forma basis to give effect to the conversion of all outstanding shares of our convertible preferred stock into 73,739,905 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 shares of common stock in this offering at an assumed initial public offering price of $ per share, after deducting estimated underwriting discounts and commissions and offering expenses payable by us; and
  - our issuance of shares of common stock upon the exercise of an outstanding warrant concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share.

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

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

	As of March 31, 2004		
	Actual	Pro Forma	Pro Forma As Adjusted
		(unaudited) (in thousands, except share and per share data)	
Total long-term obligations	$ 1,935	$ 1,935	$
Redeemable convertible preferred stock, $0.001 par value, 60,736,705 shares authorized, issued and outstanding actual; no shares authorized, issued or outstanding pro forma and pro forma as adjusted	132,276	—	
Stockholders' equity (deficit):			
Common stock, $0.001 par value, 85,000,000 shares authorized actual, pro forma and pro forma as adjusted; 1,164,524 issued and outstanding actual; shares issued and outstanding pro forma; shares issued and outstanding pro forma as adjusted	1	75	
Preferred stock, $0.001 par value, no shares authorized, issued or outstanding actual and pro forma; shares authorized and no shares issued and outstanding pro forma as adjusted	—	—	
Capital in excess of par value	6,378	115,330	
Excess of fair value of Series A preferred stock over cash received	(23,250)	—	
Common stock warrants	214	214	
Accumulated deficit	(82,818)	(82,818)	
Accumulated other comprehensive loss	(35)	(35)	
Total stockholders' equity (deficit)	(99,510)	(32,766)	
Total capitalization	$ 34,701	$ 34,701	$

The table above does not include:

- 8,024,394 shares of common stock issuable upon exercise of options outstanding as of March 31, 2004, at a weighted average exercise price of $0.64 per share, of which options to purchase 4,078,011 shares were exercisable; and
- 448,274 shares of common stock reserved for future grant under our 2000 equity incentive plan as of March 31, 2004.

DILUTION

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

The historical net tangible book value of our common stock as of March 31, 2004 was approximately $(100,089), or approximately $(85.95) per share, based on 1,164,524 shares of common stock outstanding as of March 31, 2004. Historical net tangible book value per share represents our total tangible assets less total liabilities divided by the actual number of our common stock outstanding.

As of March 31, 2004, the pro forma net tangible book value of our common stock was approximately $ million, or approximately $ per share. Pro forma net tangible book value per share represents our total tangible assets less total liabilities divided by the pro forma number of shares of our common stock outstanding, after giving effect to a one-for- reverse stock split of our common stock that will be effective prior to the completion of this offering, the conversion of all outstanding shares of our convertible preferred stock into 73,739,905 shares of common stock concurrently with the completion of this offering, and the issuance of 1,612,903 shares of common stock upon the exercise of an outstanding warrant in full for cash concurrently with the completion of this offering.

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

Assumed initial public offering price per share		$
Historical net tangible book value per share	$ (85.95)	
Increase attributable to the conversion of the convertible preferred stock		
Pro forma net tangible book value per share before this offering	( )	
Increase per share attributable to new investors		
Pro forma net tangible book value per share after this offering		
Dilution per share to new investors		$

The following table summarizes, on a pro forma basis as of March 31, 2004, the total number of shares of common stock purchased from us, the total consideration paid and the average price per share paid by existing stockholders and by new investors purchasing shares in this offering at an assumed initial public offering price of $ per share, before deducting estimated underwriting discounts and commissions and offering expenses payable by us.

	Shares Purchased		Total Consideration		
	Number	Percent	Amount	Percent	Average Price per Share
Existing stockholders		%	$	%	$
New investors					
Total		100%	$	100%	

The share data in the table above is based on shares outstanding as of March 31, 2004, counting as outstanding the 73,739,905 shares of common stock underlying all outstanding convertible preferred stock, and excludes:

- 8,024,394 shares of common stock issuable upon the exercise of options outstanding as of March 31, 2004, at a weighted average exercise price of $0.64 per share, of which options to purchase 4,078,011 shares were exercisable; and
- 448,274 shares of common stock reserved for future grant under our 2000 equity incentive plan as of March 31, 2004.

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

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

SELECTED FINANCIAL DATA

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

We have derived the statement of operations data for the years ended December 31, 2001, 2002 and 2003 and the balance sheet data as of December 31, 2002 and 2003 from our audited financial statements included in this prospectus. We have derived the statement of operations data for the year ended December 31, 2000 and the balance sheet data as of December 31, 2000 and 2001 from our audited financial statements not included in this prospectus. We became an independent company in August 2000, prior to which we were a wholly owned subsidiary of R.J. Reynolds Tobacco Company. We have derived the statement of operations data for the year ended December 31, 1999 and the balance sheet data as of December 31, 1999 from our unaudited financial statements not included in this prospectus. We have derived the statement of operations data for the three months ended March 31, 2003 and 2004 and the balance sheet data as of March 31, 2003 and 2004 from our unaudited financial statements included in this prospectus. In the opinion of our management, these unaudited financial statements reflect all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of these financial statements. Our historical results for any prior or interim period are not necessarily indicative of the results to be expected for the fiscal year ending December 31, 2004 or for any other period.

The pro forma net loss attributable to common stockholders per share information is computed using the weighted average number of common shares outstanding, after giving pro forma effect to the conversion of all outstanding shares of our convertible preferred stock into 73,739,905 shares of common stock concurrently with the completion of this offering, as if the conversion had occurred at the date of the original issuance.

	Year ended December 31,					Three months ended March 31,	
	1999	2000	2001	2002	2003	2003	2004
	(unaudited)					(unaudited)	
	(in thousands, except share and per share data)						
Statement of Operations Data:							
Net revenue	$ 2,350	$ 2,351	$ 1,703	$ 2,286	$ 2,458	$ 691	$ 497
Operating expenses:							
Research and development	2,104	3,675	8,152	16,244	18,179	4,069	6,050
General and administrative	1,436	1,653	2,302	4,135	3,600	697	1,109
Cost of product sales	—	—	—	244	743	200	182
Purchased in-process research and development	—	—	—	2,666	—	—	—
Total operating expenses	3,540	5,328	10,454	23,289	22,522	4,966	7,341
Loss from operations	(1,190)	(2,977)	(8,751)	(21,003)	(20,064)	(4,275)	(6,844)
Interest and dividend income	—	536	1,449	88	791	124	231
Interest expense	—	—	—	(103)	(122)	(34)	(25)
Loss on disposal of fixed assets	—	—	—	(54)	—	—	—
Net loss	(1,190)	(2,441)	(7,302)	(21,072)	(19,395)	(4,185)	(6,638)
Preferred stock accretion	—	(981)	(3,808)	(4,173)	(8,341)	(1,915)	(2,142)
Net loss attributable to common stockholders	$ (1,190)	$ (3,422)	$ (11,110)	$ (25,245)	$ (27,736)	$ (6,100)	$ (8,780)
Basic and diluted net loss per share applicable to common stockholders	$ (2,380.00)	$ (30.58)	$ (26.80)	$ (45.28)	$ (33.91)	$ (9.48)	$ (7.89)
Shares used to compute basic and diluted net loss per share	500	111,915	414,624	557,492	817,894	643,571	1,112,591
Pro forma basic and diluted net loss per share applicable to common stockholders (unaudited)					$ (0.27)		$ (0.09)
Shares used to compute pro forma basic and diluted net loss per share (unaudited)					71,118,629		74,852,496

	Year ended December 31,					Three months ended March 31,	
	1999	2000	2001	2002	2003	2003	2004
	(unaudited)					(unaudited)	
	(in thousands, except share and per share data)						
Balance Sheet Data:							
Cash, cash equivalents and short-term investments	$ —	$ 28,053	$ 21,180	$ 49,361	$ 42,977	$ 58,207	$ 36,847
Working capital	1,305	27,654	20,371	46,685	40,526	56,534	33,663
Total assets	1,804	29,338	24,396	54,379	47,390	62,274	40,806
Long-term debt, net of current portion	—	—	—	2,088	1,462	2,037	1,298
Redeemable convertible preferred stock	—	54,418	58,365	108,026	130,134	123,741	132,276
Accumulated deficit	(6,335)	(9,946)	(21,057)	(46,302)	(74,038)	(52,402)	(82,818)
Total stockholders' equity (deficit)	36	(27,314)	(38,268)	(63,335)	(90,796)	(69,409)	(99,510)

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

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

Overview

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

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

We have devoted substantially all of our resources to the discovery and development of our product candidates and technologies, including the design, conduct and management of preclinical and clinical studies and related manufacturing, regulatory and clinical affairs, and intellectual property prosecution. Through 1998, we received all of our funding from RJR. At the end of 1998, we entered into a collaboration agreement with the predecessor company to Aventis Pharma SA. 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, Aventis and Dr. Falk Pharma GmbH, equipment and building lease incentive financing, sales of our product Inversine and government grants.

We have never been profitable. As of March 31, 2004, we had an accumulated deficit of $82.8 million. We expect to continue to incur substantial losses for the foreseeable future. We expect our research and development expenses to increase substantially following completion of this offering as we expand our clinical trial activity, as our product candidates advance through the development cycle and as we invest in additional product opportunities and research programs. We also expect our general and administrative expenses to increase substantially as we expand our infrastructure. Clinical trials and preclinical studies are time-consuming, expensive and may never yield a product that will generate revenue. A substantial portion of our revenue for the next several years will depend on our entering into new collaborations. Our revenue may vary substantially from quarter to quarter and year to year. We believe that period-to-period comparisons of our results of operations are not meaningful and should not be relied upon as indicative of our future performance.

We currently have one product available in the market, Inversine. We acquired rights to Inversine in August 2002. Inversine is approved for the management of moderately severe to severe essential hypertension, a high

blood pressure disorder with an unknown cause. However, our market research suggests that it is prescribed predominantly for the treatment of Tourette's syndrome and other neuropsychiatric disorders. Sales of Inversine generated revenue of $815,000 for the year ended December 31, 2003 and $188,000 for the three months ended March 31, 2004.

We have entered into two collaboration agreements with Aventis. Our first collaboration agreement with Aventis covers the research, development and commercialization of a specified group of our compounds for the treatment of Alzheimer's disease. There is only one compound remaining in the collaboration, TC-4959, which is in the late preclinical evaluation stage. Our second collaboration agreement with Aventis covers the research, development and commercialization of Aventis compounds for the treatment of Alzheimer's disease and other central nervous system diseases. As of March 31, 2004, we had received a total of $8.0 million in upfront license fees and payments for research and development services under the two agreements. In addition to royalties on potential product sales, we could receive up to $30.0 million under the first agreement upon the achievement of pre-commercialization development and regulatory milestones, up to $8.0 million under the second agreement upon the achievement of pre-commercialization development and regulatory milestones related to Alzheimer's disease and up to $8.0 million under the second agreement for each other central nervous system disease upon the achievement of pre-commercialization development and regulatory milestones related to that disease. The achievement of the milestones under these agreements is uncertain. We may not receive any of these amounts or we may receive only a portion of them.

We have also entered into a collaboration agreement with Dr. Falk Pharma covering the development and commercialization of our product candidate TC-2403 for the treatment of ulcerative colitis. Upon effectiveness of the collaboration agreement in January 2001, Dr. Falk Pharma paid us a $1.0 million upfront license fee and purchased $1.0 million of our common stock. Pursuant to the terms of the agreement, we share TC-2403 development costs equally with Dr. Falk Pharma.

Critical Accounting Policies and Estimates

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

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

Revenue Recognition

Our collaboration agreements contain multiple elements, including non-refundable upfront license fees, research payments for ongoing research and development, payments associated with achieving development and regulatory milestones and royalties to be paid based on specified percentages of net product sales or net profits, if any. We consider a variety of factors in determining the appropriate method of revenue recognition under these arrangements such as whether the elements are separable, whether there are determinable fair values and whether there is a unique earnings process associated with a particular element of an agreement.

We recognize research fee revenue from research services performed under our collaboration agreements as work is performed. We defer upfront payments and amortize them over the estimated research and development

period. All revenue that we have recognized to date under these collaborations, or under government grants, is non-refundable. We recognize revenue from milestones with substantive performance risk upon achievement of the milestone. We have not yet received payment of any such milestone-based revenues. We record product sales revenues when goods are shipped, at which point title has passed, and we establish an allowance for estimated returns at that time.

Accrued Expenses

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. To date, we have not adjusted our estimate at any particular balance sheet date in any material amount. Examples of estimated accrued expenses include:

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

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

Purchased In-process Research and Development Expense

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

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

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

Stock-Based Compensation

We account for our employee stock-based compensation in accordance with Accounting Principles Board Opinion No. 25 and related interpretations, or APB 25. Under APB 25, we do not recognize compensation expense when we issue stock options to employees and non-employee directors, unless the exercise price is below the fair market value of the underlying common stock on the date of grant. We recognize this compensation expense over the vesting periods of the shares purchasable upon exercise of options. We recorded deferred stock-based compensation related to stock options granted to employees and directors of $92,600 during 2001, $129,700 during 2002 and $65,300 during 2003. We amortize our deferred stock-based compensation on a straight-line basis over the related option vesting periods, which range from immediate vesting to four years.

As required by Statement of Financial Accounting Standards, or SFAS, No. 123, *Accounting for Stock-Based Compensation,* as amended by SFAS No. 148, *Accounting for Stock-Based Compensation—Transition and Disclosure*, our financial statement footnotes disclose on a pro forma basis the amount of compensation expense that we would have recorded had we applied the fair value option methodology described in SFAS 123. Had we recorded all of our stock-based compensation using the SFAS 123 fair value methodology, our compensation expense would have been approximately $450,000 greater and our diluted net loss per share attributable to common stockholders would have been approximately $0.55 greater in 2003. For more information, you should refer to Note 2 to our financial statements included at the end of this prospectus.

Financial Operations Overview

Revenue

Inversine is our only commercial product generating revenue. Sales of Inversine generated revenue of $815,000 for the year ended December 31, 2003 and $188,000 for the three months ended March 31, 2004. We have entered into an exclusive distribution agreement with a third party for the distribution of Inversine. We do not have or use a sales force or actively promote Inversine. Accordingly, we do not anticipate any significant increase in Inversine sales. If any of the very limited number of physicians that most often prescribe Inversine were to cease to do so, revenue generated by Inversine sales would likely be substantially less. We have no other commercial products for sale and do not anticipate that we will have any other commercial products for sale for at least the next several years.

Other revenue has consisted primarily of amounts earned for providing research and development services under our two collaboration agreements with Aventis and non-refundable upfront license fees that we received in connection with our first agreement with Aventis and our collaboration agreement with Dr. Falk Pharma. We recognize these non-refundable upfront license fees over the estimated research period of each of these agreements. We received research support payments from Aventis of $1.4 million for the year ended December 31, 2002, $1.3 million for the year ended December 31, 2003 and $100,000 for the three months ended March 31, 2004. We are currently receiving research support payments from Aventis only under our collaboration agreement with Aventis that relates to Aventis compounds. The research term of that agreement ends in December 2004.

In 2003, we were awarded a grant from the National Institute of Standards and Technology through its Advanced Technology Program. The terms of the grant 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 grant provides for reimbursement of costs that we incur to perform specified work that is designed to meet the objectives of the grant. We recognize grant revenues as we perform the work and incur reimbursable costs.

Research and Development Expense

Since our inception, we have focused our activities on our drug discovery and development programs. We expense research and development expenses as they are incurred. Research and development expenses represented approximately 78% of our total expenses for the year ended December 31, 2001, 81% for the year ended December 31, 2002, 81% for the year ended December 31, 2003 and 82% for the three months ended March 31, 2004.

Research and development expenses include expenses associated with:

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

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

The following table shows, for the periods presented, total payments that we made to third parties for preclinical study support, clinical supplies and clinical trial services for each of our four clinical-stage product candidates:

	Year ended December 31,			Three months ended March 31,
Product Candidate	**2001**	**2002**	**2003**	**2004**
			(in thousands)	
TC-1734	$ —	$ 976	$3,557	$ 1,045
TC-5231	—	61	852	781
TC-2403	922	2,656	1,290	419
TC-2696	—	—	893	533
Total:	$922	$3,693	$6,592	$ 2,778

We expect to continue to incur substantial research and development expenses for the foreseeable future. We anticipate that these expenses will increase substantially in 2004 and in subsequent years as we continue to advance our clinical stage product candidates through the development process, to advance additional product candidates into clinical trials and to invest in promising product opportunities in our research programs.

Our expenditures on current and future preclinical and clinical development programs are subject to numerous uncertainties in timing and cost to completion. We test compounds in numerous preclinical studies for safety, toxicology and efficacy. We then conduct clinical trials for those product candidates that we determine to be the most promising. If we do not establish a collaboration covering the development of a particular product candidate, we fund these trials ourselves. As we obtain results from clinical trials, we may elect to discontinue or delay trials for some product candidates in order to focus our resources on more promising product candidates. Completion of clinical trials by us or our collaborators may take several years or more, but the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product candidate. The cost of clinical trials may vary significantly over the life of a project as a result of a variety of factors, including:

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

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

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

General and Administrative Expense

General and administrative expense consists principally of salaries and other related costs for personnel in executive, finance, accounting, business development, information technology and human resource functions. Other general and administrative expenses include facility costs not otherwise included in research and development expense, patent related costs, and professional fees for consulting, legal and accounting services. We expect that general and administrative expense will increase during 2004 and subsequent years due to increased payroll, expanded infrastructure, increased consulting, legal, accounting and investor relations expenses associated with being a public company and costs incurred to secure collaborations with respect to any of our product candidates.

Cost of Product Sales

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

Purchased In-process Research and Development Expense

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

Interest and Dividend Income

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

Interest Expense

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

Income Taxes

We have incurred net operating losses since our incorporation in 1997 and consequently have not paid federal, state or foreign income taxes in any period. As of December 31, 2003, we had net operating loss carryforwards of approximately $46.1 million. Pursuant to Section 382 of the Internal Revenue Code of 1986, the annual utilization of our net operating loss carryforwards may be limited if we experience a change in ownership of more than 50% within a three-year period. As a result of this offering, we may experience such an ownership change. Accordingly, our net operating loss carryforwards available to offset future federal taxable income arising before such ownership changes may be limited. 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

Three Months ended March 31, 2004 and 2003

Revenue. We recognized revenue of $497,000 for the three months ended March 31, 2004 compared to $691,000 for the corresponding period in 2003. The decrease resulted from a decrease of $178,000 in research fee revenue generated from our collaboration agreement with Aventis relating to Aventis compounds, resulting from less activity under that agreement in 2004 as we progressed in 2003 towards completion of the research requested by Aventis. We expect research fee revenues derived from that collaboration agreement throughout 2004 to decrease similarly as compared to the comparable periods in 2003. The research term of that collaboration agreement expires on December 31, 2004. The decrease in the first quarter of 2004 also resulted from a reduction of $123,000 in Inversine sales in the first quarter of 2004 compared to the first quarter of 2003. These decreases in revenue were partially offset by $107,000 of grant revenue recognized in the first quarter of 2004 in connection with work performed under a grant awarded to us in 2003 by the National Institute of Standards and Technology through its Advanced Technology Program to fund the development of sophisticated molecular simulation software. We expect this grant to provide funding to us at least through 2004. We did not recognize any grant revenue in the first quarter of 2003. The reduced level of Inversine sales in the first quarter of 2004 reflects a decrease from higher than expected Inversine sales in the first quarter of 2003. We believe that the higher sales in the first quarter of 2003 resulted from a build-up of demand for Inversine in the latter part of 2002 due primarily to a limited commercial supply of the product during the transition period following our acquisition of the rights to Inversine in August 2002. We began selling Inversine in December 2002.

Research and Development Expense. Research and development expense increased by $1.9 million, or 46%, to $6.0 million for the three months ended March 31, 2004, from $4.1 million for the corresponding period in 2003. The increase was primarily attributable to the costs associated with our four product candidates in clinical trials in the first quarter of 2004, compared to only two product candidates in clinical trials in the first quarter of 2003. During the three months ended March 31, 2004, we estimate that approximately 17% of our total research and development expenses were payments made to third parties in connection with our TC-1734 program for cognitive impairment in the elderly, 13% were payments made to third parties in connection with our TC-5231 program for ADHD, 7% were payments made to third parties in connection with our portion of the costs of our TC-2403 program for ulcerative colitis and 9% were payments made to third parties in connection with our TC-2696 program for pain. We spent the remaining 54% of our total research and development expenses on salaries, benefits, and infrastructure costs for our internal research and development capabilities and on other earlier stage programs and research efforts.

General and Administrative Expense. General and administrative expense increased by $412,000, or 59%, to $1.1 million for the three-month period ended March 31, 2004, from $697,000 for the corresponding period in 2003. This increase resulted from our investment in development of the administrative infrastructure necessary to enable us to expand our operations, to support our development efforts and to fulfill the additional reporting and regulatory requirements applicable to a public company. The increase was principally attributable to increased expenses of $229,000 related to expansion of our business development staff and an increase in spending on business development pursuits, additional patent related expenses and increases in our legal and other professional fees.

Cost of Product Sales. Cost of product sales for the three months ended March 31, 2004 was $181,000 compared to $199,000 for the corresponding period in 2003. All of these costs related to sales of Inversine.

Interest and Dividend Income. Interest and dividend income increased by $106,000 to $230,000 for the three months ended March 31, 2004, from $124,000 for the corresponding period in 2003. The increase was primarily attributable to receiving higher rates of return on our short-term investments.

Interest Expense. Interest expense was $25,000 for the three months ended March 31, 2004 compared to $34,000 for the corresponding period in 2003. The decrease was attributable to a lower average outstanding principal balance on our equipment financing facility. In April 2004, we financed an additional $1.0 million of eligible fixed assets under this facility. We expect our interest expense to increase as a result of this additional indebtedness.

Years ended December 31, 2003 and 2002

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

Research and Development Expense. Research and development expense increased by $2.0 million, or 12%, to $18.2 million for the year ended December 31, 2003, from $16.2 million for 2002. The increase resulted principally from increased spending of $2.9 million on our later stage clinical programs and increased personnel and infrastructure costs of $539,000 associated with the expansion of our internal clinical development and regulatory affairs capabilities. This was offset in part by a decrease of $1.8 million resulting from the conclusion in 2002 of a program to screen several of our preclinical candidates to select those to advance into clinical trials. During the year ended December 31, 2003, we estimate that approximately 20% of our total research and development expenses were payments made to third parties in connection with our TC-1734 program for cognitive impairment in the elderly, 5% were payments made to third parties in connection with our TC-5231

program for ADHD, 7% were payments made to third parties in connection with our portion of the costs of our TC-2403 program for ulcerative colitis and 5% were payments made to third parties in connection with our TC-2696 program for pain. We spent the remaining 63% of our total research and development expense on salaries, benefits, and infrastructure costs associated with our internal research and development capabilities and on other earlier stage programs and research efforts.

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

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

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

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

Years ended December 31, 2002 and December 31, 2001

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

Research and Development Expense. Research and development expense increased by $8.0 million, or 98%, to $16.2 million for the year ended December 31, 2002, from $8.2 million for 2001. The increase resulted principally from $1.8 million in costs attributable to a program to screen several of our preclinical candidates to ascertain those to advance into clinical trials, increased spending of $1.7 million to fund our portion of the costs of third-party services in connection with the TC-2403 program for ulcerative colitis, and $1.0 million for preclinical studies, toxicology and regulatory expenses directed towards advancing TC-1734 into clinical trials. We also incurred increased salary and benefits costs as we expanded our product development capabilities with the hiring of experienced key personnel. In addition, we incurred increased infrastructure costs in connection with our relocation in March 2002 to a new leased facility which includes expanded lab and research space. This also resulted in higher depreciation charges associated with the new equipment and furnishings that we acquired.

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

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

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

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

Liquidity and Capital Resources

Sources of Liquidity

Since we became an independent company in 2000, we have financed our operations and internal growth primarily through private placements of convertible preferred stock. We have derived aggregate net proceeds of $88.4 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 March 31, 2004, we have received $9.9 million under our collaboration agreements. We are currently receiving research support payments under only one of these agreements, and the research term of that agreement ends in December 2004. We began generating revenues from product sales of Inversine in December 2002. To date, Inversine sales have not been a significant source of cash and we do not expect them to be a significant source in the future.

Our cash, cash equivalents and short-term investments were $36.8 million as of March 31, 2004, $43.0 million as of December 31, 2003 and $49.4 million as of December 31, 2002.

