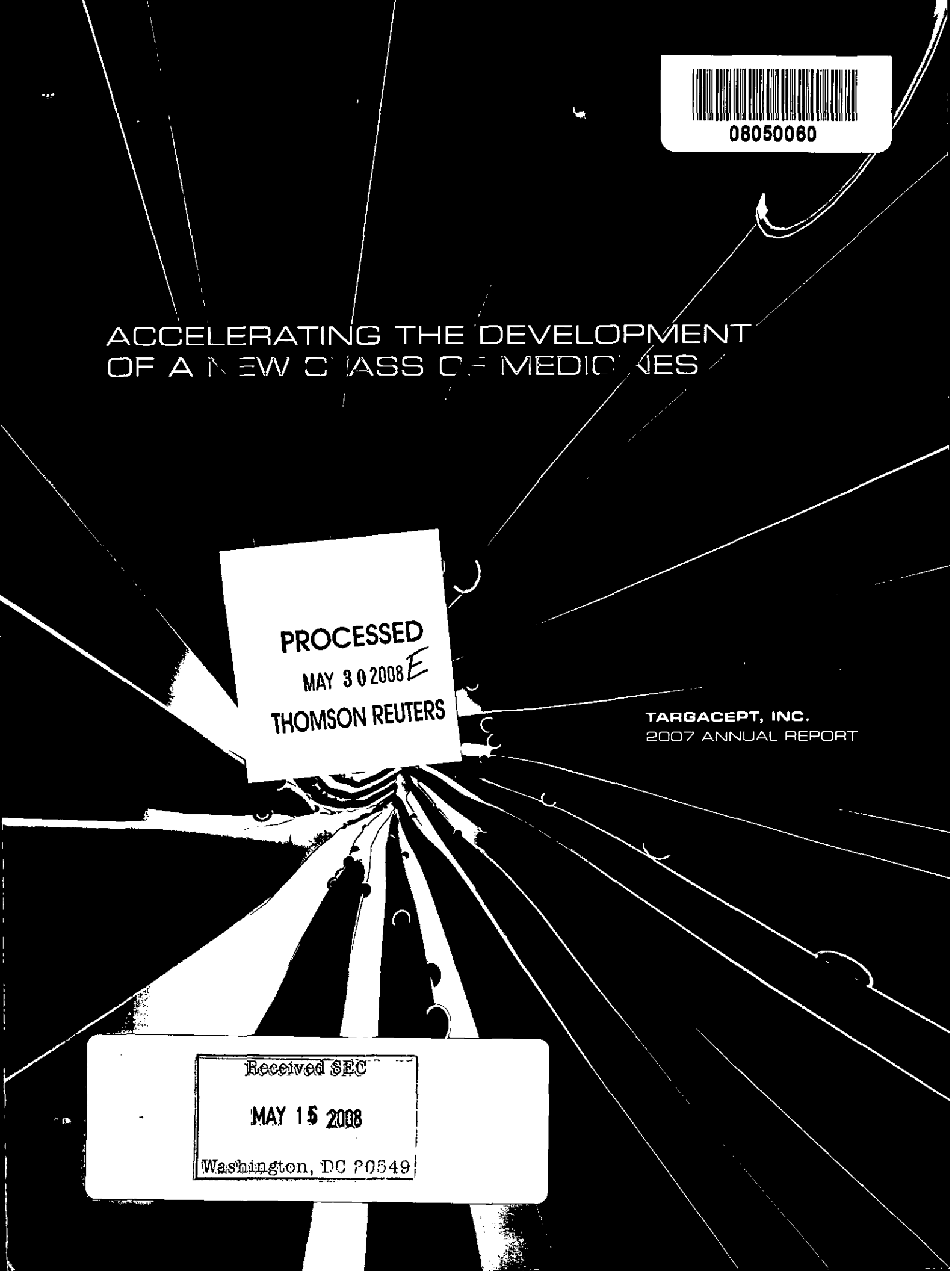
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ACCELERATING THE DEVELOPMENT
OF A NEW CLASS OF MEDICINES
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TARGACEPT, INC.
2007 ANNUAL REPORT
Received SEC
MAY 15 2008
Washington, DC 20549

ACCELERATING THE DEVELOPMENT OF A NEW CLASS OF MEDICINES

One hundred years ago, the English physiologist John Newport Langley conceptualized the existence of "receptive substances" in the body that can affect how other substances, such as drugs, behave. Today, Langley would be astonished at how his theory of pharmacological receptors has provided the foundation for a new class of medicines, with Targacept leading the way. With more than 20 years of focused research and investment, Targacept has generated a vast treasury of knowledge and built a broad pipeline of product candidates known as NNR Therapeutics™. These product candidates selectively target neuronal nicotinic receptors, or NNRs, to treat a variety of debilitating diseases and disorders of the central nervous system.

[illegible]

Formed a major alliance with GlaxoSmithKline in which Targacept is eligible to receive up to $1.5 billion in milestone payments, contingent on the achievement of specified milestone events in the five therapeutic areas of the alliance – pain, smoking cessation, addiction, obesity and Parkinson's disease.

Initiated separate Phase 2b clinical trials of Targacept's lead product candidate, AZD3480 (TC-1734), in mild to moderate Alzheimer's disease and cognitive dysfunction in schizophrenia. Both trials are being conducted by our strategic collaborator AstraZeneca.

Advanced TC-5619, a novel product candidate that modulates the activity of an NNR subtype known as alpha7, into Phase 1 clinical development.

Advanced TC-6499, a novel product candidate for the treatment of neuropathic pain, into Phase 1 clinical development, triggering a $6 million milestone payment from GlaxoSmithKline.

Therapeutics through clinical proof of concept. GlaxoSmithKline maintains options at that stage to assume responsibility and apply its substantial resources and late-stage development and commercialization capabilities. Although Phase 2 clinical results in 2007 showed that TC-2696 was not a suitable product candidate for acute post-operative pain, the scientific rationale for the NNR mechanism in the treatment of pain remains strong. In December, we initiated a Phase 1 clinical trial of TC-6499, a product candidate for neuropathic pain, triggering a $6 million milestone payment from GlaxoSmithKline.

We have retained the commercial rights to our depression program. In 2007, we made the decision to move forward aggressively with development of TC-5214, the S(+) enantiomer of mecamylamine hydrochloride, based on its more favorable overall preclinical safety and efficacy profile as compared to mecamylamine and its potential as augmentation therapy for depressed patients who are not responding well to first-line treatment. We initiated a Phase 1 trial of TC-5214 in March 2008.

We have continued to build upon a strong board of directors, with the additions of Julia Brown, with over 30 years of commercial experience in the life sciences, and Ralph Snyderman, M.D., an esteemed academician and recognized expert in personalized medicine and inflammation.

With a deep and diverse pipeline, an extensive patent estate, and financial resources bolstered by over $83 million received over the last two years from AstraZeneca and GlaxoSmithKline and $29.1 million in net proceeds from a public stock offering completed in January 2008, we are well positioned to drive additional momentum in 2008.

Sincerely,

J. Donald deBethizy, Ph.D.
President and CEO, Targacept, Inc.

J. Donald deBethizy, Ph.D.
President and Chief Executive Officer

ANTICIPATED 2008 KEY EVENTS

- ☐ AstraZeneca Collaboration:
  - Completion by AstraZeneca of proof-of-concept trials of AZD3480 in mild to moderate Alzheimer's disease and cognitive dysfunction in schizophrenia; and
  - Continued execution of a cognition-focused preclinical research collaboration
- ☐ Depression Program: Completion of a Phase 1 trial for TC-5214 and initiation of a Phase 2 proof of concept trial as augmentation therapy in major depression
- ☐ Alpha7 NNR Program: Completion of Phase 1 clinical development of TC-5619
- ☐ GlaxoSmithKline Alliance: Completion of Phase 1 clinical development of TC-6499
- ☐ Advancement of preclinical product candidates to trigger potential milestone payments

INCREASED UNDERSTANDING OF NNRs LEADS TO INCREASED POTENTIAL FOR NNR-TARGETED THERAPEUTICS

Since the 1980s, scientists have gained a deeper understanding of the nature of NNRs and the role they play in regulating the nervous system. Ongoing 21st century advances affirm the potential of NNR-targeted therapeutics to contribute to a new era of human medicine.

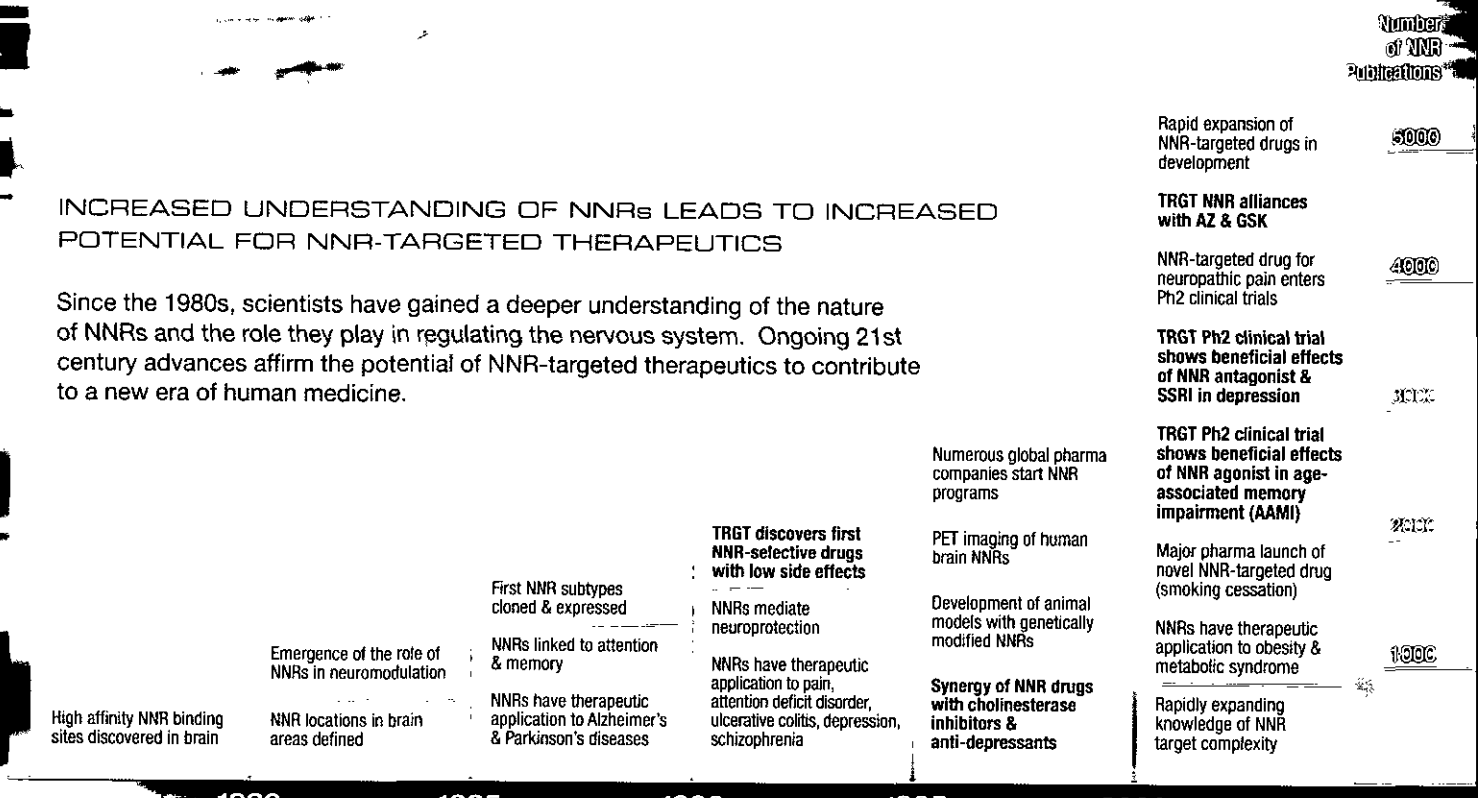


PHOTO: In Targacept's neurochemistry lab, scientists observe a compound in solution. *In vitro* screening and characterization are essential for fully understanding a compound's therapeutic potential.

TO OUR STOCKHOLDERS

Forging a new strategic alliance with GlaxoSmithKline. Leveraging a proprietary drug discovery platform to advance new product candidates into the clinic. And working with AstraZeneca to advance AZD3480 (TC-1734) into two large Phase 2b trials. In 2007, Targacept was a driving force for significant new accomplishments in business and science.

If I had just one word to describe Targacept in 2007, it would be *momentum*. Since our spinout in 2000, we have worked hard to enhance our understanding of NNRs and to advance our pipeline of NNR Therapeutics. NNRs, or neuronal nicotinic receptors, serve as key regulators of nervous system activity and have been the focus of our drug discovery efforts since inception.

We are building our business based on a foundation of strong science, proprietary technology, and a culture that values the unique contributions of a diverse workforce. We are focused on areas of large unmet medical need such as Alzheimer's disease, depression, schizophrenia, pain and smoking cessation, and are gratified to have fostered the scientific innovation necessary to discover promising compounds that target such critical diseases and disorders. The significant relationships we have formed with two premier companies that recognize our strengths and provide "big pharma" guidance and resources are helping accelerate the development of this new class of medicines.

In AstraZeneca, we have a collaborator that shares our commitment to seeking new therapies for cognitive disorders. In 2007, AstraZeneca initiated separate Phase 2b trials of AZD3480 in mild to moderate Alzheimer's disease (approximately 525 patients) and cognitive dysfunction in schizophrenia (approximately 400 patients). We expect both trials to be completed by the end of 2008.

AstraZeneca's belief in the promise of the NNR mechanism was further evidenced by our continued preclinical collaboration focused on the discovery and development of new product candidates that target the alpha4beta2 NNR for cognitive disorders and its decision in November to secure the right to license TC-5619, the lead product candidate in our alpha7 NNR program.

We are also enthusiastic about the alliance that we initiated in July 2007 with GlaxoSmithKline through its Center of Excellence in External Drug Discovery. The alliance, which is focused on pain, smoking cessation, addiction, obesity and Parkinson's disease, has potential for significant value creation, including up to $1.5 billion in possible milestone payments and stepped double-digit royalties on any product sales.

The innovative deal structure with GlaxoSmithKline allows us to accelerate several programs by leveraging our proprietary Pentad™ drug discovery platform and our development expertise to drive forward new NNR

Targacept scientists value the ongoing exchange of information and frequently participate in prominent scientific meetings. This poster, presented at the 2007 annual meeting of the Society for Neuroscience, illustrates the promising preclinical profile of TC-6499, Targacept's neuropathic pain candidate.

PROGRESSING KNOWLEDGE

"NNRs play an important role in the body's primary signaling systems, not only in essential functions such as sensation and perception, but in higher order functions such as emotion and cognition. Every breath, every move, every thought, and every mood are made possible by NNRs."

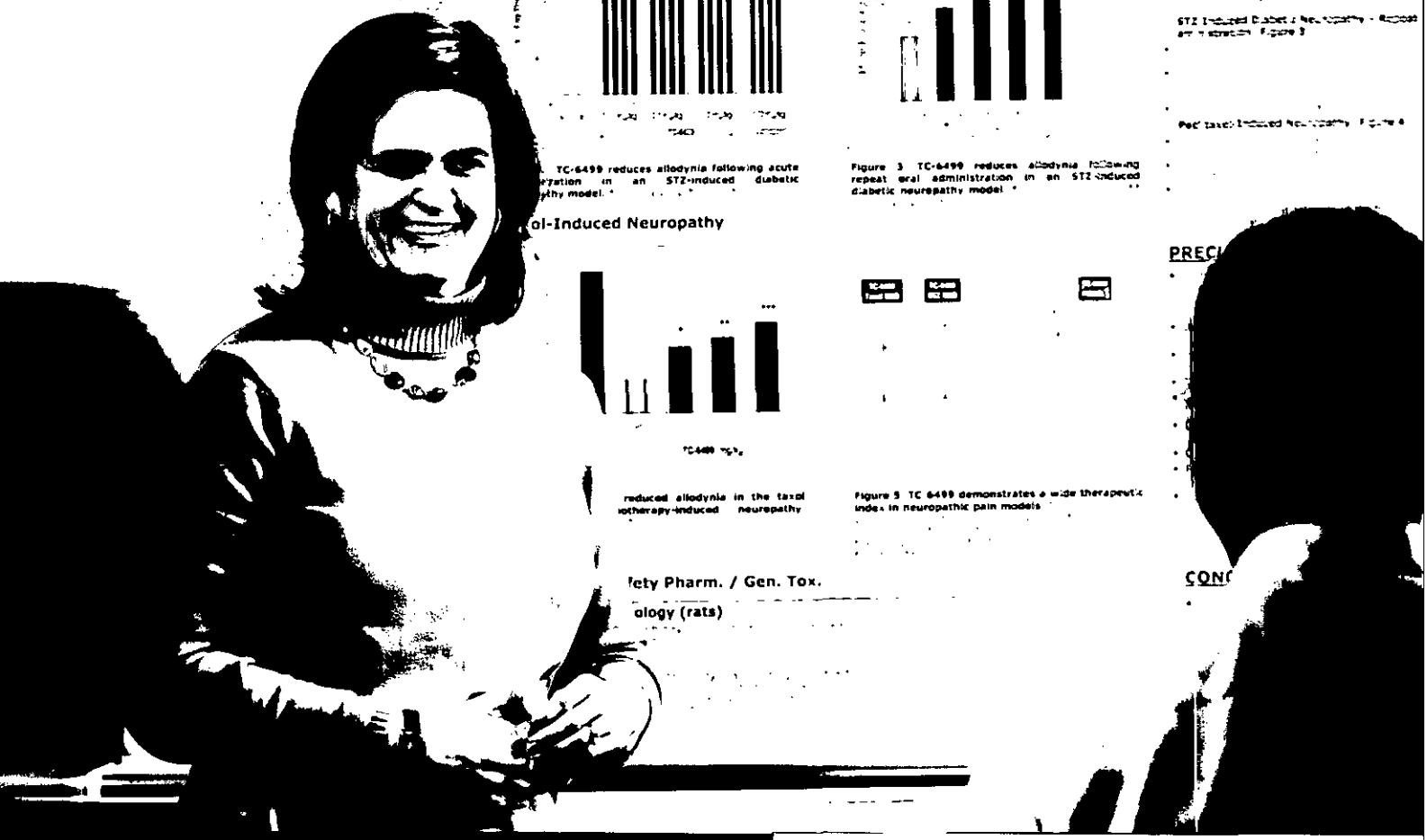
RONALD J. LUKAS, Ph.D.
Senior Staff Scientist and Director, Laboratory of Neurochemistry, Barrow Neurological Institute