Cash Flows

Net cash used for operating activities was $5.8 million for the three months ended March 31, 2004, reflecting a net loss of $6.6 million offset primarily by research support payments. Net cash used for operating activities was $19.3 million for the year ended December 31, 2003, primarily reflecting a net loss occurring for this period of $19.4 million. Net cash used for operating activities was $17.1 million for the year ended December 31, 2002, reflecting a net loss of $21.1 million partially offset by non-cash charges for acquired in-process research and development of $2.7 million and depreciation and amortization of $1.0 million. Accounts payable and accrued expenses increased by $1.5 million as of December 31, 2002, compared to December 31, 2001 primarily as a result of an increase in outsourced development activities with contract research organizations.

Net cash used in investing activities was $137,000 for the three months ended March 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. Investing activities for the year ended December 31, 2002, exclusive of cash flows from the purchase and sale of investments, included the use of $1.3 million for the purchase of equipment and furniture, the use of $3.5 million for the purchase of the marketing rights to Inversine and related assets from Layton Bioscience, Inc. and the receipt of a $2.0 million rent incentive from the owner of our facilities in connection with our entering into a lease with a minimum five-year term.

Net cash used in financing activities was $49,000 for the three months ended March 31, 2004. As of March 31, 2004, we had borrowing capacity of $2.0 million available under our equipment financing loan facility. We borrowed $1.0 million under the facility in April 2004 to finance equipment that we had previously purchased. Net cash provided by financing activities for the year ended December 31, 2003 was $13.4 million

and consisted principally of net proceeds of $13.8 million from the issuance of shares of our series C convertible preferred stock, and proceeds of $239,000 received in connection with the purchase of our common stock upon the exercise of stock options, partially offset by $637,000 of principal repayments on equipment financing. Net cash provided by financing activities for the year ended December 31, 2002 was $48.2 million and consisted principally of net proceeds of $45.5 million from the issuance of shares of our series C convertible preferred stock and proceeds of $3.0 million from long-term debt, comprised of a $2.5 million equipment financing loan repayable over 48 months and a $500,000 incentive loan from the City of Winston-Salem which requires no repayments and carries no interest charges for the initial five years, partially offset by $325,000 of equipment financing principal repayments.

In May 2002, we borrowed $2.5 million from R.J. Reynolds Tobacco Holdings, Inc. to finance equipment and other fixed assets that we had previously purchased. The borrowing bears a fixed interest rate of 6.6%, is payable in 48 equal monthly installments and matures in May 2006. In January 2004, we amended the terms of our loan facility to permit us to borrow up to an additional $2.0 million in 2004 in up to three separate borrowings. Each borrowing would bear a fixed interest rate equal to a theoretical four-year U.S. Treasury Rate on the disbursement date plus 3.5%, be payable in 48 equal monthly installments and be secured by specified tangible fixed assets determined sufficient by the lender at the time of disbursement. In April 2004, we borrowed $1.0 million under the amended loan facility to finance equipment. This borrowing bears a fixed interest rate of 5.9%, is payable in 48 equal monthly installments and matures in April 2008. All borrowings under the loan facility are secured by specified tangible fixed assets. As of June 30, 2004, the outstanding principal balance under the loan facility was $2.3 million.

Funding Requirements

We have incurred significant losses since our inception. As of March 31, 2004, we had an accumulated deficit of $82.8 million. We expect to continue to incur substantial operating losses for the foreseeable future. Our future capital requirements are difficult to forecast and will depend on many factors, including:

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

Although we currently have not specifically identified any material commitments for capital expenditures, we anticipate that implementing our strategy will require substantial increases in our capital expenditures and other capital commitments as we expand our clinical trial activity, as our product candidates advance through the development cycle, and as we invest in additional product opportunities and research programs and expand our infrastructure. We do not expect our existing capital resources and the net proceeds from this offering to be sufficient to enable us to fund the completion of the development of any of our product candidates. We expect that our existing capital resources, together with the net proceeds from this offering, will be sufficient to fund our operations through June 2006. However, our operating plan may change as a result of many factors, including those described above, and we may need additional funds sooner than planned to meet operational needs and capital requirements for product development.

We do not expect to generate sufficient cash from our operations to sustain our business for the foreseeable future. Unless we are able to do so, we expect our continuing operating losses to result in increases in our cash used in operations over the next several quarters and years. To the extent our capital resources are insufficient to meet future capital requirements, we will need to finance future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements. Additional equity or debt financing, or corporate collaboration and licensing arrangements, may not be available on acceptable terms, if at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our research and development programs, reduce our planned commercialization efforts, or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain drug candidates that we might otherwise seek to develop or commercialize independently. Additionally, any future equity funding may dilute the ownership of our equity investors.

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

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

Contractual Obligations

The following table summarizes our significant contractual obligations and commercial commitments as of December 31, 2003:

	Payments due by period (in thousands)				
Contractual Obligations	**Total**	**2004**	**2005-2007**	**2008-2009**	**After 2009**
Long-term debt	$ 2,235	$ 662	$ 1,010	$ 198	$ 365
Operating leases	5,216	1,456	2,911	849	—
Other contractual obligations	4,220	3,984	230	6	—
Total	$11,671	$6,102	$ 4,151	$ 1,053	$ 365

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

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 March 31, 2004, we had cash, cash equivalents and short-term investments of $36.8 million consisting of cash and highly liquid investments deposited in, and invested through, highly rated financial institutions in the United States. A portion of our investments may be subject to interest rate risk and could fall in value if market interest rates increase. However, because our investments are short-term in duration, we believe that our exposure to interest rate risk is not significant and a 1% movement in market interest rates would not have a significant impact on the total value of our portfolio. We actively monitor changes in interest rates. We adjusted our portfolio in April 2004 to eliminate positions in investments that were subject to potentially significant interest rate risks.

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

Recent Accounting Pronouncements

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

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

BUSINESS

Overview

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

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

- TC-1734—in Phase II clinical trials for the treatment of cognitive impairment in elderly persons classified with age associated memory impairment, commonly referred to as AAMI, or mild cognitive impairment, commonly referred to as MCI;
- TC-5231—in Phase II clinical trials for the treatment of attention deficit hyperactivity disorder, commonly referred to as ADHD;
- TC-2403—in a Phase II clinical trial for the treatment of ulcerative colitis;
- TC-2696—in a Phase I clinical trial for the treatment of pain; and
- preclinical research programs in Alzheimer's disease, schizophrenia, depression and anxiety, smoking cessation and obesity.

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

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

We develop product candidates using our proprietary databases and computer-based molecular design technologies, which we refer to collectively as Pentad. Pentad relies on extensive biological data for a library of diverse compounds that we have developed and gathered over 20 years. Together with our proprietary assays and novel screening methods, Pentad enables us to efficiently identify, prioritize, characterize and optimize novel compounds designed to selectively target specific NNR subtypes in an effort to achieve desired results while limiting or potentially eliminating side effects.

We have entered into two collaboration agreements with Aventis Pharma SA. Our first collaboration agreement with Aventis covers the research, development and commercialization of specified Targacept compounds for the treatment or prevention of Alzheimer's disease. Our second collaboration with Aventis covers the research, development and commercialization of Aventis compounds for the treatment or prevention of Alzheimer's disease and other diseases of the central nervous system. In addition, we have entered into a

collaboration agreement with Dr. Falk Pharma GmbH, a German company with a focus on treatments for gastrointestinal diseases, which covers the research, development and commercialization of our product candidate TC-2403 for the treatment or prevention of ulcerative colitis.

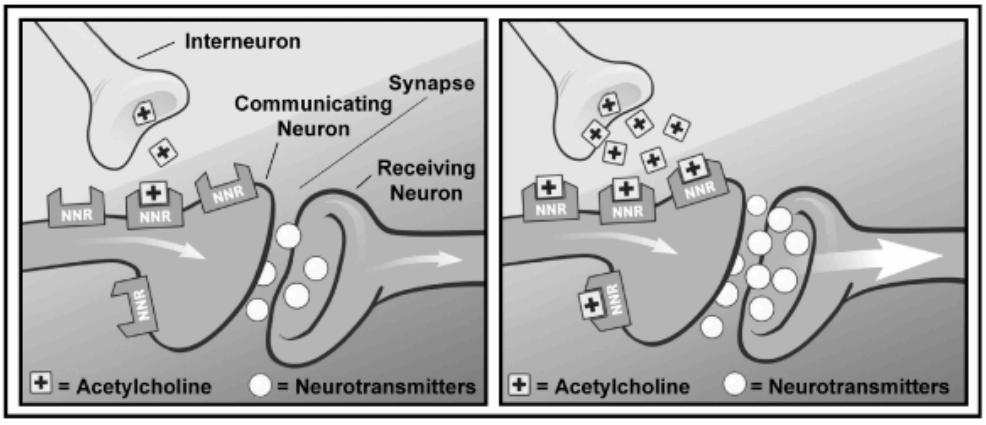
Role of NNRs in the Nervous System

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

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

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

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



NNRs are comprised of five protein subunits that are arranged like staves of a barrel around a central pore. Each different combination of five subunits represents an NNR subtype. There are several subtypes, each of which is identified by Greek letters. Scientific evidence has established that individual NNR subtypes have

particular functions in the body that are relevant to a number of debilitating diseases and disorders, as set forth below.

NNR Subtype	Primary Functions Impacted	Diseases or Disorders Potentially Implicated
$\alpha 7_5$	sensory gating; cognition	schizophrenia; cognitive impairment
$\alpha 4_2 \beta 2_3$	cognition	cognitive impairment; Alzheimer's disease; ADHD
	pain perception	acute, chronic and neuropathic pain
$\alpha 3_2 \beta 2_3$	gastrointestinal tone	ulcerative colitis
$\alpha 6 \beta 3$	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 $\alpha 4 \beta 2$ NNR and with the $\alpha 7$ NNR in the brain. Many published studies evaluating the effects of nicotine in humans and animals, as well as published studies showing the prevalence of diseases such as Alzheimer's disease and Parkinson's disease in non-smokers as compared to smokers, suggest the therapeutic effects of compounds such as nicotine that interact with NNRs. However, despite their positive effects, these compounds have historically not been desirable as therapies because they have not been sufficiently selective. This means that these compounds interact not only with NNRs, but also with nicotinic acetylcholine receptors in the muscles and ganglia that are associated with adverse effects such as increased heart rate, high blood pressure, irregular heartbeat, nausea, vomiting and a dangerous slowing of breathing known as respiratory depression.

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

Our Business Strategy

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

- *Develop and commercialize drugs that selectively target specific NNR subtypes.* Based on our understanding of the role of NNRs in the nervous system, we believe that drugs designed to selectively target specific NNR subtypes can have positive medical effects with limited or no adverse side effects. We believe that our four product candidates in clinical development may exhibit these attributes and we are aggressively pursuing their development. In addition, we use our scientific expertise and Pentad to identify additional compounds that selectively target specific NNR subtypes as potential treatments for diseases and disorders of the central nervous system and our other target indications.
- *Remain at the forefront of the commercialization of NNR research*. We have established ourselves as a leader in NNR research over the last 20 years. Our scientists and their former colleagues at RJR have published more than 150 NNR-related articles in leading scientific journals and more than 200 abstracts. Our leadership position in this area is also reflected in our extensive patent estate that includes 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.
- *Collaborate selectively to develop and commercialize product candidates.* We intend to selectively enter into collaboration agreements with leading pharmaceutical and biotechnology companies to assist us in furthering the development of our product candidates. In particular, we intend to enter into these third-party arrangements for target indications in which our potential collaborator has particular expertise or that involve a large, primary care market that must be served by large sales and marketing organizations. In entering into these collaboration agreements, our goal will be to maintain co-promotion or co-commercialization rights in the United States and, in some cases, other markets.
- *Build a specialized sales and marketing organization.* We intend to build an internal sales and marketing organization for target indications in which specialists heavily influence the market, particularly neurology and psychiatry. We believe that we can effectively serve these markets with a specialized sales force, enabling us to retain greater value from our product candidates that receive marketing approval than if we relied on a third party's sales force.

Opportunities in Our Target Indications

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

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

Our primary product development focus is on diseases and disorders of the CNS, which represent a major segment of the global healthcare environment. The Reuters Business Insight Healthcare Report estimated the total worldwide CNS pharmaceutical market to be $58 billion in 2002. Four of the top ten selling drugs in the world in 2002, Pfizer's Celebrex and Zoloft, Eli Lilly's Zyprexa and GlaxoSmithKline's Paxil/Seroxat, treat diseases and disorders of the CNS. However, despite their commercial success, many current CNS drugs are only moderately effective or are accompanied by significant side effects or other drawbacks. Accordingly, we believe that substantial opportunities exist for new therapies that address CNS disorders. We are currently conducting clinical trials for the use of our product candidates in the treatment of particular CNS disorders such as cognitive impairment in the elderly, ADHD and pain. We are also currently conducting a clinical trial of one of our product candidates for use in the treatment of the gastrointestinal disease ulcerative colitis.

Cognitive Impairment in the Elderly

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

The term AAMI describes a common condition characterized by gradual memory loss or other cognitive impairment that generally occurs with normal aging. A person who is at least 50 years of age and scores at least one standard deviation below the mean established for young adults on a standardized memory test without evidence of dementia, neurological illness or other medical cause may be classified with AAMI. The term AAMI is not currently listed in *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, or DSM-IV, the manual published by the American Psychiatric Association to establish diagnostic criteria. However, DSM-IV does list the term "age related cognitive decline," which is often used by the medical community interchangeably with AAMI, as an "objectively identified decline in cognitive functioning consequent to the aging process that is within normal limits given the person's age." A number of published clinical trials have been conducted in AAMI or similarly characterized conditions. Although estimates of the prevalence of AAMI in the elderly vary greatly because of varying methodologies and definitions of AAMI, one published study indicates that AAMI may affect as many as 38% of people over age 65. Based on a 2000 report of the Federal Interagency Forum on Aging-Related Statistics, this represents over 13 million people in the United States alone. The Federal Interagency Forum report projects that the number of people in the United States age 65 or older will double by 2030.

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

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

Attention Deficit Hyperactivity Disorder

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

Datamonitor estimates that ADHD affects approximately 8 million youths in the world's seven major pharmaceutical markets, including 4.8 million in the United States. According to Datamonitor, the worldwide market for ADHD drugs was approximately $1.3 billion in 2002.

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

Ulcerative Colitis

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

Datamonitor estimates that ulcerative colitis affects approximately 870,000 people in the world's seven major pharmaceutical markets, including approximately 320,000 people in the United States.

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

Pain

There are two general categories of pain, nociceptive and neuropathic. Pain occurs when base nerve endings known as pain receptors are activated and a pain signal is transmitted through the nervous system to the brain. With nociceptive pain, the pain signal starts with damage to tissue and is typically accompanied by inflammation. Nociceptive pain can be either acute, such as that experienced following surgery, or chronic. 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.

Datamonitor estimates that approximately 75 million people in the world's seven major pharmaceutical markets suffer annually from acute nociceptive pain following a surgical procedure. Pharmaprojects, a healthcare publication, estimates that 26 million people worldwide suffer annually from some form of neuropathic pain. According to Datamonitor, the worldwide market for pain therapies was approximately $17 billion in 2001.

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

Our Product Development Pipeline

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

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

Product Candidate	Target Indications	Stage of Development	Status of Development	Commercial Rights
TC-1734	Cognitive impairment in the elderly	Phase II	Enrollment complete for initial Phase II trials; full data expected in the second half of 2004	Targacept worldwide
TC-5231	ADHD	Phase II	Enrollment complete; data expected in 4Q 2004	Targacept worldwide
TC-2403	Ulcerative colitis	Phase II	Enrollment ongoing; data expected in 1Q 2005	Dr. Falk Pharma –Europe, Russia, Egypt and Israel Targacept –United States and rest of world
TC-2696	Acute post-operative pain	Phase I	Enrollment complete for initial Phase I trial; data expected in the second half of 2004	Targacept worldwide

We are conducting our ongoing Phase II clinical trials of TC-1734 in the United Kingdom. We are conducting our ongoing Phase II clinical trials of TC-5231 in the United States. We are conducting our ongoing Phase II clinical trial of TC-2403 in the United States, Canada and Eastern Europe. We are conducting our ongoing Phase I clinical trial of TC-2696 in France.

TC-1734

TC-1734 is a novel small molecule that we are developing as an oral treatment for a range of cognitive impairment in the elderly that includes AAMI and MCI. We are currently conducting a Phase II clinical trial of TC-1734 in 56 elderly persons classified with AAMI and have completed two arms of the trial. We are also currently conducting a Phase II clinical trial in 40 elderly persons classified with MCI. We have previously evaluated TC-1734 in 84 healthy volunteers in four Phase I clinical trials.

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

Published studies with humans have shown a reduced number of $\alpha 4\beta 2$ NNRs in persons with dementia, suggesting the involvement of $\alpha 4\beta 2$ in cognition. In our preclinical animal studies, TC-1734 triggered activity of $\alpha 4\beta 2$, enhanced the release of acetylcholine, enhanced memory and showed meaningful separation between the doses at which positive effects on memory and side effects were first seen. In two preclinical in vitro studies that we conducted, 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 $\alpha 4\beta 2$, we believe that TC-1734 has the potential to prevent or delay neurodegeneration.

We are also evaluating TC-1734 for potential additional clinical development for indications marked by cognitive impairment that are not specific to the elderly, such as ADHD, schizophrenia and various forms of dementia. We are restricted from pursuing development of TC-1734 for the treatment or prevention of Alzheimer's disease while our collaborative agreement with Aventis Pharma SA relating to the development of our compound TC-4959 remains in effect.

Clinical Development of TC-1734

Phase I Clinical Trials. During 2003, we 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 48 volunteers, the compound was well tolerated in doses of up to 320mg. We also observed an acceleration in brainwaves thought to be associated with positive effects on attention, suggesting that the compound had reached the brain.
- In a multiple rising dose trial with 24 volunteers, 50mg, 100mg and 200mg doses of TC-1734 were administered over a 10-day period. We observed a dose-dependent positive effect on attention at the end of the trial measured by the ability of the volunteers to focus on a particular task to the exclusion of other tasks.
- In a pharmacokinetic trial, six elderly volunteers were given a single 80mg dose to assess the compound's absorption, distribution, metabolism and excretion. We observed positive effects on memory and learning, including improved episodic memory based on word recall and picture recognition assessments. These effects lasted up to 48 hours after a single oral dose.
- In a food interaction trial, six volunteers were administered an 80mg dose with or without having eaten and the compound was well tolerated.

Phase II Clinical Trials. We are currently conducting a double blind, placebo-controlled Phase II clinical trial of TC-1734 in 56 elderly volunteers classified with AAMI. We are conducting the trial at multiple sites in the United Kingdom under a clinical trial exemption, the United Kingdom equivalent to an IND. The primary objective of this trial is to assess the safety and tolerability of TC-1734 in elderly subjects compared to placebo. The secondary objectives of this trial are to assess the efficacy of TC-1734 in improving cognitive function and changes in mood state.

We are also currently conducting a second double blind, placebo-controlled clinical trial of TC-1734 in 40 elderly volunteers classified with MCI. This trial has similar objectives to the AAMI trial and is also being conducted in the United Kingdom.

In the AAMI trial, the subjects have been divided into three dose groups – 20 subjects are in the 50mg group, 20 subjects are in the 100mg group and 16 subjects are in the 150mg group. In the MCI trial, the subjects have been divided into 50mg and 100mg dose groups of 20 subjects each. In both trials, each subject is 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 is changed to be dosed with either a placebo or TC-1734, as the case may be, daily for another three-week period. Each subject takes TC-1734 or a placebo before eating on the day of dosing. During the trials, routine safety measures are recorded and pharmacokinetic assessments are made for each subject. In addition, subjects are assessed for changes in cognitive function and mood state before and after dosing on the first day of the three-week dosing period and then again on the last day of the dosing period. The trials are double blind, meaning that neither the subjects nor the clinical investigators know during the trials which subjects are receiving TC-1734 and which are receiving the placebo.

In the trials, we are testing subjects for changes in cognitive function using a computer-based test battery developed by CDR Ltd. This test battery includes measures of attention, speed of cognitive processes and memory that assess the ability to react to stimuli, recognize words and pictures and recall words. CDR has indicated that its battery has been used to assess cognitive performance in over 500 clinical trials worldwide.

We also used the CDR test battery in our Phase I clinical trials of TC-1734. We selected it because of its comprehensive measures and CDR's extensive database of test results in unimpaired persons that enable assessment of statistical significance.

As of June 30, 2004, we have received data from the 50mg and 100mg arms of the AAMI trial. At each of these doses, TC-1734 was well tolerated, with no serious adverse events reported. In addition, subjects in the 50mg dose group that received TC-1734 showed improvements in measures of attention, speed of cognitive processes and memory as compared to subjects receiving placebo. These results were statistically significant. A clinical trial result is statistically significant if it is unlikely to have occurred by chance. The statistical significance of clinical trial results is determined by a widely used statistical method that establishes the p-value of the results. Under this method, a p-value of 0.05 or less represents statistical significance. The improvements observed in attention, speed of cognitive processes and memory in the 50mg dose group ranged from a p-value of 0.01 to a p-value of 0.043. These effects were consistent with the effects seen in our Phase I trials. The positive effects that we observed in the 50mg dose group were less pronounced in the 100mg dose group, which is consistent with the dose-related effects on cognition that we observed in our preclinical animal studies. In the 150mg dose group, three out of eight subjects treated with TC-1734 experienced side effects such as headache, lightheadedness, dizziness and vomiting and dropped out of the trial. In light of these effects, we ceased dosing new subjects at 150mg. The results of the AAMI trial suggest that TC-1734 is well tolerated at a dose range of up to 100mg, that 150mg is the maximum tolerated dose of TC-1734 for this trial design and that the compound had positive effects on cognition at a dose within the tolerated range.

To generate additional data related to the tolerability of TC-1734, we are currently enrolling eight additional elderly volunteers classified with AAMI to be tested at a dose of 150mg, after having eaten, using the same trial design. This will enable us to assess the impact of food on the tolerability of TC-1734 by comparing it in volunteers dosed at 150mg who have eaten and in volunteers dosed at 150mg who have not eaten. To further assess the tolerability of TC-1734, we are also enrolling additional elderly volunteers classified with AAMI to be tested at a dose of 125mg without having eaten using the same trial design.

Plans for Future Development. We plan to meet with the FDA regarding whether cognitive impairment in the elderly or one or both of AAMI and MCI are indications for which the FDA would approve a drug and, if so, the additional trials that we would need to perform to support an application for approval of TC-1734 for the treatment of one or more of these indications. Following the discussions with the FDA, we expect to evaluate the specific target indication or indications for continued clinical development of TC-1734. Subject to the results of our discussions with the FDA, we anticipate commencing a separate Phase II clinical trial designed to evaluate the efficacy of TC-1734 in the fourth quarter of 2004.

TC-5231

TC-5231 is a small molecule that we are developing as an oral treatment for ADHD. TC-5231 is a low-dose reformulation of mecamylamine hydrochloride, the active ingredient in our FDA-approved product, Inversine. Inversine is approved in the United States for the management of moderately severe to severe essential hypertension at average daily doses of 25mg. Our market research suggests, however, that Inversine is prescribed predominantly for the treatment of Tourette's syndrome and other neuropsychiatric disorders at doses ranging from 2.5mg to 7.5mg. We have reformulated mecamylamine hydrochloride as TC-5231 in a liquid gel cap. We are evaluating this product candidate in doses between 0.2mg and 1.0mg in two Phase II clinical trials, one in ADHD in children and adolescents and one in ADHD in young adults.

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

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

Although the means by which mecamylamine hydrochloride acts to cause these effects is not known, scientists have suggested that it may prevent interference with the activity of the α4ß2 NNR, which regulates neurotransmitters involved in attentional processes such as dopamine, norepinephrine and serotonin, or it may block α4ß2 from releasing the neurotransmitter GABA, which inhibits attentional processes.

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

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

Clinical Development of TC-5231

Phase II Trial in Children and Adolescents. We are conducting a flexible dose, double blind, placebo-controlled, Phase II clinical trial of TC-5231 in children and adolescents with ADHD. As of June 30, 2004, we had enrolled 192 patients between the ages of 6 and 17 at 17 sites in the United States. The trial is fully enrolled. The primary objective of this trial is to determine whether TC-5231 is effective in the treatment of symptoms of ADHD in subjects within this age group. The trial will also assess the safety, tolerability and pharmacokinetics of TC-5231. In addition, because mecamylamine hydrochloride at the Inversine dose is used to treat forms of hypertension, an independent safety board is monitoring the effects of TC-5231 on subjects' blood pressure.