The human brain is a fascinating entity that has intrigued scientists and scholars for centuries. Once thought to be a rigid collection of billions of "hard-wired" connections, the brain is now proving to be more malleable and capable of change than previously thought. This is an encouraging development for those who suffer from cognitive disorders, such as Alzheimer's disease, cognitive dysfunction in schizophrenia, and attention deficit disorder, as well as for those with other diseases and disorders of the central nervous system, such as depression and anxiety, pain and inflammation.

What is now Targacept began with a small team of researchers at R.J. Reynolds Tobacco Company in the mid 1980s. These scientists learned that neuronal nicotinic receptors (NNRs) play a key role in regulating nervous system activity and that compounds or drugs that modulate the activity of NNRs have the potential to remedy chemical imbalances in the brain associated with many different central nervous system diseases and disorders.

Over the years, Targacept scientists came to understand that the key to enhancing efficacy and limiting adverse effects lay in the development of drugs that would interact selectively with specific NNR subtypes.

In the past two decades, the momentum in the field of NNRs has continued to grow, with Targacept's leadership position reflected by its extensive patent estate



and more than 350 scientific publications and abstracts.

One of the things that most distinguishes Targacept from the rest of the field is its ability to design novel, NNR-targeted molecules with impressive efficiency. Using its proprietary Pentad drug discovery platform, Targacept is rationally developing molecules for specific NNR subtypes. This drives Targacept's deep portfolio of NNR-targeted compounds.

In the past several years, significant advances have been made in further unraveling the diversity of NNR subtypes in living systems and their relationship to health and disease.

The promise of NNR-based therapies has led many global pharmaceutical companies to invest significantly in this fertile and under-exploited area of drug development.

Targacept has been active in this field for years and has an unparalleled NNR-related patent estate.

PENTAD FUELS OUR PIPELINE

Industry-wide, the average time from idea to lead compound is 18-24 months. With Pentad, Targacept has been able to significantly reduce the front-end time for drug discovery to just 6-12 months.

Pentad also facilitates Targacept's unusually high "hit rate" in discovering compounds with the desired chemical activity. As a rule of thumb, random screening might be expected to yield only one active compound in 10,000 structures. By comparison, Targacept has achieved 40 times that success rate.

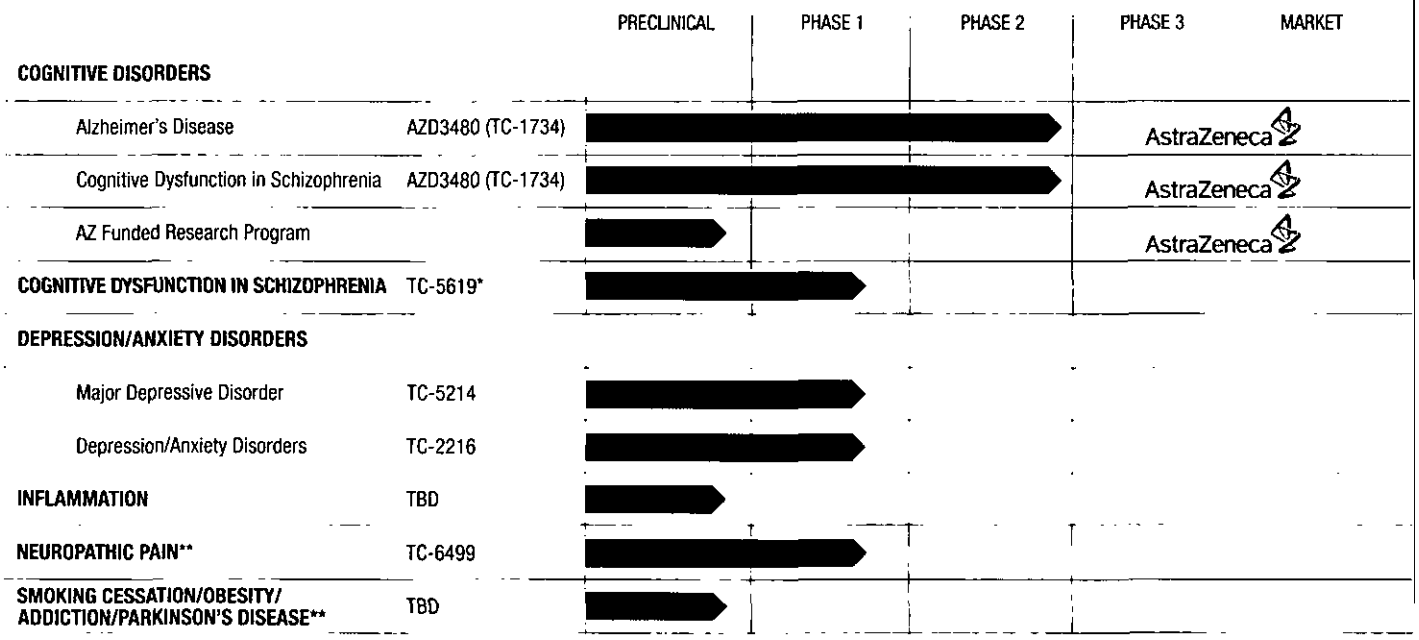
ADVANCING OUR PIPELINE

Targacept's contributions to the field of NNR-based science have been substantial and include a long list of scientific firsts, more than 150 peer-reviewed papers and over 200 abstracts. Targacept is actively applying its knowledge to the development of new NNR Therapeutics to improve the quality of life for patients and their families. Targacept seeks solutions to some of society's most critical medical issues, including Alzheimer's disease, cognitive dysfunction in schizophrenia, depression and anxiety, pain, and more.

"With the discovery of diverse receptor subtypes, there's more opportunity than ever to develop novel, effective nicotinic treatments with very low side effect profiles for a variety of disorders."

EDWARD LEVIN, Ph.D.
Professor of Psychiatry and Behavioral Sciences
Duke University Medical Center

In Targacept's process chemistry lab, a Targacept scientist assesses the crystallinity of a drug candidate, an important preparatory step for x-ray diffraction studies and the characterization of molecular structure.



* AstraZeneca has rights to obtain a global license at clinical proof of concept
** GlaxoSmithKline has rights to obtain a global license at clinical proof of concept

KEY PROGRAMS

COGNITIVE DISORDERS Alzheimer's disease strips away self-identity, robbing individuals of their ability to think clearly, concentrate and remember. Schizophrenia is a chronic, severe and disabling form of psychosis that impairs cognitive function, preventing patients from leading productive lives. Targacept's lead product candidate, AZD3480, activates the alpha4beta2 NNR and is in development for Alzheimer's disease, cognitive dysfunction in schizophrenia and potentially other cognitive disorders such as attention-deficit/hyperactivity disorder. TC-5619, the lead product candidate in Targacept's alpha7 NNR program, is also in development for cognitive dysfunction in schizophrenia and potentially other cognitive disorders.

DEPRESSION AND ANXIETY According to the National Institutes of Mental Health, there is no single cause of depression. It most likely results from a combination of factors, including biochemical disorders. TC-5214, which inhibits the activity of various NNR subtypes, entered Phase 1 development in March 2008 as an augmentation treatment for major depression. In preclinical studies, TC-5214 has exhibited a promising anti-depressant profile.

PAIN/OTHER NNRs hold great promise as therapeutic targets to address many diverse diseases and disorders, including smoking and other addictions, obesity, Parkinson's disease and inflammation. In addition, scientific evidence suggests that multiple NNRs may have potential applications for a broad range of pain states. TC-6499, a product candidate for neuropathic pain, is in Phase 1 development, and multiple compounds are in various stages of preclinical development in other programs.

PEOPLE

"The collective hearts and minds of our employees have created a winning culture at Targacept. We were delighted in 2007 to be recognized as a top ten employer by *The Scientist* magazine, which affirmed our strengths-based organization and exceptionally diverse and talented workforce. Fifteen different countries of national origin are represented and nearly half of our employees have a Ph.D. or M.D. degree. People who work at Targacept have an extraordinary opportunity to make a real difference in the lives of patients and their families. As a result, our employees embrace their work with creativity, focus and enthusiasm."

KAREN A. HICKS
Senior Director of Human Resources

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, DC 20549

FORM 10-K

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2007

or

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number: 000-51173

Targacept, Inc.

(Exact Name of Registrant as Specified in its Charter)

Delaware	**56-2020050**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification No.)**
200 East First Street, Suite 300 Winston-Salem, North Carolina	**27101**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant's telephone number, including area code: (336) 480-2100

Securities registered pursuant to Section 12(b) of the Exchange Act:

Title of each class	**Name of each exchange on which registered**
Common Stock, $0.001 par value per share	**The NASDAQ Stock Market LLC**

Securities registered pursuant to Section 12(g) of the Exchange Act: None

Indicate by check mark if the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. ☐ Yes ☒ No

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. ☐ Yes ☒ No

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark if disclosure of delinquent filers pursuant to Rule 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the registrant's knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, or a smaller reporting company. See the definitions of "large accelerated filer," "accelerated filer" and "smaller reporting company" in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ☐ Accelerated filer ☒ Non-accelerated filer ☐ (Do not check if a smaller reporting company) Smaller reporting company ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). ☐ Yes ☒ No

The aggregate market value of the registrant's common stock held by non-affiliates of the registrant as of June 30, 2007, was approximately $117,291,444, based on the price at which the registrant's common stock was last sold on June 29, 2007 ($9.15).

As of February 29, 2008, the registrant had 24,894,130 shares of common stock, $0.001 par value per share, outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant's proxy statement for its 2008 annual meeting of stockholders to be held on June 25, 2008, which is expected to be filed pursuant to Regulation 14A within 120 days after the end of the registrant's fiscal year ended December 31, 2007, are incorporated by reference into Part III of this report.

TARGACEPT, INC.

FORM 10-K
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Cautionary Note Regarding Forward-Looking Statements

This annual report includes forward-looking statements within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. For this purpose, any statements contained in this annual report regarding the progress, timing or scope of the research and development of our product candidates or related regulatory filings or clinical trials, any future payments that AstraZeneca or GlaxoSmithKline may make to us, our future operations, financial position, revenues, costs or expenses, or our strategies, prospects, plans, expectations or objectives, other than statements of historical fact, are forward-looking statements made under the provisions of The Private Securities Litigation Reform Act of 1995. In some cases, words such as "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "ongoing," "scheduled" or other comparable words identify forward-looking statements. Actual results, performance or experience may differ materially from those expressed or implied by forward-looking statements as a result of various important factors, including our critical accounting policies and risks and uncertainties relating to: our dependence on the success of our collaboration with AstraZeneca and our alliance with GlaxoSmithKline; the amount and timing of resources that AstraZeneca devotes to the development of AZD3480 (TC-1734); our ability to perform the research planned and budgeted for our preclinical research collaboration with AstraZeneca; AstraZeneca's right to terminate the preclinical research collaboration prior to the end of the planned four-year term; our ability to discover and develop product candidates under our alliance with GlaxoSmithKline; the results of clinical trials and non-clinical studies and assessments with respect to our current and future product candidates in development; the conduct of such trials, studies and assessments, including the performance of third parties that we engage to execute them and difficulties or delays in the completion of subject enrollment or data analysis; the timing and success of submission, acceptance and approval of regulatory filings; our ability to obtain substantial additional funding; our ability to establish additional strategic alliances and collaborations; and our ability to obtain, maintain and enforce patent and other intellectual property protection for our product candidates and discoveries. These and other risks and uncertainties are described in more detail under the caption "Risk Factors" in Item 1A of Part I of this annual report and in other filings that we make with the Securities and Exchange Commission, or SEC. As a result of the risks and uncertainties, the results or events indicated by the forward-looking statements may not occur. We caution you not to place undue reliance on any forward-looking statement.

Any forward-looking statements in this annual report represent our views only as of the date of this annual report and should not be relied upon as representing our views as of any subsequent date. We anticipate that subsequent events and developments may cause our views to change. Although we may elect to update these forward-looking statements publicly at some point in the future, whether as a result of new information, future events or otherwise, we specifically disclaim any obligation to do so, except as required by applicable law. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

PART I

Item 1. Business.

Overview

We are a biopharmaceutical company engaged in the design, discovery and development of NNR Therapeutics™, a new class of drugs for the treatment of multiple diseases and disorders of the central nervous system. Our NNR Therapeutics selectively target neuronal nicotinic receptors, or NNRs. NNRs are found on nerve cells throughout the nervous system and serve as key regulators of nervous system activity.

We trace our scientific lineage to a research program initiated by R.J. Reynolds Tobacco Company in 1982 to study the activity and effects of nicotine, a compound that interacts non-selectively with all nicotinic receptors. Based on years of focused research in the NNR area, we believe that compounds that interact selectively with specific NNR subtypes have the potential to achieve positive medical effects by modulating their activity. We have built an extensive patent estate covering the structure or therapeutic use of small molecules designed to regulate the central nervous system by selectively affecting specific NNR subtypes.

We currently have clinical-stage product candidates for target indications generally in three therapeutic areas: cognitive impairment, depression and anxiety, and pain. We also have preclinical programs focused in smoking cessation, addiction, obesity, pain, Parkinson's disease and inflammation. We have a collaboration with AstraZeneca and a strategic alliance with GlaxoSmithKline.

Cognitive Impairment and AstraZeneca Collaboration

AZD3480 (TC-1734). Our lead product candidate is a novel small molecule that we have historically referred to as TC-1734 and that our strategic collaborator, AstraZeneca, refers to as AZD3480. AZD3480 (TC-1734) modulates the activity of the α4ß2 NNR. We have a collaborative research and license agreement with AstraZeneca AB for the development and worldwide commercialization of AZD3480 (TC-1734) as a treatment for Alzheimer's disease, cognitive dysfunction in schizophrenia and potentially other conditions characterized by cognitive impairment such as attention deficit hyperactivity disorder, commonly referred to as ADHD, age associated memory impairment, commonly referred to as AAMI, and mild cognitive impairment, commonly referred to as MCI. AstraZeneca is currently conducting two Phase 2b clinical trials of AZD3480 (TC-1734), one in mild to moderate Alzheimer's disease and one in cognitive dysfunction in schizophrenia. Based on information provided to us by AstraZeneca, we expect that both trials will be completed by the end of 2008. If AZD3480 (TC-1734) achieves clinical proof of concept in either Alzheimer's disease or cognitive dysfunction in schizophrenia, or if AstraZeneca initiates a Phase 3 clinical trial of AZD3480 (TC-1734) in either Alzheimer's disease or cognitive dysfunction in schizophrenia, AstraZeneca has agreed in our agreement to pursue the development of AZD3480 (TC-1734) as a treatment for ADHD.

In addition, we and AstraZeneca are currently considering a single site Phase 2 clinical trial of AZD3480 (TC-1734) in adults with ADHD that would potentially be initiated in mid-2008, prior to completion of AstraZeneca's ongoing Phase 2 trials. If we and AstraZeneca proceed with the adult ADHD trial, we expect that AstraZeneca would provide clinical trial material and we would provide funding for the trial.

Our agreement with AstraZeneca became effective in January 2006. AstraZeneca paid us an initial fee of $10 million in February 2006 and an additional $20 million in January 2007 as a result of its December 2006 determination to proceed with further development of AZD3480 (TC-1734). Under the agreement, we are eligible to receive other payments of up to $249 million, contingent upon the achievement of development, regulatory and first commercial sale milestones for AZD3480 (TC-1734) for Alzheimer's disease, cognitive dysfunction in schizophrenia and ADHD, and stepped double-digit royalties on any future product sales. If AZD3480 (TC-1734) is developed under the agreement for other indications characterized by cognitive impairment, we would also be eligible to receive payments contingent upon the achievement of development, regulatory and first

commercial sale milestones for AZD3480 (TC-1734) for those indications. AstraZeneca is responsible for the commercialization of AZD3480 (TC-1734) and any compounds that arise out of the α4ß2 NNR research collaboration described below that it elects to advance. We have the option to co-promote AZD3480 (TC-1734) and any other compounds arising out of the research collaboration that are selected for advancement to specified classes of specialist physicians in the United States.

We and AstraZeneca are conducting a preclinical research collaboration under the agreement that is designed to discover and develop additional compounds that, like AZD3480 (TC-1734), act on the α4ß2 NNR as treatments for conditions characterized by cognitive impairment. AstraZeneca is responsible for funding the research collaboration, which began in January 2006 and has a planned term of four years.