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

Phase II Trial in Young Adults. We have contracted with a physician-investigator to conduct a placebo-controlled, Phase II clinical trial of TC-5231 on our behalf. This trial is being conducted in the United States with 12 ADHD patients between the ages of 17 and 24. In the trial, the investigator doses patients once per week over a five-week period. Each week patients receive one of a 0.2mg, 0.5mg or 1.0mg dose of TC-5231, nicotine administered via patch or a placebo. The primary objective of the trial is to measure effects of TC-5231 on sustained attention. In particular, the trial measures the time needed for a patient to cancel a planned movement, referred to as "stop signal reaction time," as well as other aspects of attention. In addition, the investigator is measuring performance on a word recognition test. The investigator has advised us that the trial will be completed and the results available in the second half of 2004.

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

TC-2403

TC-2403 is a small molecule that we are developing for the treatment of ulcerative colitis in collaboration with Dr. Falk Pharma GmbH. We are currently conducting a Phase II clinical trial of an enema formulation of the compound designed to induce remission of acute episodes of left-sided colitis. In addition, we are developing a delayed release oral formulation of the compound designed to deliver the drug to the entire colon to induce and maintain remission of all forms of ulcerative colitis. We expect to complete the oral formulation of this product candidate in the fourth quarter of 2004.

Ulcerative colitis is characterized by inflammation of the lining of the colon. Our preclinical studies of TC-2403 suggest that the compound interacts with the $\alpha3\beta2$ NNR that is present in nerve endings in the gastrointestinal tract. We believe that $\alpha3\beta2$ may play an important role in preventing inflammation and maintaining the lining of the colon. In other preclinical in vitro studies that we conducted, TC-2403 inhibited the release of proteins called cytokines that cause inflammation in humans and did not interact significantly with nicotinic acetylcholine receptors in the peripheral tissues associated with side effects like nausea and cardiovascular effects.

TC-2403 is related structurally to nicotine, and studies have shown that nicotine has positive effects for limited periods in treating the symptoms of ulcerative colitis. Specifically, in published third-party studies involving humans and animals, nicotine modulated the release of acetylcholine from nerves, increased secretion of mucus in the colon, inhibited the production of cytokines and reduced chemicals called prostaglandins that are involved in the process of inflammation. Collectively, these effects would help to maintain the normal structure of the colon. Also, in published studies conducted at the Mayo Clinic, nicotine was administered to non-smoking ulcerative colitis patients either via a nicotine patch or an enema. In these studies, remission of ulterative colitis symptoms and tissue healing was observed in approximately 40% of patients treated with the patch, as compared to 9% of patients treated with placebo, and approximately 70% of patients treated with an enema. Unlike the patch study, the enema study was not placebo controlled. However, serious side effects like nausea were observed in patients treated with nicotine, particularly when administered via patch. Because TC-2403 is designed to selectively target the $\alpha3\beta2$ NNR, we believe that it may have positive effects on ulcerative colitis similar to those of nicotine, but without the side effects.

Clinical Development of TC-2403

Phase I Clinical Trials. We conducted two Phase I, placebo-controlled clinical trials of the enema formulation of TC-2403, including:

- a single rising dose trial in which 32 healthy volunteers received TC-2403 enemas in dosages ranging from 5mg to 800mg; and
- a multiple rising dose trial in which 12 volunteers received TC-2403 enemas in dosages of 50mg, 200mg and 400mg over a period of 14 days.

In each trial, TC-2403 was well tolerated and we observed no clinically significant adverse events.

Phase II Clinical Trial. We are sponsoring a double blind, placebo-controlled, dose range finding Phase II clinical trial to determine whether TC-2403 in the enema formulation is effective in treating mild to moderate left-sided colitis. The trial is being conducted at 35 sites in the United States, 10 sites in Canada and 26 sites in three Eastern European countries. We plan to enroll between 176 and 240 ulcerative colitis patients for the trial. Because patient recruitment rates for ulcerative colitis are relatively low, we are using a large number of clinical sites in an effort to complete the trial by early 2005. As of June 30, 2004, 176 patients had been enrolled. Two contract research organizations are monitoring and managing the trial for us.

In the trial, patients are administered an enema with 100mg, 200mg or 400mg of TC-2403 or a placebo each day over six weeks. Endoscopic examinations of the colon are made at the beginning and end of the six-week period and routine safety assessments are made throughout the trial. The primary efficacy endpoint of the trial is the change in patients' U.S. Disease Activity Index for ulcerative colitis from baseline, as compared to placebo.

This index measures stool frequency, rectal bleeding, appearance of the lining of the colon and a physician's global rating of disease severity. A secondary endpoint is the change in patients' European Union's Clinical Activity Index for ulcerative colitis, which measures items such as number of stools, blood in stools, abdominal pain and cramps, general well-being, presence or absence of fever and clinical manifestations such as arthritis outside of the intestines, as compared to placebo.

As of June 30, 2004, five of the 176 patients who had participated in the trial experienced an elevation in liver enzymes in excess of three times the upper limit of normal. Four of these patients were withdrawn from the trial and their liver enzymes returned to within the normal range. The fifth patient continued in the trial. This patient's liver enzymes returned to the normal range during the last two weeks of the six-week dosing regimen and were within the normal range at the post-regimen follow-up visit. Because the trial is double blind, we do not know if these patients were administered TC-2403 or a placebo.

The design of this trial is adaptive, meaning that we can adjust the dosages and the number of participating patients. We plan to have an analysis of the available data from the trial conducted by an independent third party in the third quarter of 2004 to enable us to select the most relevant dosages for the remainder of the trial and to determine the total number of patients to be studied. We expect the complete results of this trial to be available in the first quarter of 2005.

Plans for Future Development. We plan to file an IND or a foreign equivalent to conduct a Phase I clinical trial of the oral formulation of TC-2403 in the first half of 2005. If the results of the planned Phase I trial of the oral formulation and the ongoing Phase II trial of the enema formulation are favorable, we expect that we and Dr. Falk Pharma will further assess the development plans for both the oral and enema formulations.

TC-2696

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

In our preclinical in vitro studies of TC-2696, we found the compound to be a potent activator of the $\alpha4\beta2$ NNR and to avoid interaction with nicotinic acetylcholine receptors in the muscles and ganglia that are associated with side effects. Published studies conducted by third parties have shown that compounds that activate $\alpha4\beta2$ have pain-relieving effects in animals. These effects may be caused in part by the activation of NNRs that are abundant in CNS pathways to block the transmission of pain signals to the brain. In our preclinical animal studies, TC-2696:

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

Clinical Development of TC-2696

Phase I Clinical Trial. We are currently conducting 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 is being conducted in France with 44 healthy volunteers divided into dose groups of 2mg, 5mg, 10mg, 20mg, 50mg, 100mg, 150mg and 200mg. In addition to evaluating safety and tolerability, we designed the trial to include a number of surrogate measures, including inflammation and pain relief. We expect this trial to be completed and the results available in the second half of 2004.

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

Inversine

Inversine is currently our only marketed product. Inversine is approved in the United States for the management of moderately severe to severe essential hypertension. Our market research suggests, however, that Inversine is prescribed predominantly for the treatment of Tourette's syndrome and other neuropsychiatric disorders. Inversine has been approved for marketing since the 1950s. We acquired marketing rights to the product in August 2002 from Layton Bioscience, Inc., which had previously acquired the rights from Merck & Co., Inc. In connection with our acquisition, we assumed Layton's obligations under the agreement pursuant to which Layton acquired the rights from Merck. Pursuant to that agreement, we pay Merck an amount each year based on annual sales of Inversine, subject to a specified annual maximum. Our annual payment obligation to Merck expires in 2008.

We have reformulated mecamylamine hydrochloride and are developing it in a lower dose as TC-5231 for the treatment of ADHD. We are also exploring the potential use of mecamylamine hydrochloride in the same dose as Inversine for additional indications such as depression.

Our Preclinical Research Programs

We focus our preclinical research efforts on indications for which we believe that selective NNR-targeted drugs have the potential for use in the treatment of disease and for which we believe we can efficiently develop marketable product candidates. In selecting our target indications, we have considered a number of factors, including:

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

Based on our consideration of these factors, we currently have ongoing preclinical research programs for Alzheimer's disease, schizophrenia, depression and anxiety, smoking cessation and obesity. Each of these indications represents a substantial market opportunity. Our current research objective is to file at least one IND or foreign equivalent each year beginning in 2005.

Alzheimer's Disease

Alzheimer's disease progressively impairs memory, reason, judgment, language and eventually the ability to carry out simple tasks. While the exact cause of Alzheimer's disease is unknown, the decline of cognitive function is linked to a progressive deterioration and death of cells in the brain. In addition, published studies have shown, among other things, that Alzheimer's patients have deficient levels of acetylcholine.

TC-4959 is our compound that we are developing in collaboration with Aventis for the treatment or prevention of Alzheimer's disease. TC-4959 induced significant increases in acetylcholine levels in preclinical in vitro studies by interacting with the $\alpha 4\beta 2$ NNR and improved memory-related performance in rodent models.

An executive committee formed under our collaboration agreement with Aventis that covers the development of TC-4959 is responsible for determining whether to advance TC-4959 into clinical trials. We expect Aventis to complete the necessary preclinical studies to enable the committee to make that determination

in the fourth quarter of 2004. If the compound is advanced into clinical trials, Aventis would be responsible for all clinical development and potential commercialization. If the compound is not advanced, this collaboration agreement with Aventis will terminate.

Schizophrenia

Schizophrenia is a chronic, severe and disabling form of psychosis. Although the precise cause of schizophrenia is unknown, the disease is thought to be associated with an imbalance of neurotransmitter levels in the brain, particularly dopamine levels. Because NNRs act to regulate levels of neurotransmitters in the brain, we believe that NNRs may be useful targets for schizophrenia therapies. A number of published studies have indicated an association between the α7 NNR and schizophrenia. In a survey of experts in connection with a National Institute of Mental Health schizophrenia initiative, α7 was selected more often than any other target as the target of most interest in the development of treatments for psychosis. In addition, because schizophrenic patients are frequently cognitively impaired, we believe that the α4ß2 NNR, which plays a role in cognition, also may be associated with schizophrenia. These studies further suggest the potential relevance of NNRs as targets for the treatment of schizophrenia. In addition, published studies have linked nicotine to improvements in the ability to filter or disregard unremarkable stimuli, a common symptom of schizophrenia, and cognitive impairment in schizophrenic patients.

We are evaluating a number of compounds for the treatment of schizophrenia in preclinical studies. Some of these compounds are designed to interact selectively with α7 and others are designed to interact selectively with both α7 and α4ß2.

Depression and Anxiety

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

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

Smoking Cessation

Due primarily to nicotine's addictive effects, it is very difficult to quit smoking. Published animal studies have linked nicotine's addictive effects to the release of dopamine in regions in the brain involved in feelings of reward and pleasure. Although the specific NNR implicated in the regulation of dopamine is not fully characterized, several reported studies suggest that the ß2 NNR may be involved. These studies have shown that selectively blocking ß2 reduced the rewarding effects of nicotine in mice. Other studies have shown that mice

deficient in ß2 failed to respond to nicotine and had reduced activity in the brain regions associated with reward and pleasure. We are evaluating a number of compounds in a variety of animal models of smoking cessation and nicotine dependence for advancement in our smoking cessation program.

Obesity

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

As part of our evaluation of our compounds for other indications, we also assess each compound for a preliminary signal of its ability to induce weight loss. We are collecting this data and currently plan to conduct additional preclinical evaluation of the most promising compounds for obesity in 2005.

Our Drug Discovery Technologies—Pentad

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

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

Pentad's virtual screening enables us to more rapidly identify clinically-viable compounds than we believe could be achieved using traditional laboratory synthesis and screening methods. This allows us to reduce drug development time by focusing our resources on compounds that we believe have a greater likelihood of clinical success. Our use of Pentad to design new classes of compounds selective for the $\alpha 7$ 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 $\alpha 7$ NNR, showed low binding affinity for NNRs involved in side effects, were bioavailable and passed the blood-brain barrier. We identified the 43 compounds in only six months and are currently evaluating many of these compounds as part of our schizophrenia program.

Strategic Collaborations

We have entered into two collaboration agreements with Aventis Pharma SA. One agreement relates to the development and potential commercialization of specified Targacept compounds and the other relates to the development and potential commercialization of Aventis compounds. We have also entered into a collaboration agreement with Dr. Falk Pharma GmbH.

Aventis Pharma SA

Targacept Compounds. In January 2002, we entered into an amended and restated collaborative research and license agreement with Aventis that replaced our original agreement entered into in December 1998. Under the agreement, we granted Aventis an exclusive, worldwide, sublicensable license under our patent rights and know-how, excluding Pentad, to develop and commercialize specified Targacept compounds for the treatment or prevention of Alzheimer's disease. The agreement restricts both us and Aventis from pursuing the development or commercialization of compounds with specified activity at the $\alpha 4\beta 2$ or $\alpha 7$ NNRs for Alzheimer's disease during the term of the agreement, except under the agreement or our other collaboration agreement with Aventis, which is described below.

Aventis paid us a non-refundable upfront license fee of $2 million at the time of execution of the original agreement in 1998. Aventis also made research support payments to us under the agreement until December 2002. In addition, we could receive up to an aggregate of $30 million from Aventis upon the achievement of specified pre-commercialization development and regulatory milestones. None of these milestones has been achieved, and the achievement of any of these milestones is uncertain. We are also entitled to receive royalties based on net sales by Aventis, its affiliates and its sublicensees of products developed under the agreement. Our right to receive royalties would continue on a country-by-country and product-by-product basis until the later of ten years from the first commercial sale of a product in that country or the expiration of the patent rights covering the product in that country.

An executive committee comprised of an equal number of representatives from Aventis and us is responsible for determining whether to advance our compounds into clinical development. Our compound TC-4959, which is in late preclinical evaluation, is the only compound that remains in consideration for continued development and potential commercialization under the agreement. If the members of the executive committee representing either Aventis or us desire to advance TC-4959 into clinical development and the members representing the other party object, TC-4959 will not advance into clinical development and neither party may then develop or commercialize the compound for any use. If the executive committee selects TC-4959 for advancement, Aventis will control clinical development and be responsible for conducting all preclinical research and clinical development activities and for obtaining all regulatory approvals. Aventis would be required to use commercially reasonable efforts to develop TC-4959 and, if Aventis receives regulatory approval, commercialize the compound for the licensed indication in the United States, the European Union and Japan.

All of our compounds that were not advanced into clinical development have been removed from the collaboration, with all rights reverting to us. For example, TC-1734, our product candidate for cognitive impairment in the elderly, was removed from the collaboration in this manner. The terms of the collaboration agreement restrict us from pursuing the development of TC-1734 for the treatment or prevention of Alzheimer's disease while the agreement remains in effect.

Unless otherwise agreed, the agreement terminates six months after the end of the research term if a compound has not advanced into clinical development. The agreement provides for the research term to end on December 31, 2002. Although neither we nor Aventis has taken action to formally extend the research term, Aventis is continuing to evaluate TC-4959 for possible advancement under the agreement and to report its progress to our project team representatives at regular meetings. If TC-4959 is not advanced into clinical development, the collaboration agreement would terminate. Either party may terminate the agreement in the event of an uncured material breach by the other party. However, if a breach by Aventis is limited to a particular key market, we can terminate the agreement only as applied to that market. Upon termination of the agreement, the licenses that we granted to Aventis terminate, except that, in the event of a partial termination, only those licenses applicable to the terminated aspects of the agreement terminate.

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

The agreement restricts us, during the research term, from developing and commercializing compounds with specified activity at the $\alpha4\beta2$ or $\alpha7$ NNRs for the treatment or prevention of Alzheimer's disease. This restriction applies only if both our collaboration agreement with Aventis relating to the development and potential commercialization of our compounds remains in effect and Aventis is using commercially reasonable efforts to develop and commercialize a compound under that agreement for the treatment or prevention of Alzheimer's disease in the United States, the European Union and Japan. Except with respect to any compounds that we in-license from Aventis under the agreement as described below, we are not restricted in any way under the agreement from developing or commercializing compounds for other CNS disorders.

We could receive up to $8 million upon the achievement of specified pre-commercialization development and regulatory milestones related to Alzheimer's disease and up to $8 million for each other CNS indication upon the achievement of specified pre-commercialization development and regulatory milestones. None of these milestones has been achieved, and the achievement of any of these milestones is uncertain. We are also entitled to receive royalties based on net sales by Aventis, its affiliates and sublicensees of each product under the agreement. Our right to receive royalties would continue on a country-by-country and product-by-product basis until the later of ten years from the first commercial sale of a product in that country or the expiration of the patent rights covering the product in that country.

An executive committee comprised of an equal number of representatives from us and Aventis is responsible for initially recommending further development of any compound under the agreement. Aventis also has the independent right to recommend further development of any compound. A scientific review board from Aventis determines whether to advance a compound into clinical development. Under the agreement, Aventis is responsible for conducting all preclinical and clinical development activities and obtaining all required regulatory approvals for compounds selected for advancement. Any compound that Aventis initially selects for advancement but ultimately rejects is terminated from the collaboration and becomes available to us for in-licensing. We would be permitted to in-license the terminated compound for use in indications other than the treatment or prevention of CNS disorders or for use in specified CNS indications if Aventis is not developing its own product for those indications, subject to our making milestone and royalty payments to Aventis.

If not terminated earlier, this agreement terminates upon expiration of all royalty and other payment obligations. In addition, either party may terminate the agreement in the event of an uncured material breach by the other party. However, if Aventis is developing or commercializing more than one compound or product, or if we are developing or commercializing more than one compound or product that has been terminated from the collaboration and in-licensed by us, and the breach relates to a particular compound or product, then the non-breaching party can terminate the agreement only as applied to that compound or product. If Aventis terminates the agreement other than as a result of an uncured breach by us and our collaboration agreement with Aventis relating to the development and commercialization of our compounds is still in effect, we would continue to be entitled to receive milestone and royalty payments for specified compounds. In that case, we would be entitled to milestone and royalty payments for any Aventis compounds subject to the agreement that Aventis later develops for use in a CNS indication or for any other compound that targets the $\alpha 4\beta 2$ or $\alpha 7$ NNR that Aventis later develops for the treatment or prevention of Alzheimer's disease.

Dr. Falk Pharma GmbH

In January 2001, we entered into a collaborative research, development and license agreement with Dr. Falk Pharma. The agreement provides for the research, development, and commercialization of our compound TC-2403 and, if selected by Dr. Falk Pharma and us, at least one additional compound for the treatment or prevention of ulcerative colitis and other gastrointestinal or liver diseases. Phase II clinical trials of TC-2403 are currently ongoing.

Under the agreement, we granted Dr. Falk Pharma a license under our patent rights and know-how relating to TC-2403 and additional compounds that may become part of the agreement, excluding Pentad, in a territory in Europe consisting of all of the major European pharmaceutical markets, Russia and the Commonwealth of Independent States countries, Egypt and Israel. The license is exclusive in the licensed territory with respect to the sale of compounds for the treatment or prevention of ulcerative colitis and other gastrointestinal or liver diseases and joint, or co-exclusive, with us with respect to all other purposes. We retained all commercialization rights in the rest of the world. Dr. Falk Pharma granted us a license under its patent rights and know-how relating to TC-2403 and additional compounds that may become part of the agreement to develop and commercialize pharmaceutical products for the treatment or prevention of ulcerative colitis and other gastrointestinal or liver diseases in the rest of the world.

Upon effectiveness of this agreement, Dr. Falk Pharma paid us a non-refundable upfront license fee of $1.0 million and purchased $1.0 million of our common stock. We are also entitled to receive a percentage of net profits from the sale of licensed products by Dr. Falk, its affiliates and its sublicensees in its licensed territory. Dr. Falk Pharma is entitled to receive royalties from us based on net sales by us, our affiliates and sublicensees of products developed under the agreement in the United States and Japan. Our right to receive a percentage of Dr. Falk Pharma's net profits and Dr. Falk Pharma's right to receive royalties would continue on a country-by-country and product-by-product basis until the earlier of 12 years from the first commercial sale of a product in that country or the expiration of the patent rights covering the product in that country.

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

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

Patents and Proprietary Rights

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

As of June 30, 2004, our patent estate includes 59 patents issued in the United States, five patent applications allowed in the United States and not yet issued, 18 patent applications pending in the United States, and numerous issued patents and patent applications pending in countries outside the United States. Our issued patents and pending patent applications in the United States include composition of matter coverage on a number of different structural families of compounds. Individual patents extend for varying periods depending on the date of filing of the patent application or the date of patent issuance and the legal term of patents in the countries in which they are obtained. The actual protection afforded by a patent varies from country to country and depends upon many factors, including the type of patent, the scope of its coverage and the availability of legal remedies in a particular country.

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

Product Candidate	Patent Scope	Patent Expiration
TC-1734	Composition of matter for a family of compounds that includes TC-1734	April 2016
	Methods of use of a family of compounds that includes TC-1734 for treatment and prevention of CNS disorders	February 2017
	Composition of matter claims to TC-1734	June 2018—allowed but not yet issued
TC-5231	Methods of use of TC-5231 for treatment of ADHD, Tourette's syndrome and nicotine-responsive neuropsychiatric disorders	September 2017
TC-2403	Methods of use of TC-2403 and analogs for inflammatory bowel disease, including ulcerative colitis	January 2015
TC-2696	Composition of matter for a family of compounds that includes TC-2696	April 2016
	Method of use of a family of compounds that includes TC-2696 for eliciting an analgesic effect	August 2017

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

License Agreements

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

University of South Florida Research Foundation

Pursuant to a license agreement with the University of South Florida Research Foundation, or USFRF, we hold an exclusive worldwide license to patents and patent applications owned by USFRF for use in the development and commercialization of mecamylamine hydrochloride, which we refer to as TC-5231, and other specified compounds. The licensed patents and patent applications include an issued patent covering methods of use for the treatment of ADHD, Tourette's syndrome and nicotine-responsive neuropsychiatric disorders and pending patent applications covering the pharmaceutical composition of the components of mecamylamine hydrochloride. Under the agreement, we are obligated to pay to USFRF:

- an annual license fee until a new drug application or its equivalent is filed to cover the use of a product subject to the license to treat a neuropsychiatric disorder;
- an annual fee to maintain our rights of first refusal to acquire rights to the licensed patents and patent applications beyond the scope of our current license;
- royalties on net sales of products subject to the license or a percentage of royalties received from a sublicensee;

- aggregate payments of up to $200,000 based on the achievement of specified regulatory milestones; and
- a percentage of other amounts that we receive from a sublicensee.

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

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

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

Virginia Commonwealth University Intellectual Property Foundation

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

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

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

Wake Forest University Health Sciences

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

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

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

University of Kentucky Research Foundation

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

Medical College of Georgia Research Institute

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

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

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

Trade Secrets

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

Sales and Marketing

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

Manufacturing

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

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

Third parties currently manufacture Inversine and its active ingredient for us. Also, we have entered into a development and production agreement with Siegfried Ltd. Under this agreement, Siegfried has agreed to provide us with process development services and clinical trial material at specified rates for product candidates that we elect to introduce into the agreement. We have also agreed, following marketing approval or anticipated marketing approval of any product candidate for which Siegfried performs services under the agreement, to negotiate for a separate multi-year commercial supply agreement with Siegfried for a substantial percentage of our contracted supply needs for that product candidate, except in limited circumstances. Beginning in February 2006, either we or Siegfried can terminate the agreement at any time on 12 months notice or immediately in the event of an uncured material breach by the other party.

Competition

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

We also face substantial competition from therapies designed to target NNRs. We are aware of several prominent pharmaceutical companies with product candidates designed to target NNRs in development, including Pfizer, with an NNR-targeted compound in Phase III for smoking cessation, and Abbott Laboratories, with an NNR-targeted compound in Phase II for Alzheimer's disease, ADHD and schizophrenia and a second NNR-targeted compound in Phase I for pain. In addition, we believe that other companies have active NNR-based research programs, including, Merck & Co., AstraZeneca, Eli Lilly, Sanofi-Synthélabo, Memory Pharmaceuticals, Critical Therapeutics and NeuroSearch A/S. We expect to face increased competition in the future if NNR-targeted therapeutics are further validated and if companies initiate or grow NNR-based programs or otherwise enter the CNS market.