TC-5619. TC-5619 is a novel small molecule that we plan to develop for cognitive dysfunction in schizophrenia and potentially one or more other conditions characterized by cognitive impairment. TC-5619 modulates the activity of the α7 NNR. We are currently conducting a Phase 1 single rising dose clinical trial of TC-5619 and plan to initiate a Phase 1 multiple rising dose clinical trial of TC-5619 in the second quarter of 2008. In a single rising dose trial, each subject in a dose group receives a single dose of the agent being evaluated, with subjects in each subsequent dose group receiving a pre-determined higher dosage than subjects in the preceding dose group. In a multiple rising dose clinical trial, each subject in a dose group receives a dosage of the agent being evaluated multiple times, with subjects in each subsequent dose group receiving a pre-determined higher dosage than subjects in the preceding dose group.

As a result of a process that we initiated under our agreement with AstraZeneca and a related election made by AstraZeneca in November 2007, we have agreed to develop TC-5619 independently through Phase 1 clinical development and a Phase 2 clinical proof of concept trial pursuant to an agreed development plan. Following our completion of the development plan, AstraZeneca has the right to license TC-5619 for any or all of schizophrenia and various conditions characterized by cognitive impairment on terms specified in the agreement. If TC-5619 achieves clinical proof of concept and AstraZeneca elects to license TC-5619, the agreement provides for AstraZeneca to make a $40 million payment to us and to assume responsibility for and fund all future development and commercialization. In that event, we would be eligible to receive additional payments of up to $226 million, contingent upon the achievement of development, regulatory and first commercial sale milestones, as well as stepped double-digit royalties on any future product sales. If TC-5619 does not achieve clinical proof of concept but AstraZeneca remains interested in a potential license, the agreement provides for us and AstraZeneca to negotiate terms.

Depression/Anxiety

TC-5214. TC-5214 is one of the two enantiomers of mecamylamine hydrochloride. Enantiomers are mirror images of each other that have the same chemical but potentially different biological properties and together form a chemical mixture known as a racemate. TC-5214 inhibits the activity of various NNR subtypes, including the α4ß2 NNR. We are currently developing TC-5214 as an augmentation treatment for major depression. We initiated a Phase 1 single rising dose clinical trial of TC-5214 in healthy volunteers in the first quarter of 2008.

In 2006, we completed a Phase 2 clinical trial of the racemate mecamylamine hydrochloride as an augmentation treatment to citalopram hydrobromide, a commonly prescribed treatment for depression marketed as Celexa in the United States, in patients who did not respond adequately to first-line treatment with citalopram. We refer to this treatment combination as TRIDMAC™. In our preclinical evaluation, TC-5214 has exhibited a more favorable overall safety and efficacy profile than mecamylamine. We have no current plans to conduct further clinical development of mecamylamine and intend instead to pursue the development of TC-5214.

Mecamylamine hydrochloride is the active ingredient in Inversine®, which is our only product approved by the U.S. Food and Drug Administration, or FDA, for marketing. Inversine is approved for the management of

moderately severe to severe essential hypertension and uncomplicated cases of malignant hypertension, which are high blood pressure disorders. However, we believe that Inversine is prescribed predominantly for the treatment of neuropsychiatric disorders, including Tourette's syndrome, autism and bipolar disorder.

TC-2216. Our depression and anxiety program also includes the novel small molecule TC-2216. TC-2216 inhibits the activity of the α4ß2 NNR. We completed a Phase 1 single rising dose clinical trial of this product candidate in healthy volunteers in the first quarter of 2008. TC-2216 is a racemate. We may in the future elect to develop one of the enantiomers of TC-2216 in lieu of further development of TC-2216. However, based on our anticipated development of TC-5214 and our current budget management plans, we do not expect that we will conduct further clinical development of TC-2216 or either of its enantiomers in 2008.

Pain

TC-6499. TC-6499 is a novel small molecule that we plan to develop as a treatment for neuropathic pain. TC-6499 modulates the activity of the α4ß2 NNR. We initiated a Phase 1 single rising dose clinical trial of TC-6499 in the fourth quarter of 2007. TC-6499 is subject to a contingent future option of GlaxoSmithKline under the terms of our alliance described below.

In addition to TC-6499, we had previously been developing another product candidate, TC-2696, as a treatment for acute post-operative pain. In December 2007, we announced that TC-2696 did not meet the primary endpoints in a Phase 2 clinical trial in third molar extraction patients. We have no current plans to conduct further development of TC-2696.

GlaxoSmithKline Alliance

In July 2007, we entered into a product development and commercialization agreement with SmithKline Beecham Corporation, doing business as GlaxoSmithKline, and Glaxo Group Limited, which are referred to collectively in this annual report as GlaxoSmithKline. The agreement sets forth the terms of an alliance designed to discover, develop and market product candidates that selectively target specified NNR subtypes in five therapeutic focus areas—pain, smoking cessation, addiction, obesity and Parkinson's disease.

Upon execution of the agreement, GlaxoSmithKline made payments to us of $35 million, which included a non-refundable initial payment of $20 million and the purchase of 1,275,502 shares of our common stock for an aggregate purchase price of $15 million pursuant to a stock purchase agreement between us and Glaxo Group Limited entered into in conjunction with the product development and commercialization agreement. We are also eligible to receive other payments of up to $1.5 billion, contingent on the achievement of specified discovery, development, regulatory and commercial milestones in the five therapeutic focus areas of the alliance, as well as stepped double-digit royalties on any future sales of products licensed by GlaxoSmithKline.

Under the agreement, we have agreed, for specified periods of time and at our sole expense, to use diligent efforts to conduct research activities designed to discover product candidates that target specified NNR subtypes, to develop the product candidate identified as the lead for each therapeutic focus area through a Phase 2 clinical proof of concept trial and to develop up to two other product candidates for each therapeutic focus area to a specified stage of preclinical development. With respect to each therapeutic focus area in the alliance, if we achieve clinical proof of concept with a lead product candidate, GlaxoSmithKline would have an exclusive option for an exclusive license to that lead product candidate and up to two other product candidates in development in the alliance for the same therapeutic focus area on a worldwide basis. If GlaxoSmithKline exercises its option and pays a non-refundable exercise fee, GlaxoSmithKline would become responsible for using diligent efforts to conduct later-stage development and commercialization of the lead product candidate at its sole expense. GlaxoSmithKline's exclusive license would include all fields of use other than those indications for which AstraZeneca has development and commercialization rights under our agreement with AstraZeneca described above.

Pentad™

Our drug discovery activities utilize sophisticated proprietary computer-based molecular design methodologies and extensive biological data for a library of diverse compounds developed and collected over more than 20 years. We refer to these technologies collectively as Pentad. We used Pentad to design or optimize AZD3480 (TC-1734), TC-5619, TC-2216 and TC-6499.

Role of NNRs in the Nervous System

The human nervous system is a massive communications network that sends and receives information throughout the body via billions of specialized nerve cells known as neurons. Neurons continually gather information about the body's internal and external environment and send signals to the brain. These signals pass from one neuron to another across a gap between a communicating neuron and a receiving neuron known as a synapse. Electrical impulses of a communicating neuron are converted into chemicals called neurotransmitters that are released by the communicating neuron and bind to specialized proteins known as receptors located across the synapse on the receiving neuron to enable the signal to continue. The major neurotransmitters in the brain include 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 modulate their activity have the potential to restore this balance and therefore promise as treatments for these diseases and disorders.

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.

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

Based on years of focused research in the NNR area, we are developing product candidates that are designed to interact selectively with specific NNR subtypes to promote positive medical effects and limit adverse side effects.

Our Business Strategy

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

- We believe that drugs designed to selectively target specific NNR subtypes can have positive medical effects with limited adverse side effects. We intend to continue to use our scientific expertise and Pentad to identify compounds that selectively target specific NNR subtypes as potential treatments for diseases and disorders of the central nervous system.
- We have a collaborative research and license agreement with AstraZeneca for the development and worldwide commercialization of AZD3480 (TC-1734) as a treatment for Alzheimer's disease, cognitive dysfunction in schizophrenia and potentially other conditions characterized by cognitive impairment. Under the agreement, we and AstraZeneca are conducting a preclinical research collaboration designed to discover and develop additional compounds that, like AZD3480 (TC-1734), act on the $\alpha 4\beta 2$ NNR as treatments for conditions characterized by cognitive impairment. We also have a product development and commercialization agreement with GlaxoSmithKline that sets forth the terms of an alliance designed to discover, develop and market product candidates that selectively target specified NNR subtypes in five therapeutic focus areas—pain, smoking cessation, addiction, obesity and Parkinson's disease. We intend to selectively seek additional alliances and collaborations 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 alliances and collaborations 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 alliances and collaborations, our goal will generally be to maintain co-promotion or co-commercialization rights in the United States and, in some cases, other markets. Under our agreement with AstraZeneca, we have the option to co-promote AZD3480 (TC-1734) and any compounds arising out of the research collaboration that are selected for advancement to specified classes of specialist physicians in the United States. Under our agreement with GlaxoSmithKline, if GlaxoSmithKline's option were to be triggered with respect to TC-6499 and exercised, we would retain an option to co-promote TC-6499 for pain to specialists and hospital-based physicians in the United States.
- We have established ourselves as a leader in NNR research over more than 20 years. Our leadership position in this area is reflected in the numerous NNR-related articles and abstracts published by our scientists in prominent scientific journals, as well as our extensive patent estate. We intend to continue to invest significant resources to remain at the forefront of NNR research, build upon our NNR expertise and expand our intellectual property portfolio. We also plan to augment our own research by collaborating with commercial and academic institutions that seek access to our proprietary knowledge and compounds.
- 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 potentially provide a medical benefit. We plan to prioritize our product development opportunities in an effort to apply our product pipeline to indications in which there is a significant medical need and commercial potential.
- We intend to maximize the value of our portfolio of product candidates by seeking generally to retain marketing rights to specialists, particularly in neurology and psychiatry, in any future alliances or collaborations that we enter into.

Our Product Development Pipeline

Our most advanced product candidates target indications generally in three therapeutic areas: cognitive impairment, depression and anxiety, and pain. The following table summarizes our product development pipeline.

Product Candidate	Target Indication(s)	Status of Development	Commercial Rights
AZD3480 (TC-1734)	Alzheimer's disease; cognitive dysfunction in schizophrenia	Two Phase 2b trials, one in mild to moderate Alzheimer's disease and one in cognitive dysfunction in schizophrenia, ongoing	AstraZeneca
TC-5619	Cognitive dysfunction in schizophrenia and one or more other conditions characterized by cognitive impairment	Phase 1 trial ongoing	subject to opt-in right of AstraZeneca*
TC-5214	Major depression (augmentation treatment)	Phase 1 trial ongoing	Targacept
TC-2216	Depression and anxiety disorders	Phase 1 single rising dose trial completed	Targacept
TC-6499	Neuropathic pain	Phase 1 trial ongoing	subject to opt-in right of GlaxoSmithKline**

* Following our completion of an agreed development plan through a Phase 2 clinical proof of concept trial, AstraZeneca has the right to license TC-5619 for any or all of schizophrenia and various conditions characterized by cognitive impairment on terms specified in our agreement.

** If TC-6499 achieves clinical proof of concept, GlaxoSmithKline would have an exclusive option for an exclusive license on a worldwide basis. GlaxoSmithKline's exclusive license would include all fields of use other than those indications for which AstraZeneca has development and commercialization rights under our agreement with AstraZeneca.

AstraZeneca is conducting its ongoing Phase 2b trial of AZD3480 (TC-1734) in mild to moderate Alzheimer's disease in Western Europe, Eastern Europe and Canada and its ongoing Phase 2b trial of AZD3480 (TC-1734) in cognitive dysfunction in schizophrenia in the United States and Canada. We are conducting our ongoing Phase 1 trial of TC-5214 in the United States. Each of our other ongoing Phase 1 trials is being conducted in Europe. We plan to initiate one or more additional Phase 1 clinical trials in the United States later in 2008.

Information regarding our research and development expenses for the fiscal years ended December 31, 2007, 2006 and 2005 is included under "Management's Discussion and Analysis of Financial Condition and Results of Operations" in this annual report.

Cognitive Impairment

AZD3480 (TC-1734)

AZD3480 (TC-1734) is a novel small molecule in development in collaboration with AstraZeneca as a treatment for Alzheimer's disease, cognitive dysfunction in schizophrenia and potentially other conditions

characterized by cognitive impairment, such as ADHD, AAMI and MCI. AZD3480 (TC-1734) modulates the activity of the α4ß2 NNR. AZD3480 (TC-1734) is currently being evaluated in two Phase 2b clinical trials conducted by AstraZeneca, one in mild to moderate Alzheimer's disease and one in cognitive dysfunction in schizophrenia. If AZD3480 (TC-1734) achieves clinical proof of concept in either Alzheimer's disease or cognitive dysfunction in schizophrenia, or if AstraZeneca initiates a Phase 3 clinical trial of AZD3480 (TC-1734) in either Alzheimer's disease or cognitive dysfunction in schizophrenia, AstraZeneca has agreed in our agreement to pursue the development of AZD3480 (TC-1734) as a treatment for ADHD.

In addition, we and AstraZeneca are currently considering a single site Phase 2 clinical trial of AZD3480 (TC-1734) in adults with ADHD that would potentially be initiated in mid-2008, prior to completion of AstraZeneca's ongoing Phase 2 trials. If we and AstraZeneca proceed with the adult ADHD trial, we expect that AstraZeneca would provide clinical trial material and we would provide funding for the trial.

We have previously evaluated AZD3480 (TC-1734) in two Phase 2 clinical trials in AAMI and a third Phase 2 clinical trial in MCI. We have also previously evaluated AZD3480 (TC-1734) in four Phase 1 clinical trials.

Clinical Development of AZD3480 (TC-1734)

Ongoing Phase 2b Clinical Trial in Mild to Moderate Alzheimer's Disease. AstraZeneca is currently conducting a double blind, placebo controlled Phase 2b clinical trial of AZD3480 (TC-1734) for the treatment of mild to moderate Alzheimer's disease. The trial, which is referred to as the "Sirocco" trial, is being conducted at sites in Western Europe, Eastern Europe and Canada. The current trial design provides for approximately 525 patients with mild to moderate Alzheimer's disease to be randomly assigned to one of three dose groups of AZD3480 (TC-1734), to the active control donepezil, or to placebo and to be dosed over a 12-week period. The dose groups of AZD3480 (TC-1734) range from a dose lower than we previously evaluated in our Phase 2 clinical trials of this product candidate to up to 100mg. The primary outcome measure of the trial is the Alzheimer's Disease Assessment Scale-cognitive subscale, or ADAS-Cog, the measure most often used to assess the efficacy of drugs for Alzheimer's disease. Some of the secondary measures include a clinician interview-based impression of change, or CIBIC, scale and a computer-based test battery developed by CDR Ltd. to test cognitive function. Based on information provided to us by AstraZeneca, we expect the trial to be completed by the end of 2008. AstraZeneca has significant control over trial design, as well as the conduct and timing of development efforts with respect to AZD3480 (TC-1734).

Ongoing Phase 2b Clinical Trial in Cognitive Dysfunction in Schizophrenia. AstraZeneca is also currently conducting a double blind, placebo controlled Phase 2b clinical trial of AZD3480 (TC-1734) for the treatment of cognitive dysfunction in schizophrenia. The trial, which is referred to as the "HALO" trial, is being conducted at sites in the United States and Canada. The current trial design provides for approximately 400 schizophrenic patients who are taking one of three commonly prescribed anti-psychotics, are active cigarette smokers and are clinically stable to be randomly assigned to one of three dose groups of AZD3480 (TC-1734) or to placebo and to be dosed, together with continued treatment with the applicable anti-psychotic, over a 12-week period. The dose groups of AZD3480 (TC-1734) range from a dose lower than we previously evaluated in our Phase 2 clinical trials of this product candidate to up to 100mg. The primary outcome measures of the trial are scores for attention/vigilance, working memory, verbal learning, speed of processing and verbal fluency as measured by a computerized test battery known as IntegNeuro that assesses several of the cognitive domains identified by a National Institute of Mental Health initiative known as Measurement and Treatment Research to Improve Cognition in Schizophrenia, or MATRICS. Some of the secondary measures include measures of life

functioning, such as performance in day-to-day tasks and social skills. Based on information provided to us by AstraZeneca, we expect the trial to be completed by the end of 2008. In parallel with the cognitive dysfunction in schizophrenia trial described above, AstraZeneca is also currently conducting multiple clinical trials designed to evaluate further the safety and pharmacology of AZD3480 (TC-1734). AstraZeneca has significant control over trial design, as well as the conduct and timing of development efforts with respect to AZD3480 (TC-1734).

Phase 2 Clinical Trial in AAMI Completed in 2006. In March 2006, we completed a placebo controlled Phase 2 clinical trial of AZD3480 (TC-1734) in AAMI. We conducted the trial at 16 sites in the United States. We recruited 193 subjects between the ages of 50 and 80, who were classified with AAMI based on inclusion criteria reflecting both subjective and objective memory impairment, to participate in the trial. The trial design provided for three dose groups—25mg of AZD3480 (TC-1734), 50mg of AZD3480 (TC-1734) and placebo. The trial was double blind, meaning that neither the subjects nor the clinical investigators knew during the trials which subjects were receiving AZD3480 (TC-1734) and which subjects were receiving placebo.

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

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

There were three co-primary efficacy endpoints for this trial, including:

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

The CDR test data are presented below on both a per protocol basis and an intent to treat basis. The per protocol dataset includes all subjects who were at least 80% compliant with the dosing regimen for the trial and completed the required cognitive function assessments at the end of the dosing period. The intent to treat data set includes all subjects who received at least one dose of trial medication (AZD3480 (TC-1734) or placebo) and completed at least one cognitive function assessment.

On both a per protocol basis and an intent to treat basis, subjects receiving AZD3480 (TC-1734) in the 50mg dose group showed improvement as compared to subjects dosed with placebo on all three co-primary efficacy endpoints. These results were statistically significant. Subjects receiving AZD3480 (TC-1734) in the 25mg dose group showed improvement as compared to subjects dosed with placebo on the power of attention endpoint. This result was statistically significant.