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

- for ADHD, stimulants such as Concerta from Johnson & Johnson, Ritalin from Novartis and Adderall from Shire Laboratories and the non-stimulant Strattera from Eli Lilly;

- for ulcerative colitis, 5-ASAs such as Asacol from Proctor & Gamble;
- for pain, non-steroidal anti-inflammatory drugs such as Celebrex from Pfizer and Vioxx from Merck and opioids such as OxyContin from Purdue Pharma;
- for Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer, Reminyl from Johnson & Johnson and Exelon from Novartis and an NMDA-receptor antagonist for moderate to late stage Alzheimer's disease, Namenda from Forest Laboratories;
- for schizophrenia, anti-psychotics such as Zyprexa from Eli Lilly, Risperdal from Johnson & Johnson and Abilify from Bristol-Myers Squibb;
- for depression, selective serotonin reuptake inhibitors such as Prozac from Eli Lilly, Paxil/Seroxar from GlaxoSmithKline, Zoloft from Pfizer, Celexa from Forest Laboratories and Lexapro from Forest Laboratories and the dual uptake inhibitor Effexor from Wyeth; and
- for smoking cessation, Zyban from GlaxoSmithKline.

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

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

Government Regulation

Drug Regulation in the United States

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

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

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

Preclinical tests typically include laboratory evaluation of product chemistry, formulation and stability, as well as animal studies to evaluate toxicity and metabolism. The results of preclinical tests are submitted to the FDA as

part of an IND. The FDA requires a 30-day waiting period after the filing of an IND before clinical testing in humans may begin. If the FDA has not advised otherwise within this 30-day period, the proposed trial may begin. If the FDA has comments or questions, they must be resolved to the satisfaction of the FDA before the trial can begin. In addition, the FDA may halt proposed or ongoing clinical trials at any time, in which event the trial cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. The IND application process may be extremely costly and substantially delay development of product candidates. Moreover, positive results in preclinical tests do not ensure positive results in clinical trials.

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

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

- Phase I clinical trials are conducted with a small number of healthy human volunteers as subjects to determine an early safety and tolerability profile, including side effects associated with increasing doses, a maximum tolerated dose and pharmacokinetics;
- Phase II clinical trials are conducted with groups of patients afflicted with the therapeutic condition for which the investigational drug is being tested with a specific disease in order to determine potential efficacy preliminarily, and an expanded safety profile that identifies possible adverse effects; and
- Phase III clinical trials are large-scale, geographically diverse, adequate and well-controlled, conducted with patients afflicted with a target disease in order to collect data to establish the safety and efficacy profile and assure compliance with the requirements of the Federal Food, Drug and Cosmetic Act.

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

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

The FDA has 45 days from its receipt of an NDA to determine if it will accept the filing for a substantive review. The FDA may refuse the filing, which would result in the loss of 50% of the application user fee. If the FDA accepts the filing, it begins an in-depth review. Under current performance goals, the FDA has either 180 or 365 days to respond, depending upon whether the review is classified by the FDA as priority or standard. The FDA often extends the review timeline by requesting additional information or clarification. The FDA may refer issues to an advisory committee for review, evaluation and recommendation as to whether the application should be approved, but the FDA is not bound by any recommendation of an advisory committee.

If the FDA's evaluation of the NDA and the manufacturing facilities are favorable, the FDA may issue an approval letter, or, in many cases, an approvable letter followed by an approval letter. An approvable letter usually contains a number of conditions that must be met in order to secure final approval. If the FDA decides that the conditions have been met, it will issue an approval letter. An approval letter makes a drug available for physicians to prescribe in the United States, but authorizes commercial marketing of the drug only for specific

indications. After a drug has been approved for a particular indication, other trials and studies may be conducted to explore its use for treatment of new indications.

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

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

Even if a drug receives regulatory approval, the FDA may require post-marketing studies, sometimes referred to as Phase IV studies, to monitor the effects of approved drugs and may limit further marketing based on the results of these post-marketing studies. Moreover, the FDA may impose restrictions on the drug or withdraw its approval if a company does not stay in compliance with pre- and post-market regulatory standards or if problems relating to safety or effectiveness of the drug occur after it reaches the marketplace. The FDA has broad post-market regulatory and enforcement powers, including the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products and withdraw approvals.

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

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

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

Until any effective 180-day exclusivity expires, the FDA cannot grant effective approval of subsequently submitted ANDAs.

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

We must also notify the FDA of any change in an approved product beyond variations already allowed in the approval. Changes to the product, its labeling or its manufacturing could require prior FDA approval and may require further clinical investigations to support the change. Such approvals may be expensive and time-consuming, and if not approved, the product will not be allowed to be marketed as modified.

The FDA also imposes a number of complex regulations on entities that advertise and promote marketed pharmaceuticals. These regulations include requirements for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet. The FDA enforces the regulations under the Federal Food Drug and Cosmetic Act. Failure to abide by these regulations can result in penalties, including the issuance of a warning letter mandating the correction of deviations from FDA standards or the publication of corrective advertising. They may also include a requirement that future advertising and promotional materials be pre-cleared by the FDA, as well as civil and criminal investigations and prosecutions.

Holders of an NDA are also subject to laws and regulations regarding non-clinical laboratory practices that support human safety and product distribution, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances. In each of these areas, the FDA has broad regulatory and enforcement powers, including the ability to levy fines and civil penalties, suspend or delay issuance of approvals, seize or recall products, and withdraw approvals.

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

Fast Track Designation

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

Drug Regulation Outside the United States

In addition to U.S. regulations, we are subject to a variety of foreign regulations governing clinical trials and potential commercial sales and distribution of our products and product candidates. Even if we obtain FDA

approval for a product, we must obtain approval of a product by the regulatory authorities of foreign countries before we can commence clinical trials or marketing of the product in those countries. The approval process varies from country to country, and the time may be longer or shorter than that required for FDA approval. The requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from country to country.

Under European Union regulatory systems, we may submit marketing authorizations either under a centralized or decentralized procedure. The centralized procedure provides for the grant of a single marketing authorization that is valid for all European Union member states. The decentralized procedure provides for mutual recognition of national approval decisions. Under this latter procedure, the holder of a national marketing authorization may submit an application to the remaining member states. Within 90 days of receiving the applications and assessment report, each member state must decide whether to recognize approval.

Third-Party Reimbursement

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

Price Controls

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

Employees

As of June 30, 2004, we had 73 full-time employees, 30 of whom are Ph.D.s, M.D.s or both. Our management believes that relations with our employees are good. None of our employees is represented under a collective bargaining agreement.

Property and Facilities

We lease approximately 40,000 square feet of laboratory and office space located in the Piedmont Triad Research Park in Winston-Salem, North Carolina. We have rights generally exercisable until August 2005 to lease additional space in this facility as and when it becomes available. The term of our lease expires August 1, 2007, and we have renewal options for an additional five-year term. The current monthly payment under our lease is approximately $120,000. We believe that these facilities are adequate to satisfy our current needs.

Legal Proceedings

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

MANAGEMENT

Executive Officers and Directors

The name, age and position of our executive officers and directors as of June 30, 2004 are as follows:

Name	Age	Position
Mark Skaletsky (1) (2)	56	Chairman of the Board of Directors
J. Donald deBethizy, Ph.D.	53	Chief Executive Officer, President and Director
Merouane Bencherif, M.D., Ph.D.	49	Vice President, Preclinical Research
Jeffrey P. Brennan	46	Vice President, Business and Commercial Development
William S. Caldwell, Ph.D.	50	Vice President, Drug Discovery and Development
Geoffrey C. Dunbar, M.D.	57	Vice President, Clinical Development and Regulatory Affairs
Alan A. Musso	42	Vice President, Chief Financial Officer, Treasurer and Secretary
M. James Barrett, Ph.D. (1)	61	Director
Charles A. Blixt (2) (3)	52	Director
G. Steven Burrill (3)	59	Director
Errol B. De Souza, Ph.D. (2)	50	Director
Elaine V. Jones, Ph.D. (1) (2)	49	Director
John P. Richard (3)	46	Director
Alan G. Walton, Ph.D.	68	Director

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

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

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

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

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

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

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

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

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

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

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

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

Elaine V. Jones, Ph.D. has been a member of our board of directors since August 2000. Since August 2003, she has been a general partner of EuclidSR Associates, L.P., which is the general partner of EuclidSR

Partners, L.P., a venture capital fund that focuses on life sciences and information technology companies. Dr. Jones was an investment manager from June 1999 to September 2001, and was a vice president from September 2001 to August 2003, for S.R. One, Limited, a venture capital subsidiary of SmithKline Beecham.

John P. Richard has been a member of our board of directors since November 2002. Since April 1999, he has been an independent biotechnology consultant. He also has been a business advisor to GPC Biotech AG, a drug discovery and development company based in Munich, Germany and traded on the Frankfurt Stock Exchange, since April 1999. Prior to April 1999, Mr. Richard served as executive vice president, business development of SEQUUS Pharmaceuticals, Inc., a publicly traded biotechnology company that became a wholly owned subsidiary of ALZA Corporation in March 1999.

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

Board Composition

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

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

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

We will determine the classification of each director after the offering has been completed. 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.

Board Committees

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

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

Compensation Committee. The members of our compensation committee are Mr. Skaletsky, Dr. Barrett and Dr. Jones. Mr. Skaletsky chairs the committee. The purpose of our compensation committee is to discharge

the responsibilities of our board of directors relating to compensation of our executive officers. Specific responsibilities of our compensation committee include:

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

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

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

Compensation Committee Interlocks and Insider Participation

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

Director Compensation

In the past, each of our directors who is not our employee has received a nonqualified stock option to purchase 25,000 shares of our common stock upon his or her initial election to our board of directors. Additionally, upon each non-employee director's annual reelection, he or she has been granted a nonqualified stock option to purchase 7,500 shares of common stock. However, our chairman received a nonqualified stock option to purchase 35,000 shares upon his or her initial election and a nonqualified stock option to purchase 12,500 shares upon his or her annual reelection. Each of these options:

- has a ten-year term;
- has an exercise price of $0.01 per share; and
- vests one year after the date of grant if the director attended at least 75% of the regular board meetings held during that year.

In lieu of any such nonqualified stock option, each non-employee director could elect to receive a restricted stock award for the same number of shares of stock at a purchase price of $0.01 per share. Each non-employee director that is not a designee of one of our investors or a group of our investors has received, in addition to the equity compensation described above, cash compensation in the amount of $10,000 per year as an annual

retainer. Each director is reimbursed for expenses incurred in connection with his or her attendance at meetings of the board of directors and its committees. We have not historically paid any additional compensation for service on any committees of the board of directors.

We have adopted a new director compensation program that will become effective concurrently with the completion of this offering. Each non-employee director will receive an annual cash retainer of $20,000 payable in quarterly installments. Each member of a committee of the board will receive an additional annual cash retainer of $2,500, the chairman of our audit committee will receive an additional annual cash retainer of $7,500 and the chairman of each of our compensation and governance and nominating committees will each receive an additional annual cash retainer of $2,500. Each non-employee director also will receive an option for 25,000 shares upon initial election as a director and an option for 7,500 shares upon annual reelection. The chairman of the board will receive an option for 10,000 shares upon initial election as chairman, in addition to the option for 25,000 shares upon initial election as a director, and an option for 12,500 shares upon annual reelection. For more information, please see "Executive Compensation—Stock-Based Plans—2004 Stock Incentive Plan."

Executive Compensation

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

Summary Compensation Table

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

(1) A portion of these options reflects grants made on January 26, 2004 under our 2000 equity incentive plan in lieu of a cash bonus for fiscal year 2003. For information regarding these options, please see "—Stock Options," below.
(2) Consists of our contributions under the Targacept Retirement Savings Plan, our 401(k) plan.
(3) Mr. Brennan joined our company in September 2003. His current annual base salary is $225,000.
(4) Salary amount includes compensation of $1,731 in lieu of accrued vacation.

Stock Options

The following table sets forth information regarding grants of stock options to purchase shares of our common stock to our named executive officers during the year ended December 31, 2003.

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

Option Grants in Last Fiscal Year

Name	Number of Securities Underlying Options Granted	Percentage of Total Options Granted to Employees in Fiscal Year	Exercise Price Per Share	Expiration Date	Potential Realizable Value at Assumed Annual Rates of Stock Price Appreciation for Option Terms (5)	
					5%	10%
J. Donald deBethizy, Ph.D.	110,000 (1)	1.9%	$ 0.68	1/14/2013	$	$
	250,000 (2)	4.3	0.68	1/31/2013		
	1,565,332 (3)	26.7	0.68	10/31/2013		
	44,000 (4)	15.8	0.75	1/26/2014		
Merouane Bencherif, M.D., Ph.D.	48,406 (1)	0.8	0.68	1/14/2013		
	120,000 (2)	2.0	0.68	1/31/2013		
	417,217 (3)	7.1	0.68	10/31/2013		
Jeffrey P. Brennan	160,000 (2)	2.7	0.68	9/1/2013		
	9,000 (4)	3.2	0.75	1/26/2014		
William S. Caldwell, Ph.D.	48,631 (1)	0.8	0.68	1/14/2013		
	120,000 (2)	2.0	0.68	1/31/2013		
	346,344 (3)	5.9	0.68	10/31/2013		
	19,410 (4)	7.0	0.75	1/26/2014		
Geoffrey C. Dunbar, Ph.D.	74,210 (1)	1.3	0.68	1/14/2013		
	120,000 (2)	2.0	0.68	1/31/2013		
	444,576 (3)	7.6	0.68	10/31/2013		
	29,610 (4)	10.7	0.75	1/26/2014		
Alan A. Musso	38,250 (1)	0.7	0.68	1/14/2013		
	125,000 (2)	2.1	0.68	1/31/2013		
	348,821 (3)	5.9	0.68	10/31/2013		
	21,600 (4)	7.8	0.75	1/26/2014		

(1) These options reflect grants made on January 14, 2003 under our 2000 equity incentive plan in lieu of a cash bonus for fiscal year 2002.
(2) These options reflect grants made under our 2000 equity incentive plan. They have a term of 10 years, an exercise price equal to the fair market value of the common stock on the date of grant and vest 25% on the grant date and then quarterly over four years.
(3) These options reflect grants made under our 2000 equity incentive plan. They have a term of 10 years, an exercise price equal to the fair market value of the common stock on the date of grant and vest 20% on the grant date and then quarterly over four years.
(4) These options reflect grants made on January 26, 2004 under our 2000 equity incentive plan in lieu of a cash bonus for fiscal year 2003.

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

Option Exercises and Year-End Option Values

The following table sets forth information regarding the number of shares of our common stock issued upon option exercises by our named executive officers during the year ended December 31, 2003 and the value realized by our named executive officers. The table also sets forth information regarding the number and value of unexercised stock options held by our named executive officers as of December 31, 2003. There was no public trading market for our common stock as of December 31, 2003. Accordingly, as permitted by the rules of the Securities and Exchange Commission, we have calculated the value of the unexercised in-the-money options at fiscal year end by determining the difference between the exercise price per share and an assumed fair market value of our common stock as of December 31, 2003 equal to an assumed initial offering price of $ per share, the mid-point of the estimated price range shown on the cover page of this prospectus.

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

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

(1) A portion of these options reflects grants made on January 26, 2004 under our 2000 equity incentive plan in lieu of a cash bonus for fiscal year 2003.

Employment Agreements

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

Under the terms of these employment agreements, Dr. deBethizy is employed as our Chief Executive Officer and President at a minimum annual base salary of $225,000; Dr. Dunbar is employed as our Vice President, Clinical Development and Regulatory Affairs at a minimum annual base salary of $246,750; Mr. Brennan is employed as our Vice President, Business and Commercial Development at a minimum annual base salary of $225,000; Mr. Musso is employed as our Vice President and Chief Financial Officer at a minimum annual base salary of $180,000; Dr. Bencherif is employed as our Vice President, Preclinical Research at a minimum annual base salary of $135,000; and Dr. Caldwell is employed as our Vice President, Drug Discovery and Development at a minimum annual base salary of $135,000. For 2004, the base salary of Dr. deBethizy is $283,250; the base salary of Dr. Dunbar is $254,150; the base salary of Mr. Brennan is $225,000; the base salary of Mr. Musso is $190,000; the base salary of Dr. Bencherif is $170,000; and the base salary of Dr. Caldwell is $170,000.

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

In addition to annual base salary, each named executive officer is eligible to receive awards under our 2000 equity incentive plan and earn an annual bonus equal to a percentage of his annual base salary. The employment agreements provide that Dr. deBethizy is eligible to earn an annual bonus of up to 35% of his annual base salary; each of Dr. Dunbar and Mr. Brennan is eligible to earn an annual bonus of up to 30% of his annual base salary; and each of Mr. Musso and Drs. Bencherif and Caldwell is eligible to earn an annual bonus of up to 25% of his annual base salary. In 2001, our board of directors increased the annual bonus for Dr. deBethizy to up to 40% of his annual base salary. In 2002, our board of directors increased the annual bonus for each of Drs. Bencherif and Caldwell to up to 30% of his annual base salary and in 2003 increased the annual bonus for Mr. Musso to up to 30% of his annual base salary. Our board of directors or compensation committee, in their discretion, may increase the annual bonus for each named executive officer beyond these percentages.

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

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

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

Stock Option and Other Compensation Plans

2000 Equity Incentive Plan

We maintain a 2000 equity incentive plan, which we refer to as our 2000 plan, that our board of directors and stockholders have approved. As of March 31, 2004, an aggregate of 9,216,657 shares of common stock had been authorized for issuance under our 2000 plan, of which options to purchase an aggregate of 8,024,394 shares of common stock were outstanding at a weighted average exercise price of $0.64 per share, 85,000 shares of common stock were issued and outstanding in the form of restricted stock and 448,274 shares of common stock were available for future grant. Upon completion of this offering, 1,113,760 shares of common stock subject to unvested options outstanding as of March 31, 2004 will immediately vest.

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

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

Options. Recipients of stock options under our 2000 plan have the right to purchase a stated number of shares of common stock at a stated exercise price, subject to any other terms and conditions that may be stated in connection with the option grant. We may grant options at an exercise price equal to, less than or greater than the fair market value of our common stock on the date of grant, except that we may not grant incentive stock options and options intended to qualify as performance-based compensation under Section 422 of the Internal Revenue Code to optionees holding more than 10% of the voting power of all shares of our capital stock at an exercise price less than 110% of the fair market value of our common stock on the date of grant. Grant recipients may pay the exercise price of stock options by various methods permitted under our 2000 plan. Unless modified with respect to any particular grant:

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

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

Significant Transactions. If:

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

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

Termination and Amendment. We may grant awards under our 2000 plan until August 21, 2010, unless our 2000 plan is terminated prior to that date. The board of directors may amend or terminate our 2000 plan at any time, subject to the rights of holders of outstanding awards. Our 2004 stock incentive plan, which we refer to as our 2004 plan, is intended to serve as the successor equity incentive program to our 2000 plan. However, our board of directors may not amend our 2000 plan without stockholder approval if stockholder approval is required in order for grants of incentive stock options to meet the requirements of Section 422 of the Internal Revenue Code, or if stockholder approval is required in order to exempt compensation under our 2000 plan from the deduction limit under Section 162(m) of the Internal Revenue Code.

2004 Stock Incentive Plan

Introduction. Our 2004 plan is intended to serve as the successor equity incentive program to our 2000 plan. Our 2004 plan will become effective on the date that the underwriting agreement for this offering is signed. At that time, all of the shares reserved for grant under our 2000 plan will be transferred to our 2004 plan and no further options will be granted under our 2000 plan.

Subject to adjustments as provided in our 2004 plan, the maximum number of shares that we may issue pursuant to awards granted under our 2004 plan may not exceed the sum of (i) shares and (ii) up to shares of common stock (a) remaining available for issuance as of the effective date under our 2000 plan or any other employee stock incentive plan that we maintain prior to the effective date and/or (b) subject to an award granted under our 2000 plan or any other prior plan, which award is forfeited, cancelled, terminated, expires or lapses for any reason, without the issuance of shares pursuant to the award. The maximum number of shares of common stock that we may issue under our 2004 plan pursuant to the grant of (i) incentive stock options is and (ii) restricted awards is . In any calendar year, (i) we may not grant to any participant options and stock appreciation rights, or SARs, that are not related to an option for more than shares of common stock; (ii) we may not grant to any participant awards for more than shares of common stock; and (iii) participants may not receive awards paid in cash having an aggregate dollar value in excess of $, subject to adjustments as provided in our 2004 plan. For purposes of these restrictions, we will treat an option and related SAR as a single award. The following will not be included in calculating the share limitations set forth above: (i) dividends, including dividends paid in shares of common stock, or dividend equivalents paid in cash in connection with outstanding awards; (ii) awards which by their terms are settled in cash rather than the issuance of shares; (iii) any shares subject to an award under our 2004 plan that is forfeited, cancelled, terminated, expires or lapses for any reason without the issuance of shares underlying the award; and (iv) any shares a participant surrenders or we withhold to pay the option or purchase price for an award or use to satisfy any tax withholding requirement in connection with the exercise, vesting or earning of an award if, in accordance with the terms of our 2004 plan, a participant pays such option or purchase price or satisfies such tax withholding by either tendering previously owned shares or having us withhold shares.

We may adjust the number of shares reserved for issuance under our 2004 plan and the terms of awards in the event of an adjustment in our capital stock structure or one of our affiliates due to a merger, stock split, stock dividend or similar event.

Purpose and Eligibility. The purpose of our 2004 plan is to encourage and enable selected employees and our directors and independent contractors to acquire or increase their holdings of common stock and other proprietary interests in us in order to promote a closer identification of their interests with those of us and our stockholders, thereby further stimulating their efforts to enhance our efficiency, soundness, profitability, growth and stockholder value. The purpose will be carried out by the granting of awards to selected participants. We may grant awards under our 2004 plan which include incentive stock options and nonqualified stock options; SARs; restricted awards in the form of restricted stock awards and restricted stock units; performance awards in

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

Administration; Amendment and Termination. Our board of directors, or upon its delegation, the compensation committee of our board of directors, will administer our 2004 plan. In this discussion, we refer to our board of directors and the compensation committee collectively as the administrator. Under the terms of our 2004 plan, the administrator has full and final authority to take any action with respect to our 2004 plan, including, without limitation, the authority to: (i) determine all matters relating to awards, including selection of individuals to be granted awards, the types of awards, the number of shares, if any, of common stock subject to an award, and the terms, conditions, restrictions and limitations of an award; (ii) prescribe the form or forms of agreements evidencing awards granted under our 2004 plan; (iii) establish, amend and rescind rules and regulations for the administration of our 2004 plan; and (iv) construe and interpret our 2004 plan, awards and award agreements made under the plan, interpret rules and regulations for administering the plan and make all other determinations deemed necessary or advisable for administering the plan.

In certain circumstances and subject to certain terms and conditions, the administrator may delegate to one or more of our officers the authority to grant awards, and to make any or all of the determinations reserved for the administrator in our 2004 plan with respect to such awards.

Our board of directors may amend, alter or terminate our 2004 plan at any time, subject to the following: (i) stockholder approval is required of any amendment if such approval is required by applicable law, rule or regulation; and (ii) except for anti-dilution adjustments made under our 2004 plan, the option price for any outstanding option or base price of any outstanding SAR may not be decreased after the date of grant, nor may any participant surrender any outstanding option or SAR to us as consideration for the grant of a new option or SAR with a lower option or base price than the original option or SAR, as the case may be, without stockholder approval of any such action.

The administrator has the authority to make adjustments to awards upon the occurrence of certain unusual or nonrecurring events, if the administrator determines that such adjustments are appropriate in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under our 2004 plan or necessary or appropriate to comply with applicable laws, rules or regulations. The administrator may cause any award granted under our 2004 plan to be cancelled in consideration of an alternative award or cash payment of an equivalent cash value, as determined by the administrator, made to the holder of the cancelled award. The administrator also may determine, in its discretion, that a participant's rights, payments and/or benefits with respect to an award, including but not limited to any shares issued or issuable and/or cash paid or payable with respect to an award, will be subject to reduction, cancellation, forfeiture or recoupment upon the occurrence of certain specified events, in addition to any otherwise applicable vesting or performance conditions of an award.

Options. Our 2004 plan authorizes the grant of both incentive stock options and nonqualified stock options, both of which are exercisable for shares of common stock, although incentive stock options may only be granted to our employees. The administrator will determine the option price at which a participant may exercise an option and the option price must be:

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

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

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

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

Director Options. Each non-employee director who is first elected or appointed to our board of directors after the public offering date will receive an initial option to purchase 25,000 shares of common stock on the fifth business day after such director is first elected or appointed to our board of directors. A non-employee director who is first elected or appointed as chairman of the board also will receive an initial option for 10,000 shares. In addition, we will grant to each non-employee director, on an annual basis commencing with the 2005 annual meeting of stockholders, a director option to purchase 7,500 shares of common stock, or, in the case of the chairman of the board, an annual option for 12,500 shares, on the fifth business day after the annual or other stockholders meeting, provided that such director continues to serve as a member of our board of directors as of such date. Director options will be designated as nonqualified options. The option price at which a director may exercise a director option will be 100% of the fair market value per share of the common stock on the date the option is granted. Each initial option will vest and become exercisable on the first anniversary of the date of grant with respect to one-third of the shares subject to the option. Each initial option will vest with respect to the remaining two-thirds of the shares subject to the option on a pro rata quarterly basis over the next two years, so that the option will be vested in full as of the third anniversary of the date of grant if the director continues in service during such period. Each annual option will vest in full on the first anniversary of the date of grant. The term of a director option may not exceed 10 years from the date of grant. Director options are also subject to certain restrictions on exercise if the director's service on our board of directors terminates. The administrator also has authority to establish other terms and conditions related to director options.

Stock Appreciation Rights. Under the terms of our 2004 plan, we may grant SARs to the holder of an option with respect to all or a portion of the shares of common stock subject to the option or we may grant SARs separately. The holder of an SAR may receive consideration paid either (i) in cash; (ii) shares of common stock valued at fair market value on the date of the SAR exercise; or (iii) a combination of cash and shares of common stock, as the administrator determines. Upon exercise of an SAR, a participant is entitled to receive from us consideration in an amount determined by multiplying:

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

Notwithstanding the foregoing, the administrator may limit the amount payable in its discretion. The base price may be no less than 100% of the fair market value per share of the common stock on the date the SAR is granted. We may pay consideration upon exercise of an SAR currently or on a deferred basis.

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

Restricted Awards. Subject to the limitations of our 2004 plan, the administrator may in its sole discretion grant restricted awards to such individuals in such numbers, upon such terms and at such times as the administrator shall determine. Restricted awards may be in the form of restricted stock awards and/or restricted stock units that are subject to certain conditions, which conditions must be met in order for the restricted award to vest and be earned, in whole or in part, and no longer subject to forfeiture. Restricted stock awards may be payable in shares of common stock. Restricted stock units may be payable in cash or whole shares of common stock, or partly in cash and partly in whole shares of common stock, in accordance with the terms of our 2004 plan and the discretion of the administrator.

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

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

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

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

The administrator has authority to determine whether and to what degree restricted awards have vested and been earned and are payable. If a participant's employment or service is terminated for any reason and all or any part of a restricted award has not vested or been earned pursuant to the terms of our 2004 plan and the individual award, the participant will forfeit the award unless the administrator determines otherwise.

Performance Awards. Subject to the limitations of our 2004 plan, the administrator may in its discretion grant performance awards to such eligible individuals upon such terms and conditions and at such times as the administrator shall determine. Performance awards may be in the form of performance shares and/or performance units. An award of a performance share is a grant of a right to receive shares of our common stock, the cash value thereof or a combination thereof in the administrator's discretion, which is contingent upon the achievement of performance or other objectives during a specified period and which has a value on the date of grant equal to the fair market value of a share of our common stock. An award of a performance unit is a grant of a right to receive shares of our common stock or a designated dollar value amount of common stock that is contingent upon the achievement of performance or other objectives during a specified period, and that has an initial value determined in a dollar amount established by the administrator at the time of grant.

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

The administrator has authority to determine whether and to what degree performance awards have been earned and are payable. If a participant's employment or service is terminated for any reason and all or part of a performance award has not been earned pursuant to the terms of our 2004 plan and the individual award agreement, the participant will forfeit the award unless the administrator determines otherwise.

Phantom Stock Awards. Subject to the limitations of our 2004 plan, the administrator may in its discretion grant phantom stock awards to such eligible individuals in such numbers, upon such terms and at such times as the administrator shall determine. An award of phantom stock is an award of a number of hypothetical share units with respect to shares of our common stock, with a value based on the fair market value of a share of common stock.

The administrator has the authority to determine whether and to what degree phantom stock awards have vested and are payable. Upon vesting of all or part of a phantom stock award and satisfaction of other terms and conditions that the administrator determines, the holder of a phantom stock award will be entitled to a payment of an amount equal to the fair market value of one share of our common stock with respect to each such phantom stock unit that has vested. We may make payment in cash, shares of common stock, or a combination of cash and stock, as determined by the administrator. The administrator may determine the forms and terms of payment of phantom stock awards in accordance with our 2004 plan. If a participant's employment or service is terminated for any reason and all or any part of a phantom stock award has not vested and become payable pursuant to the terms of our 2004 plan and the individual award, the participant will forfeit the award unless the administrator determines otherwise.

Dividend and Dividend Equivalents. The administrator may, in its sole discretion, provide that awards granted under our 2004 plan earn dividends or dividend equivalents. We may pay such dividends or dividend equivalents currently or credit such dividends or dividend equivalents to a participant's account, subject to such restrictions and conditions as the administrator may establish with respect to the crediting of an account, including reinvestment in additional shares of common stock or share equivalents.

Change in Control. Upon a change in control as defined in our 2004 plan, and unless an award agreement provides otherwise, our 2004 plan provides that: (i) all options and SARs outstanding as of the date of the change in control will become fully exercisable, whether or not then otherwise exercisable; and (ii) any restrictions applicable to any restricted award, performance award and/or phantom stock award will be deemed to have been

met, and such awards will become fully vested, earned and payable to the fullest extent of the original grant of the applicable award. However, our 2004 plan authorizes the administrator, in the event of a merger, share exchange, reorganization or other business combination affecting us or one of our affiliates, to determine that any or all awards will not vest or become exercisable on an accelerated basis, if we or the surviving or acquiring corporation takes action, including but not limited to the assumption of awards or the grant of substitute awards, that, in the opinion of the administrator, is equitable or appropriate to protect the rights and interest of participants under our 2004 plan.

Transferability. Incentive stock options are not transferable other than by will or the laws of intestate succession or, in the administrator's discretion, as may otherwise be permitted in accordance with Section 422 of the Internal Revenue Code and related regulations. Nonqualified stock options, director options and SARs are not transferable other than by will or the laws of intestate succession, except as permitted by the administrator in a manner consistent with the registration provisions of the Securities Act. Restricted awards, performance awards and phantom stock awards that have not vested and been earned are not transferable, including by sale, assignment, pledge or hypothecation, other than by will or the laws of intestate succession, and participants may not sell, transfer, assign, pledge or otherwise encumber shares subject to such awards until the restriction period and/or performance period has expired and until all conditions to vesting and/or earning the award have been met.

General Federal Income Tax Consequences. Under current federal laws, in general, recipients of awards and grants of nonqualified stock options, SARs, restricted stock, dividend equivalents, performance awards and stock payments under our 2004 plan are taxable under Section 83 of the Internal Revenue Code upon their receipt of common stock or cash with respect to such awards or grants and, subject to Section 162(m) of the Internal Revenue Code and certain reporting requirements, we will be entitled to an income tax deduction with respect to the amounts taxable as ordinary income to such recipients. Under Sections 421 and 422 of the Internal Revenue Code, recipients of incentive stock options are generally not taxable on their receipt of common stock upon their exercises of incentive stock options if the option stock is held for specified minimum holding periods and, in such event, we would not be entitled to income tax deductions with respect to such exercises.

Performance-Based Compensation—Section 162(m) Requirements. Our 2004 plan is structured to comply with the requirements imposed by Section 162(m) of the Internal Revenue Code and related regulations in order to preserve, to the extent practicable, our tax deduction for awards made under our 2004 plan to covered employees. Section 162(m) of the Internal Revenue Code generally denies an employer a deduction for compensation paid to covered employees, which are generally the named executive officers, of a publicly held corporation in excess of $1,000,000 unless the compensation is exempt from the $1,000,000 limitation because it is performance-based compensation.

In order to qualify as performance-based compensation, we must pay the compensation under our 2004 plan to covered employees under pre-established objective performance goals that a committee comprised of outside directors determines and certifies. In addition to other requirements for the performance-based exception, we must advise stockholders, and stockholders must approve, the material terms or changes in material terms of the performance goals under which compensation is to be paid. Material terms include the individuals eligible to receive compensation, a description of the business criteria on which the performance goals are based, and either the maximum amount of the compensation to be paid or the formula used to calculate the amount of compensation if the performance goals are met.

As proposed, our 2004 plan limits the maximum amount of awards that we may grant to any employee. In particular, in any calendar year, (i) we may not grant to any participant options and SARs that are not related to an option for more than shares of common stock; (ii) we may not grant to any participant awards for more than shares of common stock; and (iii) no participant may receive awards paid in cash having an aggregate dollar value in excess of $. Further, with respect to performance-based restricted awards and performance awards, and in some cases, certain other types of awards, payable to covered employees that are intended to be eligible for the compensation limitation exception available under Section 162(m) and related regulations, our 2004 plan limits performance measures to one or more of the following: cash flow, return on

equity, return on assets, earnings per share, achievement of clinical development or regulatory milestones, operations expense efficiency milestones, consolidated earnings before or after taxes and including earnings before interest, taxes, depreciation and amortization, net income, operating income, book value per share, return on investment, return on capital, improvements in capital structure, expense management, profitability of an identifiable business unit or product, maintenance or improvement of profit margins, stock price or total stockholder return, market share, revenues or sales, costs, working capital, economic wealth created, strategic business criteria, efficiency ratios, achievement of division, group, function or corporate financial, strategic or operational goals and comparisons with stock market indices or performances of metrics of peer companies.

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

Targacept Retirement Savings Plan—401(k) Plan

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

Limitation of Liability and Indemnification

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

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

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

CERTAIN RELATIONSHIPS AND RELATED PARTY TRANSACTIONS

Since August 22, 2000, we have engaged in the following transactions with our directors and executive officers and holders of more than 5% of our voting securities and affiliates of our directors, executive officers and 5% stockholders.

Stock Issuances

Issuance of Common Stock

On August 22, 2000, at the time that we became an independent company, we issued and sold an aggregate of 309,424 shares of our common stock at a purchase price per share of $0.001 for an aggregate purchase price of approximately $309. The following table sets forth the number of shares of common stock sold to our founders.

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

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

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

Issuance of Series A Convertible Preferred Stock

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

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

Issuance of Series B Convertible Preferred Stock

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

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

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

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

Issuance of Series C Convertible Preferred Stock

On November 26, 2002 and March 14, 2003, we issued and sold an aggregate of 49,169,138 shares of our series C convertible preferred stock at a purchase price per share of $1.21 for an aggregate purchase price of approximately $59.5 million. The following table sets forth the number of shares of series C convertible preferred stock sold to our 5% stockholders and their affiliates.

Name	Number of Shares of Series C Preferred Stock	Aggregate Purchase Price
New Enterprise Associates 10, Limited Partnership	12,396,694	$ 15,000,000
Nomura International plc	8,264,462	9,999,999
Oxford Bioscience Partners IV L.P.	6,198,347	7,500,000
EuclidSR Partners, L.P.	5,123,966	6,199,999
Burrill & Company LLC	1,540,440	1,863,932
Advent Private Equity Fund II	1,540,440	1,863,932

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

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. Dr. Walton, one of our directors, is a general partner of OBP Management IV L.P., the general partner of Oxford Bioscience Partners IV L.P.

Registration Rights

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

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

In May 2002, we borrowed $2.5 million from R.J. Reynolds Tobacco Holdings, Inc. to finance equipment and other fixed assets. The borrowing bears a fixed interest rate of 6.6%, is payable in 48 equal monthly installments and matures in May 2006. In January 2004, we amended the terms of our loan facility to permit us to borrow up to an additional $2.0 million in 2004 in up to three separate borrowings. Each borrowing would bear a fixed interest rate equal to a theoretical four-year U.S. Treasury Rate on the disbursement date plus 3.5%, be payable in 48 equal monthly installments and be secured by specified tangible fixed assets that R.J. Reynolds determined to be sufficient at the time of disbursement. In April 2004, we borrowed $1.0 million under the amended loan facility to finance equipment. The borrowing bears a fixed interest rate of 5.9%, is payable in 48 equal monthly installments and matures in April 2008. All borrowings under the loan facility are secured by specified tangible fixed assets. We believe that the terms of the loan facility are no less favorable than those that we could have obtained from an unaffiliated third party. As of June 30, 2004, the outstanding principal balance under the loan facility was $2.3 million.

Payments to R.J. Reynolds Tobacco Company

Prior to December 31, 2003, we used the services of an R.J. Reynolds Tobacco Company employee for toxicology studies and purchased materials used for research and development through R.J. Reynolds Tobacco Company. We paid $201,000 for these services during 2003.

Director Compensation

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

Executive Compensation and Employment Agreements

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

PRINCIPAL STOCKHOLDERS

The following table sets forth information regarding the beneficial ownership of our common stock as of June 30, 2004 and on an as adjusted basis to reflect the sale of the common stock offered in this offering by:

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

The number of shares of common stock beneficially owned by each stockholder is determined under rules issued by the Securities and Exchange Commission and includes voting or investment power with respect to securities. Under these rules, beneficial ownership includes any shares as to which the individual or entity has sole or shared voting power or investment power and includes any shares that an individual or entity has the right to acquire beneficial ownership of within 60 days of June 30, 2004 through the exercise of any warrant, stock option or other right. Unless otherwise indicated, the address of all listed stockholders is c/o Targacept, Inc., 200 East First Street, Suite 300, Winston-Salem, North Carolina 27101. Each of the stockholders listed has sole voting and investment power with respect to the shares beneficially owned by the stockholder unless noted otherwise, subject to community property laws where applicable.

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned (1)	
		Before Offering	After Offering
5% Stockholders	13,425,357	17.7%	
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	10,396,226	13.7%	
Nomura International plc (4) Nomura House 1 St. Martins le Grand London EC1A 4NP England	8,928,571	11.8%	
Entities affiliated with Oxford Bioscience Partners (5) 222 Berkeley Street, Suite 1650 Boston, Massachusetts 02116	6,728,928	8.9%	
R.J. Reynolds Tobacco Holdings, Inc. (6) 401 North Main Street Winston-Salem, North Carolina 27102	6,669,628	8.6%	
Entities affiliated with Burrill & Company LLC (7) One Embarcadero Center, Suite 2700 San Francisco, California 94111	4,268,328	5.6%	
Entities affiliated with Advent Private Equity Fund II (8) 25 Buckingham Gate London SW1E 6LD England	4,228,328	5.6%	

Name and Address of Beneficial Owner	Number of Shares Beneficially Owned	Percentage of Shares Beneficially Owned (1) Before Offering	After Offering
Executive Officers and Directors			
J. Donald deBethizy, Ph.D. (9)	1,433,663	1.9%	
Merouane Bencherif, M.D., Ph.D. (10)	509,014	*	
Jeffrey P. Brennan (11)	65,667	*	
William S. Caldwell, Ph.D. (12)	503,963	*	
Geoffrey C. Dunbar, M.D. (13)	474,273	*	
Alan A. Musso (14)	341,155	*	
Mark Skaletsky	60,000	*	
M. James Barrett, Ph.D. (15)	13,425,357	17.7%	
Charles A. Blixt (16)	6,669,628	8.6%	
G. Steven Burrill (17)	4,268,328	5.6%	
Errol B. De Souza, Ph.D.	—	—	
Elaine V. Jones, Ph.D. (18)	10,396,226	13.7%	
John P. Richard (19)	32,500	*	
Alan G. Walton, Ph.D. (20)	6,728,928	8.9%	
All executive officers and directors as a group (14 persons) (21)	44,908,702	56.3%	

* Indicates less than one percent.

(1) Our calculation of the percentage of shares of common stock beneficially owned before this offering is based on 75,612,681 shares of our common stock and common stock equivalents outstanding as of June 30, 2004, assuming conversion of all outstanding shares of our series A, series B and series C convertible preferred stock. Our calculation of the percentage of shares beneficially owned after this offering is based on shares of common stock to be outstanding after this offering, including the shares that we are selling in this offering and our issuance of shares of common stock upon the exercise of an outstanding warrant that will be cancelled if not exercised concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share.

(2) Includes 13,369,197 shares owned of record by New Enterprise Associates 10, Limited Partnership, for which voting and investment power is shared by M. James Barrett, Stewart Alsop, Peter J. Barris, C. Richard Kramlich, Peter T. Morris, Charles W. Newhall, III, Mark W. Perry, Scott D. Sandell and Eugene A. Trainor, III, each of whom is a general partner of NEA Partners 10, Limited Partnership, the general partner of New Enterprise Associates 10, Limited Partnership; 23,660 shares owned of record by NEA Ventures 2002, Limited Partnership, for which voting and investment power is held by its general partner, Pamela J. Clark; and 32,500 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004 held by NEA Development Corp., for which voting and investment power is shared by Charles W. Newhall, III, Mark W. Perry, Peter J. Barris, C. Richard Kramlich and Peter T. Morris as a result of their ownership of New Enterprise Associates, LLC. New Enterprise Associates, LLC is the sole owner of NEA Development Corp. Dr. Barrett, one of our directors, and each of the other general partners of NEA Partners 10, Limited Partnership disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his pecuniary interest therein.

(3) Includes 8,695,512 shares owned of record by, and 40,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004 held by, EuclidSR Partners, L.P., for which voting and investment power is shared by Elaine V. Jones, Graham D.S. Anderson, Barbara J. Dalton, A. Bliss McCrum, Milton J. Pappas, Stephen K. Reidy and Raymond J. Whitaker, each of whom are general partners of EuclidSR Associates, L.P., the general partner of EuclidSR Partners, L.P.; and 1,660,714 shares owned of record by EuclidSR Biotechnology Partners, L.P., for which voting and investment power is shared by Elaine V. Jones, Graham D.S. Anderson, Barbara J. Dalton, A. Bliss McCrum, Milton J. Pappas, Stephen K. Reidy and Raymond J. Whitaker, each of whom are general partners of EuclidSR Biotechnology Associates, L.P., the general partner of EuclidSR Biotechnology Partners, L.P. Dr. Jones, one of our directors, and each of the other general partners of EuclidSR Associates, L.P. and EuclidSR Biotechnology Associates, L.P. disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his or her pecuniary interest therein.

(4) The board of directors of Nomura International plc has delegated voting and investment power to Mr. Yasushi Ii, the Head of Merchant Banking Europe, Nomura International plc. Mr. Ii acts in consultation with Dr. Denise Pollard-Knight, the Head of Nomura Phase4 Ventures. Each member of the board of directors, Mr. Ii and Dr. Pollard-Knight disclaims beneficial ownership of these shares.

(5) Includes 6,629,907 shares owned of record by Oxford Bioscience Partners IV L.P. and 66,521 shares owned of record by mRNA Fund II L.P., for which voting and investment power is shared by Alan G. Walton, Jonathan J. Fleming, Jeffrey T. Barnes, Mark P. Carthy and Michael Lytton, each of whom are general partners of OBP Management IV L.P., the sole general partner of Oxford Bioscience Partners IV L.P. and mRNA Fund II L.P.; and 32,500 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004 held by Oxford Bioscience IV Corporation, for which voting and investment power is shared by Alan G. Walton and Jonathan J. Fleming, each of whom are directors of Oxford Bioscience IV Corporation. Each of Oxford Bioscience Partners IV L.P. and mRNA Fund II L.P. disclaim beneficial ownership of any shares held of record by the other. Dr. Walton, one of our directors, and each of the other general partners of OBP Management IV L.P. disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his pecuniary interest therein.

(6) Includes 31,725 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004 and 1,612,903 shares issuable upon the exercise of an outstanding warrant, assuming that the warrant is exercised in full for cash. Voting and investment power is held by Andrew J. Schindler, the chief executive officer of R.J. Reynolds Tobacco Holdings, Inc. Mr. Blixt, one of our directors, is executive vice president, general counsel and assistant secretary of R.J. Reynolds Tobacco Holdings, Inc. and disclaims beneficial ownership of these shares.

(7) Includes 4,228,328 shares owned of record by Burrill Biotechnology Capital Fund, L.P., for which voting and investment power is shared by G. Steven Burrill, John H. Kim, Roger E. Wyse, Michael K. Ullman and Ann F. Hanham, members of Burrill & Company (Biotechnology GP), LLC, the general partner of Burrill Biotechnology Capital Fund, L.P.; and 40,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004 held by Burrill & Company LLC, for which voting and investment power is held by G. Steven Burrill, the chief executive officer of Burrill & Company LLC. Mr. Burrill, one of our directors, and each of the other members of Burrill & Company (Biotechnology GP), LLC disclaims beneficial ownership of the shares held by Burrill Biotechnology Capital Fund, L.P. except to the extent of his or her pecuniary interest therein.

(8) Includes 1,546,846 shares owned of record by Advent Private Equity Fund II 'A' Limited Partnership; 943,405 shares owned of record by Advent Private Equity Fund II 'B' Limited Partnership; 1,404,485 shares owned of record by Advent Private Equity Fund II 'C' Limited Partnership; and 333,592 shares owned of record by Advent Private Equity Fund II 'D' Limited Partnership. Patrick Lee is a director of Advent Limited and a general partner of Advent Venture Partners LLP, which owns 100% of Advent Limited. Advent Limited owns 100% of Advent Management II Limited, which is the general partner of Advent Management II Limited Partnership, the general partner of each of the partnerships constituting Advent Private Equity Fund II. Voting and investment power over the shares held by each of the partnerships constituting Advent Private Equity Fund II is exercised by Advent Limited in its role as manager. The board of directors of Advent Limited consists of Sir David James Scott Cooksey (chairman), Peter Anthony Baines, Jerry Christopher Benjamin, David Cheesman, Leslie Ian Gabb, Patrick Pak-tin Lee, Martin Alexander McNair, James Anthony McNaught-Davis and Nicholas James Teasdale. Each director disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein.

(9) Includes 729,899 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004.

(10) Includes 450,997 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004.

(11) Consists of 65,667 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004.

(12) Includes 445,946 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004.

(13) Includes 304,751 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004.

(14) Includes 329,155 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004.

(15) Includes 13,369,197 shares owned of record by New Enterprise Associates 10, Limited Partnership, for which voting and investment power is shared by M. James Barrett, Stewart Alsop, Peter J. Barris, C. Richard Kramlich, Peter T. Morris, Charles W. Newhall, III, Mark W. Perry, Scott D. Sandell and Eugene A. Trainor, III, each of whom is a general partner of NEA Partners 10, Limited Partnership, the general partner of New Enterprise Associates 10, Limited Partnership; 23,660 shares owned of record by NEA Ventures 2002, Limited Partnership, for which voting and investment power is held by its general partner, Pamela J. Clark; and 32,500 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004 held by NEA Development Corp., for which voting and investment power is shared by Charles W. Newhall, III, Mark W. Perry, Peter J. Barris, C. Richard Kramlich and Peter T. Morris through their ownership of New Enterprise Associates, LLC. New Enterprise Associates, LLC is the sole owner of NEA Development Corp. Dr. Barrett, one of our directors, and each of the other general partners of NEA Partners 10, Limited Partnership disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his pecuniary interest therein.

(16) Includes 31,725 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004 and 1,612,903 shares issuable upon the exercise of an outstanding warrant, assuming that the warrant is exercised in full for cash. Voting and investment power is held by Andrew J. Schindler, the chief executive officer of R.J. Reynolds Tobacco Holdings, Inc. Mr. Blixt is executive vice president, general counsel and assistant secretary of R.J. Reynolds Tobacco Holdings, Inc. and disclaims beneficial ownership of these shares.

(17) Includes 4,228,328 shares owned of record by Burrill Biotechnology Capital Fund, L.P., for which voting and investment power is shared by G. Steven Burrill, John H. Kim, Roger E. Wyse, Michael K. Ullman and Ann F. Hanham, members of Burrill & Company (Biotechnology GP), LLC, the general partner of Burrill Biotechnology Capital Fund, L.P.; and 40,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004 held by Burrill & Company LLC, for which voting and investment power is held by G. Steven Burrill, the chief executive officer of Burrill & Company LLC. Mr. Burrill, one of our directors, and each of the other members of Burrill & Company (Biotechnology GP), LLC disclaims beneficial ownership of the shares held by Burrill Biotechnology Capital Fund, L.P. except to the extent of his or her pecuniary interest therein.