A clinical trial result is statistically significant if it is unlikely to have occurred by chance. The statistical significance of clinical trial results is determined by a widely used statistical method that establishes the p-value of the results. Under this method, a p-value of 0.05 or less generally represents statistical significance. If a p-value is above 0.05, the result is generally not statistically significant, or NS. The p-values for the primary endpoints for the AZD3480 (TC-1734) dose groups are set forth below.

Primary Endpoint	25mg AZD3480 (TC-1734)		50mg AZD3480 (TC-1734)	
	Per Protocol	*Intent to treat*	*Per Protocol*	*Intent to treat*
CDR— Power of Attention	0.023	0.025	0.010	0.014
CDR—Episodic Memory	NS	NS	0.030	0.029
Subject Global Impression	NS	NS	0.008	0.015

AZD3480 (TC-1734) was generally well tolerated in this trial as compared to placebo. We reported two serious adverse events experienced by subjects dosed with AZD3480 (TC-1734). One of these subjects was diagnosed with lung cancer after being assigned to a dose group. The principal investigator for the trial site for this subject described the event as not related to AZD3480 (TC-1734). The other subject was diagnosed with a myocardial infarction, commonly known as a heart attack, after being dosed for approximately 12 weeks. The principal investigator for the trial site for this subject described the event as possibly related to AZD3480 (TC-1734). Because of the age range of the subject population for this trial, the types of the two serious adverse events that we observed were not unexpected.

Previous Phase 2 Clinical Trials. Prior to the Phase 2 clinical trial of AZD3480 (TC-1734) described above, we completed two double blind, placebo controlled Phase 2 clinical trials of AZD3480 (TC-1734). One trial evaluated 71 persons at least 60 years of age classified with AAMI and the other trial evaluated 36 persons at least 60 years of age classified with MCI, in each case on a per protocol basis.

Both trials utilized a crossover design. This means that each subject initially received AZD3480 (TC-1734) or placebo for three weeks, then did not receive any trial medication for two weeks, and then received AZD3480 (TC-1734) or placebo (whichever the subject had not received initially) for three weeks. In the AAMI trial, we evaluated four doses—50mg, 100mg, 125mg and 150mg. In the MCI trial, we evaluated two doses—50mg and 100mg. Subjects were assessed for changes in cognitive function using the CDR test battery before dosing and at various time points after dosing on the first and last day of each dosing period.

In the 50mg, 100mg and 125mg arms of the AAMI trial, AZD3480 (TC-1734) was well tolerated, with no serious adverse events reported. In the 150mg dose group, three out of eight subjects treated with AZD3480 (TC-1734) experienced side effects such as headache, lightheadedness, dizziness and vomiting and dropped out of the trial.

The results of the AAMI trial were most favorable in the 50mg dose group. In that dose group, we observed statistically significant results in favor of AZD3480 (TC-1734) in four of the five CDR factors—power of attention, continuity of attention, episodic memory, and speed of memory. The results on the continuity of attention, episodic memory and speed of memory factors included only the first dosing period due to treatment-by-period interaction.

Treatment-by-period interaction refers to a situation where the initial dosing period may have had an effect on performance on one or more factors in the cognitive test battery in the second dosing period and is identified

by a statistical analysis of a dose group's performance on a particular test factor in the first dosing period versus the dose group's performance on that test factor in the second dosing period. In instances in which our statistical analysis indicated that a treatment-by-period interaction might have occurred for a particular dose group and a particular test factor, we have described in this report only the first dosing period for that dose group for that test factor. The effect of including only the first dosing period in the results described in this report for a particular dose group and a particular test factor is to reduce, by 50%, both the number of evaluated subjects in that dose group for that test factor that were dosed with AZD3480 (TC-1734) and the number of subjects in that dose group for that test factor that were dosed with placebo.

The positive effects that we observed in the 50mg dose group were less pronounced in the other dose groups. However, in each of the other dose groups, we observed a statistically significant result in favor of AZD3480 (TC-1734) on at least one of the CDR test factors at at least one of the time points evaluated.

To generate additional data related to the tolerability of AZD3480 (TC-1734), we also tested eight elderly persons who met the inclusion criteria at a dose of 150mg, after having eaten, using the same trial design. The results indicated that the 150mg dose of AZD3480 (TC-1734) was better tolerated in subjects who had eaten than in subjects who had not eaten. There were no serious adverse events in this dose group.

As in the AAMI trial, AZD3480 (TC-1734) was well tolerated in the MCI trial, with only one serious adverse event reported. A subject who had a history of an abnormally slow heart rate lost consciousness and was hospitalized approximately one-and-one-half weeks following the end of the dosing phase of the trial. We do not believe that this adverse event was related to AZD3480 (TC-1734). In the 100mg dose group of the trial, we observed a statistically significant result in favor of AZD3480 (TC-1734) on the episodic memory factor. The results in the 50mg dose group did not favor AZD3480 (TC-1734).

Phase 1 Clinical Trials. Prior to our Phase 2 clinical trials of AZD3480 (TC-1734), we had completed four Phase 1 clinical trials in a total of 84 healthy volunteers in which the compound was well tolerated. The trials included a single rising dose trial, a multiple rising dose trial, a trial designed to evaluate the compound's pharmacokinetic profile and a food interaction trial. We enrolled volunteers ranging in age from 18 to 45 in the single rising dose, multiple rising dose and food interaction trials and from 64 to 73 in the pharmacokinetic trial. Pharmacokinetics refers to a compound's absorption, distribution and metabolism in, and excretion from, the body.

Other AZD3480 (TC-1734) Development Studies. During 2006, AstraZeneca conducted various studies of AZD3480 (TC-1734) at its expense to generate further data with respect to AZD3480 (TC-1734), including:

- in vitro studies to assess whether AZD3480 (TC-1734), when administered at a therapeutically-relevant dose, activates a particular protein that can activate an enzyme known as CYP1A1;
- a clinical trial to characterize the cardiovascular effects of various doses of AZD3480 (TC-1734) in persons who break down and eliminate, or metabolize, AZD3480 (TC-1734) at varying rates;
- a single-dose study in dogs to further assess the cardiovascular effects of AZD3480 (TC-1734);
- a clinical trial to evaluate the interaction and combined effects of AZD3480 (TC-1734) with paroxetine, a known inhibitor of a key enzyme involved in the primary metabolic pathway of AZD3480 (TC-1734);
- in vitro and animal studies to further characterize the mechanism of action of AZD3480 (TC-1734); and
- a Phase 1 clinical trial in healthy volunteers of Japanese descent to support the potential future pursuit of regulatory approval of AZD3480 (TC-1734) in Japan.

TC-5619

TC-5619 is a novel small molecule that we plan to develop for cognitive dysfunction in schizophrenia and potentially one or more other conditions characterized by cognitive impairment. We are currently conducting a

Phase 1 single rising dose clinical trial of TC-5619 and plan to initiate a Phase 1 multiple rising dose clinical trial of TC-5619 in the second quarter of 2008.

TC-5619 modulates the activity of the α7 NNR. In a 2004 survey of 46 cognitive neuroscientists and neuropharmacologists conducted in connection with the MATRICS initiative, α7 was selected more often than any other target as the target of most interest in the development of treatments for cognitive dysfunction in schizophrenia.

In 2007, we initiated a process under our agreement with AstraZeneca pursuant to which we offered AstraZeneca the right to license TC-5619 for specified conditions characterized by cognitive impairment. As permitted by the agreement, AstraZeneca elected in November 2007 to allow us to develop TC-5619 independently through Phase 1 clinical development and a Phase 2 clinical proof of concept trial in accordance with an agreed development plan, following which AstraZeneca would have the right to license TC-5619 for any or all of schizophrenia and various conditions characterized by cognitive impairment on terms specified in the agreement. As a result, AstraZeneca made a $2 million payment to us in the fourth quarter of 2007. If TC-5619 achieves clinical proof of concept and AstraZeneca elects to license TC-5619, the agreement provides for AstraZeneca to make a $40 million payment to us and to assume responsibility for and fund all future development and commercialization. In that event, we would be eligible to receive additional payments of up to $226 million, contingent upon the achievement of development, regulatory and first commercial sale milestones, as well as stepped double-digit royalties on any future product sales. If TC-5619 does not achieve clinical proof of concept but AstraZeneca remains interested in a potential license, the agreement provides for us and AstraZeneca to negotiate terms. Under the agreement, we would not have been permitted to develop TC-5619 for specified conditions characterized by cognitive impairment without first offering AstraZeneca the right to license the product candidate.

Depression/Anxiety

TC-5214

TC-5214 is one of the two enantiomers of mecamylamine hydrochloride. TC-5214 inhibits the activity of various NNR subtypes, including the α4β2 NNR. We have licensed patent rights from the University of South Florida Research Foundation covering the pharmaceutical composition of TC-5214 and are currently developing TC-5214 as an augmentation treatment for major depression. We initiated a Phase 1 single rising dose clinical trial of TC-5214 in healthy volunteers in the first quarter of 2008. We plan to initiate a Phase 2 clinical trial of TC-5214 using a substantially similar trial design as we used in the Phase 2 trial of TRIDMAC described below later in 2008.