(18) Includes 8,695,512 shares owned of record by, and 40,000 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004 held by, EuclidSR Partners, L.P., for which voting and investment power is shared by Elaine V. Jones, Graham D.S. Anderson, Barbara J. Dalton, A. Bliss McCrum, Milton J. Pappas, Stephen K. Reidy and Raymond J. Whitaker, each of whom are general partners of EuclidSR Associates, L.P., the general partner of EuclidSR Partners, L.P.; and 1,660,714 shares owned of record by EuclidSR Biotechnology Partners, L.P., for which voting and investment power is shared by Elaine V. Jones, Graham D.S. Anderson, Barbara J. Dalton, A. Bliss McCrum, Milton J. Pappas, Stephen K. Reidy and Raymond J. Whitaker, each of whom are general partners of EuclidSR Biotechnology Associates, L.P., the general partner of EuclidSR Biotechnology Partners, L.P. Dr. Jones, one of our directors, and each of the other general partners of EuclidSR Associates, L.P. and EuclidSR Biotechnology Associates, L.P. disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his or her pecuniary interest therein.

(19) Includes 7,500 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004.

(20) Includes 6,629,907 shares owned of record by Oxford Bioscience Partners IV L.P. and 66,521 shares owned of record by mRNA Fund II L.P., for which voting and investment power is shared by Alan G. Walton, Jonathan J. Fleming, Jeffrey T. Barnes, Mark P. Carthy and Michael Lytton, each of whom are general partners of OBP Management IV L.P., the sole general partner of Oxford Bioscience Partners IV L.P. and mRNA Fund II L.P.; and 32,500 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004 held by Oxford Bioscience IV Corporation, for which voting and investment power is shared by Alan G. Walton and Jonathan J. Fleming, each of whom are directors of Oxford Bioscience IV Corporation. Dr. Walton and each of the other general partners of OBP Management IV L.P. disclaims beneficial ownership of the shares held by each of the aforementioned entities except to the extent of his pecuniary interest therein.

(21) Includes 2,682,162 shares of common stock issuable upon exercise of stock options exercisable within 60 days of June 30, 2004 and 1,612,903 shares issuable upon the exercise of an outstanding warrant, assuming that the warrant is exercised in full for cash.

DESCRIPTION OF CAPITAL STOCK

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

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

As of March 31, 2004, we had outstanding:

- 1,164,524 shares of common stock held by 53 stockholders of record;
- 5,000,000 shares of series A convertible preferred stock;
- 6,567,567 shares of series B convertible preferred stock; and
- 49,169,138 shares of series C convertible preferred stock.

As of March 31, 2004, we also had outstanding a warrant to purchase 1,612,903 shares of common stock at an exercise price of $1.95 per share.

All of our outstanding shares of preferred stock will convert into 73,739,905 shares of common stock concurrently with the completion of this offering. In addition, the warrant will be cancelled if it is not exercised prior to the completion of this offering. If R.J. Reynolds exercises the warrant in full for cash, we would issue 1,612,903 shares of common stock and receive cash proceeds of approximately $3.1 million. If R.J. Reynolds exercises the warrant on a cashless basis, we would issue shares of common stock, based on an assumed initial public offering price of $ per share.

Common Stock

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

Preferred Stock

Upon completion of this offering, our board of directors will be authorized, without stockholder approval, to issue up to an aggregate of shares of preferred stock in one or more series and to fix the rights, preferences, and powers granted to or imposed upon the preferred stock, including voting rights, dividend rights, conversion rights, redemption privileges and liquidation preferences. We cannot state with certainty the actual

effects of the issuance of any shares of preferred stock upon the rights of holders of common stock until the board of directors determines the specific rights of the holders of the preferred stock. Some of these effects might potentially include:

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

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

Options

As of March 31, 2004, options to purchase 8,024,394 shares of common stock at a weighted average exercise price of $0.64 per share were outstanding.

Registration Rights

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

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

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

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

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

Anti-Takeover Provisions

We are subject to Section 203 of the Delaware General Corporation Law, an anti-takeover statute. Subject to certain exceptions, Section 203 prohibits a publicly held Delaware corporation from engaging in a business combination with an interested stockholder for three years following the date that the person became an interested stockholder, unless the interested stockholder attained such status with the approval of our board of directors or unless the business combination is approved in a prescribed manner. A business combination includes, among other things, a merger or consolidation involving us and the interested stockholder and the sale of more than 10% of our assets. In general, an interested stockholder is any entity or person beneficially owning 15% or more of our outstanding voting stock and any entity or person affiliated with or controlling or controlled by that entity or person.

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

In particular, our certificate of incorporation or bylaws provide for the following:

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

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

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

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

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

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

Transfer Agent and Registrar

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

NASDAQ National Market

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

SHARES ELIGIBLE FOR FUTURE SALE

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

Upon completion of this offering, we will have outstanding shares of common stock, after giving effect to the conversion of all outstanding shares of our convertible preferred stock into 73,739,905 shares of common stock concurrently with the completion of this offering and our issuance of shares of common stock upon the exercise of an outstanding warrant that will be cancelled if not exercised concurrently with the completion of this offering, assuming that the warrant is exercised on a cashless basis based on an assumed initial public offering price of $ per share. If the warrant is exercised in full for cash, we would issue 1,612,903 shares of our common stock.

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

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

Rule 144

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

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

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

Rule 144(k)

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

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

Rule 701

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

Lock-up Agreements

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

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

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

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

Stock Options

After the completion of this offering, we intend to file a registration statement on Form S-8 under the Securities Act to register all of the shares of common stock subject to issuance upon exercise of outstanding options granted under, or reserved for future issuance under, our 2000 plan and our 2004 plan. Shares of common stock issued under the Form S-8 upon exercise of options will be available for sale in the public market, subject to Rule 144 volume limitations applicable to affiliates and subject to the contractual restrictions described above. As of March 31, 2004, options to purchase 8,024,394 shares of common stock were outstanding under our 2000 plan with a weighted average exercise price of $0.64, of which approximately 4,078,011 were vested and exercisable with a weighted average exercise price of $0.62 and an additional 448,274 shares were reserved for issuance under our 2000 plan. Upon completion of this offering, an additional shares of common stock will be reserved for issuance under our 2004 plan.

Registration Rights

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

UNDERWRITERS

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

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

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

The underwriters initially propose to offer part of the shares of common stock directly to the public at the public offering price listed on the cover page of this prospectus and part to certain dealers at a price that represents a concession not in excess of $ per share under the public offering price. No underwriter may allow, and no dealer may reallow, any concession to other underwriters or to certain dealers. After the initial offering of the shares of common stock, the offering price and other selling terms may from time to time be varied by the representatives.

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

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

We and all of our directors and officers and holders of substantially all of our outstanding stock have agreed that, without the prior written consent of Morgan Stanley & Co. Incorporated on behalf of the underwriters, we and they will not, during the period ending 180 days after the date of this prospectus:

- offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant to purchase, lend or otherwise transfer or dispose of directly or indirectly, any shares of our common stock or any securities convertible into or exercisable or exchangeable for shares of our common stock; or

- enter into any swap or other arrangement that transfers to another, in whole or in part, any of the economic consequences of ownership of shares of our common stock,

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

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

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

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

These restrictions do not apply to:

- the sale of shares to the underwriters;
- the issuance by us of shares of our common stock upon the exercise of an option or a warrant or the conversion of a security outstanding on the date of this prospectus of which the underwriters have been advised in writing;
- the issuance by us of shares or options to purchase shares of our common stock pursuant to our 2000 equity incentive plan or our 2004 stock incentive plan, provided that the recipient of the shares agrees to be subject to the restrictions described above;
- transactions by any person other than us relating to shares of common stock or other securities acquired in open market transactions after the completion of the offering of the shares;
- transfers of shares as a gift or charitable contribution, or by will or intestacy;
- transfers of shares to any trust the sole beneficiaries of which are the transferee or a member of the immediate family of the transferee; or
- transfers to certain entities or persons affiliated with the stockholder;

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

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

	Paid by Targacept	
	No Exercise	**Full Exercise**
Per share	$	$
Total	$	$

In addition, we estimate that the expenses of this offering payable by us, other than underwriting discounts and commissions, will be $.

In order to facilitate the offering of the common stock, the underwriters may engage in transactions that stabilize, maintain or otherwise affect the price of the common stock. Specifically, the underwriters may sell

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

We have applied for quotation of our common stock on the NASDAQ National Market under the symbol "TRGT."

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

Directed Share Program

At our request, the underwriters have reserved for sale, at the initial public offering price, up to shares offered by this prospectus to directors, officers, employees and other individuals associated with us and members of their respective families and friends through a directed share program. The number of shares of our common stock available for sale to the general public in the offering will be reduced to the extent these persons purchase these reserved shares. Any reserved shares not purchased by these persons will be offered by the underwriters to the general public on the same basis as the other shares offered by this prospectus. Recipients of reserved shares will be required to agree with the underwriters not to sell, transfer, assign, pledge or hypothecate these shares for a period of 180 days after purchasing the shares.

Pricing of the Offering

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

LEGAL MATTERS

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

EXPERTS

Ernst & Young LLP, independent registered public accounting firm, have audited our financial statements as of December 31, 2003 and 2002 and for each of the three years in the period ended December 31, 2003, as set forth in their report. We have included our financial statements in the prospectus and elsewhere in the registration statement in reliance on Ernst & Young LLP's report, given on their authority as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock to be sold in this offering. This prospectus does not contain all of the information set forth in the registration statement. You should refer to the registration statement for additional information regarding us and the shares of our common stock to be sold in this offering. Whenever we reference any contract, agreement or other document in this prospectus, the reference is not necessarily complete and you should refer to the exhibits to the registration statement for the actual contract, agreement or other document. In each instance, reference is made to such exhibits and each such statement is qualified in all respects by such reference. In addition, when this offering is completed, we will become subject to the information and reporting requirements of the Exchange Act and, in accordance with the Exchange Act, will file periodic reports, proxy statements and other information with the Securities and Exchange Commission.

You can read the registration statement and our future filings with the Securities and Exchange Commission over the Internet at the Securities and Exchange Commission's website at http://www.sec.gov. You may also read and copy any document that we file with the Securities and Exchange Commission at its public reference room at 450 Fifth Street, N.W., Washington, D.C. 20549.

You may obtain copies of the documents at prescribed rates by writing to the Public Reference Section of the Securities and Exchange Commission at 450 Fifth Street, N.W., Washington, D.C. 20549. Please call the Securities and Exchange Commission at 1-800-SEC-0330 for further information on the operation of the public reference room. Upon approval of our common stock for listing on the NASDAQ National Market, such reports, proxy and information statements and other information may also be inspected at the offices of NASDAQ Operations, 1735 K Street, N.W., Washington, D.C. 20006.

INDEX TO THE FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors
Targacept, Inc.

We have audited the accompanying balance sheets of Targacept, Inc. as of December 31, 2002 and 2003, and the related statements of operations, redeemable convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2003. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Targacept, Inc. at December 31, 2002 and 2003, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2003, in conformity with U.S. generally accepted accounting principles.

ERNST & YOUNG LLP

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

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

/S/ ERNST & YOUNG LLP

July 9, 2004
Greensboro, North Carolina

Targacept, Inc.

Balance Sheets

	December 31,		March 31,	Pro forma Stockholders' equity as of March 31, 2004
	2002	2003	2004	
			(unaudited)	
Assets				
Current assets:				
Cash and cash equivalents	$ 44,353,320	$ 11,609,157	$ 5,482,910	$
Short-term investments	5,008,139	31,367,500	31,364,260	
Research fees and accounts receivable	1,335,648	818,618	224,674	
Inventories	169,536	118,520	114,812	
Prepaid expenses	423,016	514,552	698,488	
Total current assets	51,289,659	44,428,347	37,885,144	
Property and equipment, net	2,462,944	2,373,035	2,342,108	
Intangible assets, net of accumulated amortization of $15,735, $53,499 and $62,940 at December 31, 2002, 2003 and March 31, 2004, respectively	626,265	588,501	579,060	
Total assets	$ 54,378,868	$ 47,389,883	$ 40,806,312	$
Liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)				
Current liabilities:				
Accounts payable	$ 1,503,170	$ 1,246,975	$ 1,224,603	$
Accrued expenses	1,477,034	1,406,778	1,687,928	
Current portion of long-term debt	586,816	576,072	637,137	
Current portion of deferred rent incentive	402,647	402,647	402,647	
Current portion of deferred license fee revenue	634,881	269,537	269,537	
Total current liabilities	4,604,548	3,902,009	4,221,852	
Long-term debt, net of current portion	2,088,293	1,461,554	1,298,317	
Deferred rent incentive, net of current portion	1,442,818	1,040,171	939,509	
Deferred license fee revenue, net of current portion	1,551,875	1,647,687	1,580,303	
Total liabilities	9,687,534	8,051,421	8,039,981	
Commitments				
Redeemable convertible preferred stock:				
Series A, $0.001 par value, 5,000,000 shares authorized, issued and outstanding, aggregate liquidation preference of $26,826,253, $28,496,497 and $28,914,058 at December 31, 2002, 2003, and March 31, 2004, respectively, or $4.65 per share plus accreted redemption value	26,826,253	28,496,497	28,914,058	—
Series B, $0.001 par value, 6,567,567 shares authorized, issued and outstanding, aggregate liquidation preference of $35,346,675, $37,484,419 and $38,018,854 at December 31, 2002, 2003, and March 31, 2004, respectively, or $4.65 per share, plus accreted redemption value	35,346,675	37,484,419	38,018,854	—
Series C, $0.001 par value, 37,764,180, 49,169,138 and 49,169,138 shares authorized, issued and outstanding at December 31, 2002, 2003, and March 31, 2004, respectively, aggregate liquidation preference of $45,853,329, $64,153,421 and $65,343,314 at December 31, 2002, 2003, and March 31, 2004, or $1.21 per share, plus accreted redemption value	45,853,329	64,153,421	65,343,314	—
Total redeemable convertible preferred stock	108,026,257	130,134,337	132,276,226	—
Stockholders' equity (deficit):				
Common stock, $0.001 par value, 75,000,000, 85,000,000 and 85,000,000 shares authorized at December 31, 2002, 2003, and March 31, 2004, respectively, 624,584, 1,082,771 and 1,164,524 shares issued and outstanding at December 31, 2002, 2003, and March 31, 2004, respectively.	625	1,083	1,165	
Capital in excess of par value	6,002,692	6,306,513	6,377,745	
Excess of fair value of Series A preferred stock over cash received	(23,250,000)	(23,250,000)	(23,250,000)	
Common stock warrants	213,710	213,710	213,710	
Accumulated deficit	(46,301,950)	(74,037,899)	(82,817,723)	
Accumulated other comprehensive loss	—	(29,282)	(34,792)	
Total stockholders' equity (deficit)	(63,334,923)	(90,795,875)	(99,509,895)	
Total liabilities, redeemable convertible preferred stock and stockholders' equity (deficit)	$ 54,378,868	$ 47,389,883	$ 40,806,312	$

See accompanying notes.

Targacept, Inc.

Statements of Operations

	Year ended December 31,			Three months ended March 31,	
	2001	2002	2003	2003	2004
				(unaudited)	
Revenue:					
Research fee revenue	$ 1,100,000	$ 1,388,824	$ 1,302,500	$ 312,500	$ 134,674
License fee revenue	602,807	634,881	269,532	67,383	67,384
Product sales	—	242,861	814,724	310,913	187,511
Other	687	19,792	71,529	—	107,370
Net revenue	1,703,494	2,286,358	2,458,285	690,796	496,939
Operating expenses:					
Research and development	8,151,785	16,243,888	18,179,542	4,069,188	6,049,828
General and administrative	2,302,161	4,135,262	3,599,673	697,269	1,109,254
Cost of product sales	—	243,718	742,941	199,404	181,450
Purchased in-process research and development	—	2,666,000	—	—	—
Total operating expenses	10,453,946	23,288,868	22,522,156	4,965,861	7,340,532
Loss from operations	(8,750,452)	(21,002,510)	(20,063,871)	(4,275,065)	(6,843,593)
Other income (expense):					
Interest and dividend income	1,448,182	87,691	791,339	124,341	230,187
Interest expense	—	(102,891)	(122,789)	(34,318)	(24,529)
Loss on disposal of fixed assets	—	(53,996)	—	—	—
Total other income (expense)	1,448,182	(69,196)	668,550	90,023	205,658
Net loss	(7,302,270)	(21,071,706)	(19,395,321)	(4,185,042)	(6,637,935)
Preferred stock accretion	(3,807,988)	(4,173,545)	(8,340,628)	(1,914,958)	(2,141,889)
Net loss attributable to common stockholders	$ (11,110,258)	$ (25,245,251)	$ (27,735,949)	$ (6,100,000)	$ (8,779,824)
Basic and diluted net loss attributable to common stockholders per share	$ (26.80)	$ (45.28)	$ (33.91)	$ (9.48)	$ (7.89)
Weighted average common shares outstanding—basic and diluted	414,624	557,492	817,894	643,571	1,112,591
Pro forma basic and diluted net loss per share attributable to common stockholders assuming conversion of preferred stock (unaudited)			$ (0.27)		$ (0.09)
Pro forma weighted average shares outstanding—basic and diluted (unaudited)			71,118,629		74,852,496

See accompanying notes.

Targacept, Inc.

Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)

	Redeemable Convertible Preferred Stock			Common Stock								
	Series A	Series B	Series C	Shares	Amount	Capital in Excess of Par Value	Excess of Fair Value of Series A Preferred over Cash Received	Common Stock Warrants	Deferred Compensation	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Deficit
Balances at December 31, 2000	$23,485,765	$30,932,000	$ —	309,424	$ 309	$5,760,958	$(23,250,000)	$ 213,710	$ (92,638)	$ (9,946,441)	$ —	$ (27,314,102)
Stock issuance costs	—	—	—	—	—	(42,496)	—	—	—	—	—	(42,496)
Issuance of 29,933 shares of Series B redeemable convertible preferred stock at $4.65 per share	—	139,188	—	—	—	—	—	—	—	—	—	—
Issuance of 111,111 shares of common stock valued at $0.68 per share, related to collaborative research and development agreement	—	—	—	111,111	111	75,445	—	—	—	—	—	75,556
Issuance of 65,565 shares of common stock at $0.001 per share par value, related to exercise of stock options	—	—	—	65,565	66	30,749	—	—	—	—	—	30,815
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock	42,744	—	—	—	—	—	—	—	—	(42,744)	—	(42,744)
Accreted redemption value for Series A and Series B redeemable convertible preferred stock	1,627,500	2,137,744	—	—	—	—	—	—	—	(3,765,244)	—	(3,765,244)
Amortization of deferred compensation	—	—	—	—	—	—	—	—	92,638	—	—	92,638
Net loss	—	—	—	—	—	—	—	—	—	(7,302,270)	—	(7,302,270)
Balances at December 31, 2001	25,156,009	33,208,932	—	486,100	486	5,824,656	(23,250,000)	213,710	—	(21,056,699)	—	(38,267,847)
Stock issuance costs	—	—	(206,887)	—	—	—	—	—	—	—	—	—
Issuance of 37,764,180 shares of Series C redeemable convertible preferred stock at $1.21 per share	—	—	45,694,658	—	—	—	—	—	—	—	—	—
Issuance of 138,484 shares of common stock at $0.001 per share par value, related to exercise of stock options	—	—	—	138,484	139	178,036	—	—	—	—	—	178,175
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock	42,744	—	—	—	—	—	—	—	—	(42,744)	—	(42,744)
Accreted redemption value for Series A, Series B, and Series C redeemable convertible preferred stock	1,627,500	2,137,743	365,558	—	—	—	—	—	—	(4,130,801)	—	(4,130,801)
Net loss	—	—	—	—	—	—	—	—	—	(21,071,706)	—	(21,071,706)
Balances at December 31, 2002	$26,826,253	$35,346,675	$45,853,329	624,584	$ 625	$6,002,692	$(23,250,000)	$ 213,710	$ —	$ (46,301,950)	$ —	$ (63,334,923)

Targacept, Inc.

Statements of Redeemable Convertible Preferred Stock and Stockholders' Equity (Deficit)—(continued)

	Redeemable Convertible Preferred Stock			Common Stock								
	Series A	Series B	Series C	Shares	Amount	Capital in Excess of Par Value	Excess of Fair Value of Series A Preferred over Cash Received	Common Stock Warrants	Deferred Compensation	Accumulated Deficit	Accumulated Other Comprehensive Loss	Total Stockholders' Deficit
Balances at December 31, 2002 (carried forward)	$26,826,253	$35,346,675	$45,853,329	624,584	$ 625	$6,002,692	$(23,250,000)	$ 213,710	$ —	$ (46,301,950)	$ —	$ (63,334,923)
Stock issuance costs	—	—	(32,548)	—	—	—	—	—	—	—	—	—
Issuance of 11,404,958 shares of Series C redeemable convertible preferred stock at $1.21 per share	—	—	13,800,000	—	—	—	—	—	—	—	—	—
Issuance of 458,187 shares of common stock at $0.001 per share par value, related to exercise of stock options	—	—	—	458,187	458	303,821	—	—	—	—	—	304,279
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock	42,744	—	—	—	—	—	—	—	—	(42,744)	—	(42,744)
Accreted redemption value for Series A, Series B, and Series C redeemable convertible preferred stock	1,627,500	2,137,744	4,532,640	—	—	—	—	—	—	(8,297,884)	—	(8,297,884)
Net change in unrealized holding loss on available-for-sale securities	—	—	—	—	—	—	—	—	—	—	(29,282)	(29,282)
Net loss	—	—	—	—	—	—	—	—	—	(19,395,321)	—	(19,395,321)
Comprehensive loss												(19,424,603)
Balances at December 31, 2003	28,496,497	37,484,419	64,153,421	1,082,771	1,083	6,306,513	(23,250,000)	213,710	—	(74,037,899)	(29,282)	(90,795,875)
Issuance of 81,753 shares of common stock at $0.001 per share par value, related to exercise of stock options (unaudited)	—	—	—	81,753	82	71,232	—	—	—	—	—	71,314
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock (unaudited)	10,686	—	—	—	—	—	—	—	—	(10,686)	—	(10,686)
Accreted redemption value for Series A Series B and Series C redeemable convertible preferred stock (unaudited)	406,875	534,435	1,189,893	—	—	—	—	—	—	(2,131,203)	—	(2,131,203)
Net change in unrealized holding loss on available-for-sale securities (unaudited)	—	—	—	—	—	—	—	—	—	—	(5,510)	(5,510)
Net loss (unaudited)	—	—	—	—	—	—	—	—	—	(6,637,935)		(6,637,935)
Comprehensive loss (unaudited)												(6,643,445)
Balances at March 31, 2004 (unaudited)	$28,914,058	$38,018,854	$65,343,314	1,164,524	$ 1,165	$6,637,745	$(23,250,000)	$ 213,710	$ —	$ (82,817,723)	$ (34,792)	$ (99,509,895)

See accompanying notes.

Targacept, Inc.

Statements of Cash Flows

	Year ended December 31,			Three months ended March 31,	
	2001	2002	2003	2003	2004
				(unaudited)	
Operating activities					
Net loss	$ (7,302,270)	$ (21,071,706)	$ (19,395,321)	$ (4,185,042)	$ (6,637,935)
Adjustments to reconcile net loss to net cash used in operating activities:					
Depreciation and amortization	308,594	958,105	672,927	162,616	177,423
Loss on disposal of equipment	—	53,996	—	—	—
Write-off of in-process research and development	—	2,666,000	—	—	—
Non-cash compensation expense	92,638	129,710	65,325	4,188	18,444
Recognition of deferred rent incentive	—	(167,769)	(402,647)	(100,662)	(100,662)
Realized loss on sale of investments	—	—	20,978	—	10,482
Amortization of discount on held-to-maturity investments	(460,701)	(48,446)	—	—	—
Changes in operating assets and liabilities, excluding the effects from acquired assets and liabilities:					
Research fees and accounts receivable	(210,448)	(713,109)	517,030	731,483	593,944
Inventories	—	22,464	51,016	6,340	3,708
Prepaid expenses and accrued interest receivable	(555,929)	158,605	(205,054)	125,276	(102,852)
Accounts payable and accrued expenses	742,837	1,503,132	(326,451)	(1,535,622)	258,778
Deferred license fee revenue	1,321,637	(634,881)	(269,532)	(67,383)	(67,384)
Net cash used in operating activities	(6,063,642)	(17,143,899)	(19,271,729)	(4,858,806)	(5,846,054)
Investment activities					
Purchase of investments	(29,284,891)	(11,500,000)	(84,796,103)	(43,500,000)	(22,144,148)
Proceeds from sale of investments	32,700,000	26,400,000	58,500,000	—	22,050,312
Purchase of property and equipment	(1,522,064)	(1,281,840)	(545,254)	(99,715)	(137,055)
Proceeds from rent incentive	—	2,013,234	—	—	—
Purchase of Inversine product	—	(3,500,000)	—	—	—
Net cash provided by (used in) investing activities	1,893,045	12,131,394	(26,841,357)	(43,599,715)	(230,891)
Financing activities					
Proceeds from borrowing of long-term debt	—	3,000,000	—	101,289	—
Principal payments on long-term debt	—	(324,891)	(637,483)	(143,102)	(102,172)
Proceeds from issuance of redeemable convertible preferred stock, net of transaction costs	96,692	45,487,771	13,767,452	13,767,452	—
Proceeds from issuance of common stock	106,371	48,465	238,954	54,014	52,870
Net cash provided by (used in) financing activities	203,063	48,211,345	13,368,923	13,779,653	(49,302)
Net (decrease) increase in cash and cash equivalents	(3,967,534)	43,198,840	(32,744,163)	(34,678,868)	(6,126,247)
Cash and cash equivalents at beginning of period	5,122,014	1,154,480	44,353,320	44,353,320	11,609,157
Cash and cash equivalents at end of period	$ 1,154,480	$ 44,353,320	$ 11,609,157	$ 9,674,452	$ 5,482,910

See accompanying notes.

Targacept, Inc.

Notes to Financial Statements
December 31, 2003

1. The Company and Nature of Operations

Targacept, Inc., a Delaware corporation (the "Company"), was formed on March 7, 1997. The Company is a biopharmaceutical company engaged in the design, discovery and development of a new class of drugs to treat multiple diseases and disorders by selectively targeting a class of receptors known as neuronal nicotinic acetylcholine receptors, or NNRs. Its facilities are located in Winston-Salem, North Carolina.

The accompanying financial statements have been prepared on a going concern basis. The Company has incurred operating losses since its inception and expects to incur substantial additional losses for the forseeable future. As a result, the Company will require substantial additional funds, and plans to seek collaborative agreements, research funding, and private or public equity or debt financing to meet such needs. If such funds are not available, management may need to reassess its plans. Even if the Company does not have an immediate need for additional cash, it may seek access to the private or public equity markets if and when conditions are favorable. There is no assurance that such additional funds will be available for the Company to finance its operations on acceptable terms, if at all.

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

2. Summary of Significant Accounting Policies

Cash and Cash Equivalents

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

Investments

In accordance with the Company's investment policy, surplus cash is invested with high quality financial institutions in money market accounts, certificates of deposit, and a mutual fund that invests in Government National Mortgage Association and other mortgage-backed securities, United States Government debt and other asset-backed securities with AAA credit ratings. The Company determines the appropriate classification of marketable securities at the time of purchase and reevaluates such designation as of each balance sheet date. All marketable securities have been classified as available-for-sale and are stated at market value with the unrealized holding gains and losses reported as a component of stockholders' equity in comprehensive loss. Interest and dividend income on investments, as well as realized gains and losses, are included in "Interest and dividend income." The cost of securities sold is based on the specific identification method.

Research Fees and Accounts Receivable

Substantially all of the Company's research fees and accounts receivable are related to the collaborative research and license agreements discussed in Note 15, and trade sales of Inversine. All of the Company's trade

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

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

During 2001, 2002, 2003 and the three months ended March 31, 2004, the Company recognized revenues of $1,703,000, $2,024,000, $1,572,000 and $202,000, respectively, or 99%, 89%, 64% and 40%, respectively, of total revenues, from two collaborative research and license agreements discussed in Note 15.

Inventories

Inventories are stated at the lower of cost or market. Cost is determined by the weighted-average method.

Property and Equipment and Intangible Assets

Property and equipment consists primarily of lab equipment, office furniture and fixtures and leasehold improvements and is recorded at cost. Depreciation is computed using the straight-line method over the estimated useful lives of the assets ranging from three to ten years. Lab equipment is typically depreciated over 3-5 years, office furniture and fixtures are typically depreciated over 7-10 years, and leasehold improvements are amortized over the life of the applicable lease.

Intangible assets consist of patents acquired (See Note 16). The intangible assets are being amortized to research and development expense on a straight-line basis over the remaining useful life of the patents, or a period of 17 years from the date of acquisition.

The Company assesses the net realizable value of its long-lived assets and evaluates such assets for impairment whenever events or changes in business circumstances indicate that the carrying amount of an asset may not be recoverable. An impairment loss would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. An impairment loss, if recognized, would be based on the excess of the carrying value of the impaired asset over its respective fair value. Through March 31, 2004, there has been no such impairment.

Patents

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

Research and Development Costs

Research and development costs are expensed as incurred and include related salaries of personnel involved in research and development activities, contractor fees, administrative expenses and allocations of research-related overhead costs. Administrative expenses and research-related overhead costs included in research and development consist of allocations of facility and equipment lease charges, depreciation and amortization of assets, and insurance, legal and supply costs that are directly related to research and development activities.

The Company directly reduces research and development expenses for amounts reimbursed pursuant to cost-sharing agreements. During 2001, 2002 and 2003 and the three months ended March 31, 2004, research and development expenses were reduced by $412,000, $514,000, $131,000 and $69,000, respectively, for costs reimbursed primarily by Dr. Falk Pharma, GmbH and under the terms of the collaboration described in Note 15.

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

Clinical Trials Accounting

The Company records accruals based on estimates of the services received, efforts expended and amounts owed pursuant to contracts with numerous clinical trial centers and contract research organizations. In the normal course of business, the Company contracts with third parties to perform various clinical trial activities in the ongoing development of potential products. The financial terms of these agreements are subject to negotiation and variation from contract to contract and may result in uneven payment flows. Payments under the contracts depend on factors such as the achievement of certain events, the successful recruitment of patients, the completion of portions of the clinical trial or similar conditions. The objective of the Company's accrual policy is to match the recording of expenses in its financial statements to the actual services received and efforts expended. As such, expense accruals related to clinical trials are recognized based on the Company's estimate of the degree of completion of the event or events specified in the specific clinical study or trial contract.

Deferred Rent Incentive

In August 2002, the Company received $2,013,000 as an incentive to lease its current office space. The incentive is being recognized monthly over the life of the lease on a straight-line basis as a reduction to the lease expense in general and administrative expenses. The Company recognized $168,000, $403,000 and $101,000 of the incentive during 2002, 2003 and the three months ended March 31, 2004, respectively.

Redeemable Convertible Preferred Stock

The carrying value of redeemable convertible preferred stock is increased by periodic accretions so that the carrying amount will equal the redemption amount at the earliest redemption date. These increases are affected through charges to accumulated deficit.

Fair Value of Financial Instruments

The carrying amounts of cash and cash equivalents, short-term investments, accounts receivable, accounts payable, accrued expenses and redeemable convertible preferred stock are considered to be representative of their respective fair values. The fair value of long-term debt is $2,590,000, $1,961,000 and $1,867,000 at December 31, 2002, 2003 and March 31, 2004, respectively. The Company estimates that the fair value of long-term debt using discounted cash flows based on its incremental borrowing rates for similar debt.

Credit Risk

Financial instruments that potentially subject the Company to credit risk consist principally of cash and short-term investments. The Company places its cash and cash equivalents with high-credit quality financial institutions. The Company has established guidelines for investment of its excess cash designed to emphasize safety, liquidity and preservation of capital.

Revenue Recognition

The Company uses revenue recognition criteria in Staff Accounting Bulletin No. 101, *Revenue Recognition in Financial Statements,* as amended by Staff Accounting Bulletin No. 104, *Revision of Topic 13*. Revenues are recorded under collaboration agreements at the time of performance of services. Research fee revenues are earned and recognized in accordance with contract provisions. License fees for access to the Company's

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

intellectual properties are recognized ratably over the contracted period in accordance with the provisions of the contract. Amounts received in advance of performance are recorded as deferred revenue and amortized in the statements of operations into revenue over the estimated life of the research and development period. Revenues from milestones are only recognized upon achievement of the milestone criteria. Product sales revenues are recorded when goods are shipped, at which point title has passed.

Shipping and Handling Costs

During 2002, 2003 and the three months ended March 31, 2004, $22,000, $173,000 and $41,000, respectively, of shipping and handling costs were included in cost of product sales.

Income Taxes

The liability method is used in accounting for income taxes as required by Statement of Financial Accounting Standards ("SFAS") No. 109, *Accounting for Income Taxes*. Under this method, deferred tax assets and liabilities are recognized for operating loss and tax credit carryforwards and for the future tax consequences attributable to the differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the results of operations in the period that includes the enactment date. A valuation allowance is recorded to reduce the carrying amounts of deferred tax assets unless it is more likely than not that such assets will be realized. Currently there is no provision for income taxes as the Company has incurred net losses to date.

Comprehensive Loss

SFAS No. 130, *Reporting Comprehensive Income*, requires components of other comprehensive loss, including unrealized gains and losses on available-for-sale securities, to be included as part of total comprehensive loss. The components of comprehensive loss are included in the statements of redeemable convertible preferred stock and stockholders' equity (deficit).

Net Loss Per Share Attributable to Common Stockholders

The Company computes net loss per share attributable to common stockholders in accordance with SFAS No. 128, *Earnings Per Share* ("SFAS 128"). Under the provisions of SFAS 128, basic net loss per share attributable to common stockholders ("Basic EPS") is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares outstanding. Diluted net loss per share attributable to common stockholders ("Diluted EPS") is computed by dividing net loss attributable to common stockholders by the weighted average number of common shares and dilutive common share equivalents then outstanding. Common share equivalents consist of the incremental common shares issuable upon the conversion of preferred stock, shares issuable upon the exercise of stock options and shares issuable upon the exercise of warrants. For the periods presented, Diluted EPS is identical to Basic EPS because common share equivalents are excluded from the calculation, as their effect is antidilutive.

Pro Forma Stockholders' Equity and Pro Forma Net Loss Per Share

The Company's Board of Directors has authorized management of the Company to file a registration statement with the Securities and Exchange Commission permitting the Company to sell shares of its common stock to the public in an initial public offering (the "IPO"). If the IPO is closed under the terms presently

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

anticipated, all of the redeemable convertible preferred stock outstanding at the time of the IPO will automatically convert into 73,739,905 shares of common stock. Unaudited pro forma stockholders' equity, as adjusted for the assumed conversion of the preferred stock, is set forth on the accompanying balance sheets. Unaudited pro forma basic and diluted net loss per share is computed using the weighted average number of common shares outstanding, including the pro forma effects of the conversion of outstanding redeemable convertible preferred stock into shares of the Company's common stock effective upon the completion of the Company's planned IPO as if such conversion had occurred at January 1, 2003, or the date of issuance, if later.

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

	Year ended December 31,			Three months ended March 31,	
	2001	2002	2003	2003	2004
				(unaudited)	
Historical					
Numerator:					
Net loss attributable to common stockholders	$ (11,110,258)	$ (25,245,251)	$ (27,735,949)	$ (6,100,000)	$ (8,779,824)
Denominator:					
Weighted-average common shares outstanding	414,624	557,492	817,894	643,571	1,112,591
Basic and diluted net loss per share attributable to common stockholders	$ (26.80)	$ (45.28)	$ (33.91)	$ (9.48)	$ (7.89)
Pro forma					
Numerator:					
Net loss attributable to common stockholders			$ (19,395,321)		$ (6,637,935)
Denominator:					
Shares used above			817,894		1,112,591
Pro forma adjustments to reflect assumed conversion of preferred stock, on a weighted average basis (unaudited)			70,300,735		73,739,905
Shares used to compute pro forma basic and diluted net loss per share attributable to common stockholders (unaudited)			71,118,629		74,852,496
Pro forma basic and diluted net loss per share attributable to common stockholders (unaudited)			$ (0.27)		$ (0.09)

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

The Company has excluded all outstanding stock options and warrants from the calculation of net loss per share attributable to common stockholders because such securities are antidilutive for all periods presented. Had the Company been in a net income position, these securities may have been included in the calculation. These potentially dilutive securities consist of the following on a weighted average basis:

	Year Ended December 31,			Three Months ended March 31,	
	2001	2002	2003	2003	2004
Outstanding common stock options	1,496,707	2,150,650	4,601,270	3,604,941	8,000,521
Redeemable convertible preferred stock	11,567,567	15,980,048	70,300,735	59,792,159	73,739,905
Outstanding warrants	1,612,903	1,612,903	1,612,903	1,612,903	1,612,903
Total	14,677,177	19,743,601	76,514,908	65,010,003	83,353,329

Stock-Based Compensation

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

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

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

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

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

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

	Year Ended December 31,			Three months ended March 31,	
	2001	2002	2003	2003	2004
Net loss attributable to common stockholders, as reported	$ (11,110,258)	$ (25,245,251)	$ (27,735,949)	$ (6,100,000)	$ (8,779,824)
Add: Stock-based employee compensation expense included in reported net income, net of related tax effects	92,638	129,710	65,325	4,188	18,444
Deduct: Stock-based employee compensation expense determined under fair value based method for all awards, net of related tax effects	(205,710)	(312,830)	(515,405)	(87,714)	(233,319)
Pro forma net loss	$ (11,223,330)	$ (25,428,371)	$ (28,186,029)	$ (6,183,526)	$ (8,994,699)
Net loss per share:					
Basic and diluted, as reported	$ (26.80)	$ (45.28)	$ (33.91)	$ (9.48)	$ (7.89)
Basic and diluted, pro forma	$ (27.06)	$ (45.61)	$ (34.46)	$ (9.61)	$ (8.08)

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

Recent Accounting Pronouncements

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

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

Targacept, Inc.

Notes to Financial Statements—(continued)

2. Summary of Significant Accounting Policies (continued)

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Reclassifications

Certain reclassifications have been made to the prior year financial statements to conform to the current year presentation. These reclassifications had no impact on net loss or previously recorded amounts.

3. Short-term investments

The following is a summary of available-for-sale securities as of December 31, 2002, 2003 and March 31, 2004:

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

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

March 31, 2004	Amortized Cost	Unrealized Gains	Unrealized Losses	Fair Value
Adjustable rate mortgage fund	$ 15,377,586	$ —	$(34,793)	$ 15,302,793
Certificates of deposit	16,020,895	—	—	16,020,895
Interest receivable	40,572	—	—	40,572
Total	$ 31,439,053	$ —	$(34,793)	$ 31,364,260

The adjustable rate mortgage fund investment has remained in an unrealized loss position for less than 6 months. Accordingly the Company believes this is a temporary decline. The Company recognized $1,448,000, $88,000, $591,000 and $59,000 of interest income during 2001, 2002, 2003 and the three months ended March 31, 2004, respectively. The Company recognized $200,000 and $171,000 of dividend income during 2003 and the three months ended March 31, 2004, respectively.

Targacept, Inc.

Notes to Financial Statements—(continued)

4. Inventories

Inventories consisted of the following:

	December 31,		March 31,
	2002	2003	2004
Raw materials	$137,706	$ 46,988	$ 46,988
Work-in-process	9,042	6,892	6,892
Finished goods	22,788	64,640	60,932
	$169,536	$118,520	$114,812

5. Property and equipment

Property and equipment consists of the following:

	December 31,		March 31,
	2002	2003	2004
Lab equipment	$ 4,674,369	$ 5,057,345	$ 5,056,768
Office furniture and fixtures	1,030,406	1,192,685	1,295,933
Leasehold improvements	87,875	87,875	87,875
	5,792,650	6,337,905	6,440,576
Less: accumulated depreciation	3,329,706	3,964,870	4,098,468
Property and equipment, net	$ 2,462,944	$ 2,373,035	$ 2,342,108

The Company recorded $309,000, $577,000, $635,000 and $168,000 of depreciation expense during 2001, 2002, 2003 and the three months ended March 31, 2004, respectively.

6. Intangible Assets

Intangible assets consist of the following:

	December 31,		March 31,
	2002	2003	2004
Patents (See Note 16)	$642,000	$642,000	$642,000
Less: accumulated amortization	(15,735)	(53,499)	(62,940)
Total	$626,265	$588,501	$579,060

The Company recognized amortization expense of $0, $16,000, $38,000 and $9,000 in 2001, 2002, 2003 and the three months ended March 31, 2004, respectively. The Company expects to recognize $38,000 of amortization expense in each of the next five years.

7. Accrued Expenses

Accrued expenses consists of the following:

	December 31,		March 31,
	2002	2003	2004
Clinical trials costs	$ 361,119	$ 623,158	$ 1,265,409
Employee compensation	860,368	676,900	311,273
Other	255,547	106,720	111,246
	$ 1,477,034	$ 1,406,778	$ 1,687,928

Targacept, Inc.

Notes to Financial Statements—(continued)

8. Long-term debt

During 2002, the Company entered into agreements to borrow $500,000 from the City of Winston-Salem and $2,500,000 from R.J. Reynolds Tobacco Company ("RJRT"). The note payable to the City of Winston-Salem matures on April 19, 2012, is non-interest bearing until April 2007 and, thereafter, bears interest between 5% and 7% depending on the gross revenues of the Company until maturity. No payments are due on the City of Winston-Salem note until the 5-year anniversary of the loan. The note payable to RJRT accrues interest at 6.6%, is repayable in monthly payments of $59,403 through the maturity date of May 1, 2006, and is secured by equipment owned by the Company with a book value of approximately $2,373,000, net of accumulated depreciation, at December 31, 2003. The Company paid $91,000, $135,000 and $25,000 for interest under the RJRT note during 2002, 2003 and the three months ended March 31, 2004, respectively.

Maturities of long-term debt are as follows at December 31, 2003:

2004	$ 576,072
2005	669,379
2006	292,175
2007	69,438
2008	93,830
Thereafter	336,732
	$ 2,037,626

9. Redeemable Preferred Stock

In August 2000, the Company issued 5,000,000 shares of its Series A redeemable convertible preferred stock (the "Series A") to RJRT, and completed a private placement of 6,537,634 of its Series B redeemable convertible preferred stock (the "Series B") generating cash of $29,073,000, net of offering costs.

In January 2001, the Company issued 29,933 shares of Series B to three consultants in partial payment of consulting fees owed by the Company.

In November 2002, the Company completed a private placement of 37,764,180 shares of its Series C redeemable convertible preferred stock (the "Series C") and received cash of $45,488,000, net of offering costs.

In March 2003, the Company completed a private placement of an additional 11,404,958 shares of Series C and received cash of $13,767,452, net of offering costs.

The following is a summary of the rights, preferences and terms of the Company's outstanding series of redeemable convertible preferred stock:

Conversion

Each share of Series A, Series B and Series C is convertible, at the option of the holder thereof, at any time and from time to time, and without the payment of additional consideration by the holder thereof, into fully paid and nonassessable shares of the Company's common stock. As of December 31, 2003 and March 31, 2004, conversion of the Series A, Series B and Series C would result in the issuance of 5,000,000, 15,619,675, and 53,120,230 shares of common stock, respectively. Future sales of equity at prices below the respective conversion prices could result in adjustments to the number of shares of common stock into which each series of preferred stock is convertible.

Targacept, Inc.

Notes to Financial Statements—(continued)

9. Redeemable Preferred Stock (continued)

Automatic conversion of the Series A, Series B and Series C into fully paid and nonassessable shares of common stock, without the payment of additional consideration by the holders thereof, would occur immediately upon the closing of the sale of the Company's common stock in a firm commitment, underwritten public offering registered under the Securities Act of 1933 in which (i) the price per share equals or exceeds $3.60 (subject to certain adjustments) and (ii) the gross proceeds to the Company are not less than $50,000,000. The accrued but unpaid cumulative dividend on the Series C shall, if not yet declared, be forfeited upon conversion of the Series C.

Dividends

Dividends accrue daily on each share of Series C on a cumulative basis at the rate of 8% per annum and are recorded as an increase to Series C and an increase to accumulated deficit. Cumulative dividends may be declared and paid at any time and shall be payable upon liquidation or redemption. At December 31, 2003 and March 31, 2004, cumulative accrued dividends on the Series C stock totaled $4,898,000 and $6,088,000, respectively.

Dividends on the Series A, Series B and Series C are payable when and if declared by the Board of Directors. No dividend may be paid on the common stock without the approval of the holders of a majority of the then outstanding shares of Series A and Series B, considered together on an as-converted basis, and the holders of 65% of the Series C. No dividend may be declared or paid on either the Series A or the Series B unless, simultaneously with such declaration or payment, the same dividend per share is declared or paid on both the Series A and the Series B, as well as the Series C, and any unpaid cumulative dividends on the Series C are declared and paid in full.

Voting

Each holder of the Series A, Series B and Series C is entitled to the number of votes equal to the number of shares of common stock into which such holder's shares are convertible on the applicable record date. In addition, certain actions by the Company require the approval of one or more of (i) the holders of a majority of the outstanding shares of Series A, (ii) the holders of at least two-thirds of the outstanding shares of Series B, (iii) the holders of a majority of the outstanding shares of Series A and Series B, considered together on an as-converted basis, and/or (iv) the holders of at least 65% of the outstanding shares of Series C.

Liquidation Preference

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

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

Targacept, Inc.

Notes to Financial Statements—(continued)

9. Redeemable Preferred Stock (continued)

Mandatory Redemption

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

At any time after the later of August 22, 2005 or the date on which no shares of Series C are outstanding, a number of outstanding shares of Series A or Series B elected upon demand by the holders of a majority of the outstanding shares of Series A (in the case of Series A) or a majority of the outstanding shares of Series B (in the case of Series B) shall be redeemed in an amount per share equal to $4.65 (subject to certain adjustments) plus (i) any previously declared but unpaid dividends on such share and (ii) an amount equal to $0.081375 per share (subject to certain adjustments) multiplied by the number of complete three-month periods that have elapsed from the date such share was originally issued to the redemption date. The Company may satisfy its redemption obligation with respect to the Series A and/or the Series B in cash or by paying a portion in cash and issuing a promissory note that meets certain prescribed conditions for the remaining amount.

10. Stockholders' Equity (Deficit)

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

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

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

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

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

Targacept, Inc.

Notes to Financial Statements—(continued)

10. Stockholders' Equity (Deficit) (continued)

conversion price of the warrant was adjusted to $1.95. The warrant is exercisable only upon the earlier of an initial public offering or a change in control. The fair value of the warrant is a direct cost of obtaining capital. As such, the fair value has been recorded in stockholders' equity, with the offset recorded as a decrease in the redemption value of the Series A. The Company will accrete to the redemption value of the Series A at the earliest date of redemption, or until August 2005 through an increase in redemption value to Series A and an increase to retained deficit. The fair value of the warrant to purchase 1,612,903 shares of the Company's common stock was estimated at the grant date to be $213,710 or $0.53 per share. The Company considered the anti-dilution features, the contingencies surrounding the limited opportunities for exercise, and the warrant's priorities over common stock options in relation to the fair value of the Company's common stock at the date of issuance when estimating the fair value of the warrant.

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

	December 31, 2003	March 31, 2004
Convertible preferred stock	73,739,905	73,739,905
Warrant	1,612,903	1,612,903
Options	8,554,421	8,472,668
	83,907,229	83,825,476

11. Income Taxes

There is no income tax provision (benefit) for federal or state income taxes as the Company has incurred operating losses since inception.

The Company's effective tax rate differs from the federal income tax rate for the following reasons:

	Year ended December 31,			Three months ended March 31,
	2001	2002	2003	2004
Expected federal income tax benefit at statutory rate	(34)%	(34)%	(34)%	(34)%
Increase (decrease) resulting from:				
Research and development credits	—	(1)	(6)	(2)
Purchased in-process research and development	—	4	—	—
State income tax expense, net of federal benefit	(5)	(4)	(5)	(5)
Change in valuation allowance	38	35	44	41
Other	1	—	1	—
	—%	—%	—%	—%

At December 31, 2002 and 2003 and March 31, 2004, the Company had net operating loss carryforwards for income tax purposes of approximately $25,317,000, $46,090,000 and $53,007,000, respectively, and research and development tax credits of approximately $299,000, $1,456,000 and $1,594,000, respectively. The federal net operating loss carryforwards begin to expire in 2020. State net operating loss carryforwards begin to expire in 2015. The research and development tax credits will begin to expire in 2021.

Targacept, Inc.

Notes to Financial Statements—(continued)

11. Income Taxes (continued)

Utilization of the net operating loss carryforwards and credits may be subject to a substantial annual limitation due to ownership change limitations provided by the Internal Revenue Code of 1986, as amended, and similar state provisions. The Company has not performed a detail analysis to determine whether an ownership change under Section 382 of the Internal Revenue Code occurred. The effect of an ownership change would be the imposition of an annual limitation on the use of net operating loss carryforwards attributable to periods before the change.

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company's net deferred tax assets relate primarily to its net operating loss carryforwards. A valuation allowance has been recognized to offset the deferred tax assets related to those carryforwards. If and when recognized, the tax benefit for those items will be reflected in current operations of the period in which the benefit is recorded as a reduction of income tax expense. The utilization of the loss carryforwards to reduce future income taxes will depend on the Company's ability to generate sufficient taxable income prior to the expiration of the net operating loss carryforwards. For the years ended December 31, 2002, 2003 and the three months ended March 31, 2004, the valuation allowance increased approximately $7,380,000, $8,617,000 and $2,694,000, respectively.

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

	December 31,		March 31,
	2002	2003	2004
Deferred tax assets:			
Net operating loss carryforward	$ 9,760,723	$ 17,769,377	$ 20,436,139
Research and development tax credit	299,266	1,456,438	1,594,235
Equipment and other	226,338	—	—
Patents	682,413	641,008	641,008
Unearned revenue	843,084	739,167	635,251
Total gross deferred tax assets	11,811,824	20,605,990	23,306,633
Valuation allowance	(11,811,824)	(20,428,878)	(23,122,851)
Net deferred tax asset	—	177,112	183,782
Deferred tax liabilities:			
Equipment and other	—	(177,112)	(183,782)
Net deferred tax asset	$ —	$ —	$ —

Targacept, Inc.

Notes to Financial Statements—(continued)

12. Equity Incentive Plan

On August 22, 2000, the Company established an Equity Incentive Plan (the "Plan") and authorized the issuance of up to 2,011,259 shares under the Plan to attract and retain employees, directors and certain independent contractors, consultants and advisors and to allow them to participate in the growth of the Company. During 2001, the number of shares authorized for issuance under the Plan was increased to 2,611,259. In conjunction with the Series C financing, the Company authorized the issuance of an additional 3,000,000 shares, increasing the number of authorized shares to 5,611,259. Upon the issuance of the additional Series C shares in March 2003, the number of authorized shares was increased to 9,216,657. Awards may be made to participants under the Plan in the form of incentive and nonqualified stock options, restricted stock, stock appreciation rights, stock awards, and performance awards. Eligible participants under the Plan include employees, directors and certain independent contractors, consultants or advisors of the Company or a related corporation. The vesting periods for awards made under the Plan are determined at the discretion of the Plan administrator. The exercise price of incentive options granted under the Plan may not be less than 100% of the fair market value of the common stock on the date of grant, as determined by the Plan Administrator. The following summarizes stock option activity and balances:

	Options Granted	Price	Weighted Average Exercise Price Per Share
Outstanding at January 1, 2001	1,234,999	0.47	$ 0.47
Granted	440,000	0.47-4.65	0.90
Forfeited	(31,717)	0.47	0.47
Exercised	(65,565)	0.47	0.47
Outstanding at December 31, 2001	1,577,717	0.47-4.65	0.59
Granted	838,550	0.01-0.68	0.58
Forfeited	(18,672)	0.56	0.56
Exercised	(90,984)	0.47-0.68	0.53
Outstanding at December 31, 2002	2,306,611	0.47-4.65	0.59
Granted	5,996,095	0.01-0.75	0.67
Forfeited	(35,980)	0.01-0.68	0.26
Exercised	(458,187)	0.01-0.68	0.52
Outstanding at December 31, 2003	7,808,539	0.01-0.75	0.65
Granted	322,608	0.01-0.75	0.69
Forfeited	(25,000)	4.65	4.65
Exercised	(81,753)	0.47-0.75	0.65
Outstanding at March 31, 2004	8,024,394	$ 0.01-0.75	$ 0.64

Targacept, Inc.

Notes to Financial Statements—(continued)

12. Equity Incentive Plan (continued)

The weighted average fair value of options granted during 2001, 2002, 2003 and the three months ended March 31, 2004 was $0.38, $0.46, $0.41 and $0.47, respectively. At December 31, 2001, 2002, 2003 and March 31, 2004, 83,305, 958,059, 3,538,218 and 4,078,011 options, respectively, were exercisable at a weighted-average price of $0.47, $0.64, $0.63 and $0.62, respectively.

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

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

A summary of options outstanding as of March 31, 2004 (unaudited) is as follows:

	Options Outstanding			Options Exercisable	
Exercise Price	Number Outstanding	Weighted Average Remaining Contractual Exercise Life	Weighted Average Exercise Price	Number Exercisable	Weighted Average Price
0.01	209,225	8.9	$ 0.01	184,225	$ 0.01
0.47	901,142	6.5	0.47	748,519	0.47
0.68	6,583,523	9.1	0.68	2,884,713	0.68
0.75	330,504	9.8	0.75	260,554	0.75
	8,024,394	8.9	$ 0.64	4,078,011	$ 0.62

During 2001, the Company granted 25,000 options above fair value at a weighted-average exercise price of $4.65. The options had a weighted-average fair value of $0. During 2002 and 2003, respectively, the Company granted 130,000 and 97,500 options below fair value at an exercise price of $0.01 and fair value of $0.67 per share. The fair value of these shares was recorded as compensation expense in the amounts $129,710 and $65,325, during 2002 and 2003, respectively. During the three months ended March 31, 2004, the Company granted 25,000 options below fair value at an exercise price of $0.01 and a fair value of $0.74 per share. The fair value of these shares was recorded as compensation expense in the amount of approximately $18,000.

13. Leases

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

Targacept, Inc.

Notes to Financial Statements—(continued)

13. Leases (continued)

On March 1, 2002, the Company entered into an agreement with Wake Forest University to lease an office and research facility in Winston-Salem, North Carolina with an initial term that extends through July 31, 2007. The lease contains a renewal option for up to one additional five-year term, with a lease rate similar to the original agreement. Rent expense incurred by the Company under this lease was approximately $904,000, $1,456,000 and $364,000 for the years ended December 31, 2002, 2003 and the three months ended March 31, 2004, respectively. Rent expense is offset by the monthly recognition of the deferred rent incentive discussed in Note 2. At December 31, 2003, the Company has the following future minimum lease payments in relation to this lease:

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

14. Retirement Savings Plan

The Company has a 401(k) retirement plan that covers substantially all of its employees. This plan provides for the Company to make 100% matching contributions up to a maximum of 6% of employees' eligible compensation. The Company contributed $171,000, $290,000, $298,000 and $114,000 to the plan for the years ended December 31, 2001, 2002, 2003 and the three months ended March 31, 2004, respectively.

15. Collaborative Research and License Agreements

Aventis Pharma

In December 1998, the Company entered into a collaborative research and license agreement with Aventis Pharma ("Aventis") whereby the Company and Aventis agreed to collaborate on the discovery, development and commercialization of nicotinic agonists for use in prevention of certain human diseases. Under the agreement, Aventis was granted a license under certain patent rights and knowledge to develop, manufacture and commercialize certain compounds. The agreement provides for the payment of research fees on a "fee for service" basis for development work that the Company agreed to perform. For the years ended December 31, 2001, 2002, and 2003 and the three months ended March 31, 2004, these fees were $1,100,000, $1,389,000, $1,303,000 and $135,000, respectively. The Company is entitled to receive milestone payments under the contract at specified dates during the development period. The Company did not receive milestone payments under the agreement during 2001, 2002, 2003 or the three months ended March 31, 2004. In addition, Aventis agreed to make royalty payments based on net sales of products developed and sold. In general, either party may terminate the agreement in the event of a material breach by the other party, including a material breach of research obligations or the issuance of third-party patent rights to a competitor. Additionally, Aventis may terminate the agreement without cause by providing the Company with 30 days, written notice at any time after the research term, in which case all rights to the product candidate would revert to the Company. All royalty and other payment obligations of the parties survive any termination of the agreement.

During 1999, the Company received a one-time non-refundable license fee payment of $2,000,000 to enter into this agreement. The product candidate subject to the agreement has not completed the research and clinical development process. Accordingly, the Company has deferred recognition of the license fee and is amortizing it

Targacept, Inc.

Notes to Financial Statements—(continued)

15. Collaborative Research and License Agreements (continued)

over the expected term of the research and development period. The Company recognized $250,000, $250,000, $100,000 and $25,000 of the license fee payment during 2001, 2002, 2003 and the three months ended March 31, 2004, respectively.

On January 21, 2002, the Company entered into a second collaborative research and license agreement with Aventis to discover and develop drugs, derived from the Aventis library of compounds for the treatment of Alzheimer's disease and other disorders of the central nervous system. The second agreement was structured similarly to the first agreement. The research terms of the agreement will extend for two years.

Dr. Falk Pharma

On January 26, 2001, the Company entered into a collaborative research development and license agreement with Dr. Falk Pharma GmbH ("Dr. Falk Pharma"), a German corporation, pursuant to which the parties agreed to collaborate to research, develop and commercialize nicotinic therapeutics for use in the prevention or treatment of ulcerative colitis and other gastrointestinal and liver diseases. Upon execution of the agreement, Dr. Falk Pharma paid the Company a $1,000,000 license fee and purchased 111,111 shares of the Company's common stock for $1,000,000. The Company is continuing to advance the compound subject to the agreement through the research and clinical development process. Therefore, the Company has deferred recognition of the license fee payment and is amortizing it over the expected term of the research and development period. To account for the $1,000,000 in proceeds for the common stock, the Company used the estimated fair value of the common stock to value the shares issued to arrive at a total equity value of $75,556, with the remaining proceeds of $924,494 allocated to deferred revenue. This deferred revenue is also being amortized over the expected term of the research and development period. The Company recognized $353,000, $385,000, $170,000 and $41,000 of deferred revenue under this agreement during 2001, 2002, 2003 and the three months ended March 31, 2004, respectively. As of March 31, 2004, deferred revenue under this agreement was approximately $975,000 and was included in deferred license fee revenue in the accompanying balance sheet.

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

16. Acquisition of Inversine product

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

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

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

Targacept, Inc.

Notes to Financial Statements—(continued)

16. Acquisition of Inversine product (continued)

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

17. Related Party Transactions

RJRT is the holder of 5,000,000 shares of Series A redeemable preferred stock convertible to 5,000,000 shares of common stock, a warrant to purchase 1,612,903 shares of common stock, and options to purchase 31,725 shares of common stock. The Company has entered into the following transactions and agreements with RJRT in the ordinary course of business.

During 2002, the Company entered into an agreement to borrow $2,500,000 from RJRT accruing interest at 6.6%. The note is repayable in monthly installments of $59,403 through the maturity date of May 1, 2006, and is secured by equipment owned by us with a book value of approximately $2,373,000, net of accumulated depreciation, at December 31, 2003. Under this related party note payable, the Company paid RJRT $416,000, $713,000 and $178,000 during 2002, 2003 and the three months ended March 31, 2004, respectively.

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

A member of the Company's board of directors serves as an officer of RJRT. Equity compensation for such director's service has been made, at the director's request, directly to RJRT. The numbers of shares subject to stock options granted to RJRT during the years ended December 31, 2001, 2002 and 2003 and the three months ended March 31, 2004 in connection with the director's services are 0, 32,500, 7,500 and 0, respectively. In addition, a stock option for an additional 32,500 shares was granted to RJRT during the year ended December 31, 2002 in connection with the services of a former director. A portion of that option, representing 15,775 shares, was forfeited when that director ceased to serve as a director. In connection with the issuance of the stock options, the Company recognized compensation expense of $0, $43,550, $2,512 and $1,256 during 2001, 2002, 2003 and the three months ended March 31, 2004, respectively.

Prior to December 31, 2003, the Company used the services of a RJRT employee for toxicology studies and purchased materials used for research and development through RJRT. The Company paid RJRT $810,000, $525,000 and $201,000 for these services during 2001, 2002, and 2003, respectively.

18. Subsequent Event

On , 2004 the Company's Board of Directors adopted, and on , 2004 the stockholders approved, a to reverse stock split of the Company's common stock effective as of . All common stock and per common share amounts for all periods presented in the accompanying financial statements have been restated to reflect the effect of this common stock split.

Targacept, Inc.

Notes to Financial Statements—(continued)

19. Selected Quarterly Financial Data (Unaudited)

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

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

Diluted EPS is identical to Basic EPS since common stock equivalent shares are excluded from the calculation, as their effect is anti-dilutive.

(1) Per common share amounts for the quarters and full years have been calculated separately. Accordingly, quarterly amounts do not add to the annual amount because of differences in the weighted-average common shares outstanding during each period principally due to the effect of the Company's issuing shares of its common stock during the year.


TARGACEPT

Part II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 13. Other Expenses of Issuance and Distribution.

The following table sets forth the expenses in connection with the offering, all of which will be borne by us. All amounts shown are estimates except for the Securities and Exchange Commission registration fee, the NASDAQ National Market listing fee and the NASD filing fee.

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

* To be filed by amendment.

Item 14. Indemnification of Directors and Officers.

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

Section 145 of the DGCL empowers a corporation to indemnify its directors and officers against expenses (including attorneys' fees), judgments, fines and amounts paid in settlements actually and reasonably incurred by them in connection with any action, suit or proceeding brought by third parties by reason of the fact that they were or are directors or officers of the corporation, if they acted in good faith, in a manner they reasonably believed to be in or not opposed to the best interests of the corporation and, with respect to any criminal action or proceeding, had no reason to believe that their conduct was unlawful. The DGCL provides further that the indemnification permitted thereunder shall not be deemed exclusive of any other rights to which the directors and officers may be entitled under the corporation's bylaws, any agreement, a vote of stockholders or otherwise. The Certificate provides that, to the fullest extent permitted by Section 145 of the DGCL, we shall indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding (whether civil, criminal, administrative or investigative) by reason of the fact that such person is or was a director or officer of us, or is or was serving at our request as a director, officer or trustee of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, against expenses

(including attorneys' fees), judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding. At present, there is no pending litigation or proceeding involving any director or officer as to which indemnification will be required or permitted under the Certificate and we are not aware of any threatened litigation or proceeding that may result in a claim for such indemnification.

Section 145 of the DGCL also empowers a corporation to purchase insurance for its officers and directors for such liabilities. We maintain liability insurance for our officers and directors.

Item 15. Recent Sales of Unregistered Securities.

Set forth below is information regarding shares of common stock and preferred stock issued, and options and warrants granted, by us since August 22, 2000. Also included is the consideration, if any, received by us for such shares, options and warrants and information relating to the section of the Securities Act, or rule of the Securities and Exchange Commission, under which exemption from registration was claimed.

(a) Issuance of Securities

1. On August 22, 2000, at the time that we became an independent company, we issued an aggregate of 309,424 shares of our common stock at a purchase price per share of $0.001 to each of Dr. deBethizy, Dr. Bencherif, Dr. Caldwell and Dr. Patrick M. Lippiello for an aggregate purchase price of approximately $309.

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

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

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

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

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

7. On August 8, 2002 and June 11, 2003, we issued and sold an aggregate of 60,000 shares of restricted stock to Mr. Skaletsky for an aggregate purchase price of $600.

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

9. On March 14, 2003, we issued and sold an aggregate of 11,404,958 shares of our series C convertible preferred stock at a purchase price per share of $1.21 to investors affiliated with JAFCO G-9(A) Venture Capital, Rock Castle Ventures, Cogene Biotech Ventures Five, Bison Capital, LLC and Oxford Bioscience Partners IV L.P. for an aggregate purchase price of approximately $13.8 million. These shares will convert into common stock at the rate of approximately 1.08 shares of common stock for each share of series C convertible preferred stock concurrently with the completion of this offering.

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

11. Since inception to June 30, 2004, we have granted:

- options to purchase an aggregate of 8,637,319 shares of common stock at exercise prices ranging from $0.01 to $4.65 per share under our 2000 Equity Incentive Plan, as amended, with a weighted average exercise price of $0.66 per share, to employees, directors and individual consultants;
- restricted stock awards for an aggregate of 85,000 shares of common stock at a purchase price of $0.01 per share under our 2000 Equity Incentive Plan, as amended; and
- options to purchase an aggregate of 217,500 shares of common stock at an exercise price of $0.01 per share to non-individual consultants under our 2000 Equity Incentive Plan, as amended.

The weighted average exercise price of all options to purchase shares of common stock granted since inception and outstanding on June 30, 2004 is $0.66 per share. As of June 30, 2004, there were 55 holders of record of shares of our common stock.

(b) No underwriters were involved in the foregoing sales of securities. The securities described in paragraphs (a)(1)—(10) of this Item 15 were issued to a combination of foreign and U.S. investors in reliance upon the exemption from the registration requirements of the Securities Act, as set forth in Sections 3(a)(9) or 4(2) under the Securities Act and Rule 506 of Regulation D promulgated thereunder relative to sales by an issuer not involving any public offering, to the extent an exemption from such registration was required. All purchasers of shares of our convertible preferred stock described in paragraph (a)(1)—(10) of this Item 15 represented to us in connection with their purchase that they were accredited investors and were acquiring the shares for investment and not distribution, that they could bear the risks of the investment and could hold the securities for an indefinite period of time. The purchasers received written disclosures that the securities had not been registered under the Securities Act and that any resale must be made pursuant to a registration or an available exemption from such registration.

All of the foregoing securities are deemed restricted securities for purposes of the Securities Act. All certificates representing the issued shares of common stock described in this Item 15 included appropriate legends setting forth that the securities had not been registered and the applicable restrictions on transfer.

The issuance of stock options and the common stock issuable upon the exercise of such options as described in paragraph (a)(11) of this Item 15 were issued pursuant to written compensatory plans or arrangements with our employees, directors and consultants, in reliance on the exemption provided by Rule 701 promulgated under the Securities Act. All recipients either received adequate information about us or had access, through employment or other relationships, to such information.

Item 16. Exhibits and Financial Statement Schedules.

(a) Exhibits.

Exhibit No.	Description
1.1*	Form of Underwriting Agreement.
3.1(a)**	Second Amended and Restated Certificate of Incorporation of the Company, as amended.
3.1(b)*	Certificate of Amendment to Second Amended and Restated Certificate of Incorporation of the Company.
3.1(c)*	Form of Third Amended and Restated Certificate of Incorporation of the Company, to be effective upon completion of this offering.
3.2(a)**	Amended and Restated Bylaws of the Company.
3.2(b)*	Form of Bylaws of the Company, to be effective upon completion of this offering.
4.1*	Specimen common stock certificate.
4.2*	Third Amended and Restated Investor Rights Agreement, dated May 12, 2004, by and among the Company and certain stockholders of the Company.
4.3**	Warrant to Purchase Common Stock, dated August 22, 2000, granted to R.J. Reynolds Tobacco Company and subsequently assigned to R.J. Reynolds Tobacco Holdings, Inc.
5.1*	Opinion of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C.
5.2*	Opinion of Womble Carlyle Sandridge & Rice, PLLC.
10.1*	Form of Indemnification Agreement between the Company and each of its directors and officers.
10.2**	Lease Agreement, dated as of August 1, 2002, by and between the Company and Wake Forest University Health Sciences.
10.3**	Loan Agreement, dated as of April 19, 2002, between the Company and the City of Winston-Salem.
10.4**	Amended and Restated Note and Security Agreement, dated January 30, 2004, issued by the Company in favor of R.J. Reynolds Tobacco Holdings, Inc.
10.5**	2000 Equity Incentive Plan, as amended.
10.6*	2004 Stock Incentive Plan.
10.7**	Employment Agreement, dated as of August 22, 2000, by and between the Company and J. Donald deBethizy.
10.8**	Employment Agreement, dated as of August 22, 2000, by and between the Company and Merouane Bencherif.
10.9**	Employment Agreement, dated as of August 22, 2000, by and between the Company and William S. Caldwell.

Exhibit No.	Description
10.10**	Employment Agreement, dated as of April 24, 2001, by and between the Company and Geoffrey Dunbar.
10.11**	Employment Agreement, dated as of February 8, 2002, by and between the Company and Alan Musso.
10.12**	Employment Agreement, dated as of September 1, 2003, by and between the Company and Jeffrey P. Brennan.
10.13(a)+**	Collaborative Research and License Agreement, dated as of January 21, 2002, by and between the Company and Aventis Pharma SA.
10.13(b)+**	Amended and Restated Collaborative Research and License Agreement, dated as of January 21, 2002, by and between the Company and Aventis Pharma SA.
10.13(c)**	Letter Agreement, dated March 18, 2003, amending the Amended and Restated Collaborative Research and License Agreement, dated as of January 21, 2002, by and between the Company and Aventis Pharma SA and the Collaborative Research and License Agreement, dated as of January 21, 2002, by and between the Company and Aventis Pharma SA.
10.14+**	Collaborative Research, Development and License Agreement, dated as of January 26, 2001, by and between the Company and Dr. Falk Pharma GmbH.
10.15**	Asset Purchase Agreement, dated as of June 28, 2002, by and between the Company and Layton Bioscience, Inc.
10.16+**	Asset Purchase and Trademark Assignment Agreement, dated March 19, 1998, by and between the Company (as assignee of Layton Bioscience, Inc.) and Merck & Co., Inc.
10.17+**	Amended and Restated License Agreement, dated as of March 9, 2004, by and between the Company and the University of South Florida Research Foundation, Inc.
10.18(a)+**	License Agreement, dated October 6, 1997, by and between the Company (as assignee of R.J. Reynolds Tobacco Company) and Virginia Commonwealth University Intellectual Property Foundation.
10.18(b)+**	Amendment to License Agreement, dated February 11, 2004, to the License Agreement, dated October 6, 1997, by and between the Company (as assignee of R.J. Reynolds Tobacco Company) and Virginia Commonwealth University Intellectual Property Foundation.
10.19+**	License Agreement, dated as of June 9, 2002, by and between the Company and the Medical College of Georgia Research Institute, Inc.
10.20+**	License Agreement, dated May 26, 1999, by and between the Company and the University of Kentucky Research Foundation.
10.21+**	License Agreement, dated as of August 12, 2002, between the Company and Wake Forest University Health Sciences.
10.22+**	Development and Production Agreement for Active Pharmaceutical Ingredients, dated as of February 1, 2004, by and between the Company and Siegfried Ltd.
23.1	Consent of Ernst & Young LLP.
23.2*	Consent of Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C. (included in Exhibit 5.1).
23.3*	Consent of Womble Carlyle Sandridge & Rice, PLLC (included in Exhibit 5.2).
24.1**	Power of Attorney (included on signature page).

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

(b) Financial Statement Schedules.

All information for which provision is made in the applicable accounting regulations of the Securities and Exchange Commission is either included in the financial statements or is not required under the related instructions or is inapplicable, and therefore has been omitted.

Item 17. Undertakings.

The undersigned registrant hereby undertakes to provide to the underwriters at the closing specified in the underwriting agreement, certificates in such denominations and registered in such names as required by the underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the provisions described herein, or otherwise, the registrant has been advised that in the opinion of the Commission such indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by such director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of such issue.

The undersigned registrant hereby undertakes that:

(1) For purposes of determining any liability under the Securities Act of 1933, the information omitted from the form of prospectus filed as a part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this registration statement as of the time it was declared effective.

(2) For the purpose of determining any liability under the Securities Act of 1933, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant has duly caused this Amendment No. 2 to the registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Winston-Salem, State of North Carolina, on July 9, 2004.

TARGACEPT, INC.

By: /S/ J. DONALD DEBETHIZY

J. Donald deBethizy
Chief Executive Officer and President

Pursuant to the requirements of the Securities Act of 1933, this Amendment No. 2 to the registration statement has been signed by the following persons in the capacities indicated on July 9, 2004.

/S/ J. DONALD DEBETHIZY	/S/ ALAN A. MUSSO
Name: J. Donald deBethizy **Title:** Chief Executive Officer, President and Director (Principal Executive Officer)	**Name:** Alan A. Musso **Title:** Vice President and Chief Financial Officer (Principal Financial Officer and Principal Accounting Officer)
*	*
Name: Mark Skaletsky **Title:** Chairman of the Board of Directors	**Name:** M. James Barrett **Title:** Director
*	*
Name: Charles A. Blixt **Title:** Director	**Name:** G. Steven Burrill **Title:** Director
*	*
Name: Errol B. De Souza **Title:** Director	**Name:** Elaine V. Jones **Title:** Director
*	*
Name: John P. Richard **Title:** Director	**Name:** Alan G. Walton **Title:** Director

*By: /s/ ALAN A. MUSSO

Alan A. Musso
Attorney-in-fact

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

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the reference to our firm under the caption "Experts" and to the use of our report dated January 22, 2004 (except Note 18 as to which the date is , 2004), in Amendment No. 2 to the Registration Statement (Form S-1 No. 333-115538) and related Prospectus of Targacept, Inc. dated June 18, 2004.

Ernst & Young LLP

Greensboro, North Carolina
, 2004

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

/s/ Ernst & Young LLP

Greensboro, North Carolina
July 9, 2004