Completed Phase 2 Clinical Trial of Mecamylamine Hydrochloride

In 2006, we completed a Phase 2 clinical trial of the racemate mecamylamine hydrochloride as an augmentation treatment to citalopram hydrobromide, a commonly prescribed treatment for depression marketed as Celexa in the United States, in patients who did not respond adequately to first-line treatment with citalopram. We refer to this treatment combination as TRIDMAC. We conducted the Phase 2 trial at one site in the United States and eight sites in India. The trial design included two phases. In the first phase, 450 patients with a diagnosis of major depressive disorder were given open label citalopram over six weeks and evaluated based on improvement on two scales—the Hamilton Depression Rating Scale (HAM-D), a commonly used 17-item scale that evaluates depressed mood and other symptoms of depression and anxiety, and the Clinical Global Impression subscale for severity of illness (CGI-SI)—to determine the extent of any response. Patients whose score on the HAM-D scale was at least equal to 14 and whose score on the CGI-SI scale was at least equal to 4 were enrolled into the second phase of the trial. The second phase was double blind and placebo controlled. We dosed 184 patients in the second phase. In the second phase, patients received either mecamylamine or placebo, in each case together with continued citalopram therapy, for an additional eight weeks. The dose group that received mecamylamine together with continued citalopram therapy is referred to below as the TRIDMAC dose group. Patients in the TRIDMAC dose group initially received 5mg of mecamylamine daily, titrating potentially up to 10mg over the dosing period at the clinician's discretion based on tolerability and therapeutic response.

The primary endpoints of the trial were group mean change from baseline and achievement of remission, in each case as measured by HAM-D and compared to continued citalopram therapy plus placebo. Secondary outcome measures used in the trial included rating scales to assess symptoms of depression and anxiety, disability, irritability, global improvement or severity of illness. Data from the trial were evaluated on both an intent to treat and per protocol basis. With respect to the primary endpoints, the intent to treat population included 160 patients who received at least one dose of blinded study medication and were assessed using HAM-D at least once after determination of baseline. With respect to the secondary outcome measures, the intent to treat population included 184 patients who received at least one dose of blinded study medication and were assessed using the applicable measure at least once after determination of baseline. The per protocol population included 151 patients who were at least 80% compliant with the dosing regimen called for by the protocol and were assessed at the end of the dosing period.

The result on the group mean change endpoint was statistically significant in favor of TRIDMAC on an intent to treat basis, with a p-value of 0.041, and showed a strong trend, but not statistical significance, on a per protocol basis (p-value of 0.059). The result on the achievement of remission endpoint favored the TRIDMAC group over the placebo group in both the intent to treat and per protocol populations, although these results were not statistically significant. With respect to the secondary outcome measures, the results on all five rating scales favored the TRIDMAC group over the placebo group on a per protocol basis. Each of these results was statistically significant, with a p-value of less than 0.05. On an intent to treat basis, the results on the rating scales assessing disability, irritability and severity of illness were statistically significant, with p-values less than 0.05.

TRIDMAC was generally well tolerated in the trial. There was one serious adverse event reported in each of the TRIDMAC and placebo groups. In the TRIDMAC group, a patient experienced an upper respiratory tract infection and irregular heartbeat and discontinued participation in the trial.

In our preclinical evaluation, TC-5214 has exhibited a more favorable overall safety and efficacy profile than mecamylamine. We have no current plans to conduct further clinical development of mecamylamine and intend instead to pursue the development of TC-5214.

TC-2216

Depression and anxiety disorders often occur together, and anti-depressants are often also used to treat anxiety disorders. Our depression and anxiety program also includes the novel small molecule TC-2216. TC-2216 inhibits the activity of the $\alpha 4\beta 2$ NNR. We completed a Phase 1 single rising dose clinical trial of this product candidate in healthy volunteers in the first quarter of 2008. TC-2216 is a racemate. We may in the future elect to develop one of the enantiomers of TC-2216 in lieu of further development of TC-2216. However, based on our anticipated development of TC-5214 and our current budget management plans, we do not expect that we will conduct further clinical development of TC-2216 or either of its enantiomers in 2008.

Pain

TC-6499

TC-6499 is a novel small molecule that we plan to develop as a treatment for neuropathic pain. TC-6499 modulates the activity of the $\alpha 4\beta 2$ NNR. We initiated a Phase 1 single rising dose clinical trial of TC-6499 in the fourth quarter of 2007. In our preclinical animal studies, TC-6499 demonstrated pain-relieving activity in multiple models of neuropathic pain. TC-6499 is subject to a contingent future option of GlaxoSmithKline under the terms of our alliance.

TC-2696

In December 2007, we announced results of a Phase 2 clinical trial of our product candidate TC-2696, which was originally subject to our alliance with GlaxoSmithKline. In the trial, 181 patients received a single

dose of one of three doses of TC-2696 or ibuprofen or placebo following third molar extraction surgery. TC-2696 did not meet the primary endpoints, superior pain relief four or six hours after dosing as compared to placebo. GlaxoSmithKline subsequently notified us that it had determined not to make the payment required under our agreement in order to maintain its contingent future option to TC-2696. As a result, under the terms of the agreement, TC-2696 is no longer subject to an option of GlaxoSmithKline. We have no current plans to conduct further development of TC-2696.

Our Preclinical Research Programs

We focus our preclinical research efforts in areas in which we believe NNRs can be exploited for medical benefit and on indications for which we believe we can efficiently develop marketable product candidates. We are conducting a preclinical research collaboration with AstraZeneca to discover and develop additional compounds that act on the α4ß2 NNR as treatments for conditions characterized by cognitive impairment. We also have preclinical research programs in smoking cessation, addiction, obesity, pain and Parkinson's disease, which are therapeutic focus areas of our agreement with GlaxoSmithKline. In addition, we have a program focused on the role of NNRs in inflammation.

Smoking Cessation

Due primarily to nicotine's addictive effects, it is very difficult to quit smoking. Published 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 NNRs implicated in the regulation of dopamine are not fully characterized, several reported studies suggest that the α6, α4, ß2 and ß4 NNR subunits may be involved. These studies have shown that selectively modulating α6, α4 or ß4 reduced the rewarding effects of nicotine in mice. Other studies have shown that mice deficient in the ß2 NNR failed to self-administer 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. In addition, we are a named subcontractor on a grant awarded by the National Institute on Drug Abuse, part of the National Institutes of Health, to The California Institute of Technology to fund research on innovative NNR-based approaches to the development of therapies for smoking cessation. In addition to The California Institute of Technology, we are collaborating with University of Colorado at Boulder to conduct this research.

Addiction

There is also a need for more effective treatments to help addicts reduce or eliminate their intake of other drugs of abuse besides nicotine. Although other drugs of abuse may activate different targets in the brain than nicotine, they act generally by increasing levels of dopamine. The dopamine system is thought to be the common pathway by which these drugs produce feelings of pleasure and reward. As described above, compounds that modulate NNRs may have the potential to decrease the rewarding effects of drugs of abuse such as alcohol and cocaine.

Obesity

The incidence of obesity has grown substantially in recent years. A number of published studies have demonstrated that smokers generally weigh significantly less than non-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 nicotine administration is stopped. A number of NNRs are thought to play a role in appetite and metabolism.

Pain

Pain is a common endpoint for many different conditions, injuries and disease states. Pain can be short-term or persistent and nociceptive or neuropathic in nature. Multiple NNR subunits are found in pain pathways.

Scientific evidence suggests that multiple NNRs, particularly the $\alpha4\beta2$ and $\alpha7$ NNRs, may have potential therapeutic application for a broad range of pain states.

Parkinson's disease

Parkinson's disease is a movement disorder associated with a deficit in dopamine in the brain resulting from a progressive deterioration and death of cells in the brain, which is known as neurodegeneration. As noted above, several reported studies suggest that the $\alpha6$, $\alpha4$, ß2 and ß4 NNR subunits may be involved in regulating dopamine release. As a result, NNRs that contain one or more of these subunits may have promise as therapeutic targets for the treatment of Parkinson's disease. Moreover, the existence of many published studies showing the greater prevalence of Parkinson's disease in non-smokers as compared to smokers further suggests the potential application of compounds that interact with NNRs as treatments for Parkinson's disease.

Inflammation

Published studies suggest that nicotine, acting upon specific NNRs, may modulate the inflammatory response and support the targeting of NNRs in the development treatments for inflammatory disorders. In addition, compounds that act selectively on the $\alpha7$ NNR have been shown to be active in various preclinical models of inflammatory activity.

Our Drug Discovery Technologies—Pentad

Our drug discovery activities utilize sophisticated proprietary computer-based molecular design methodologies and extensive biological data from a library of diverse compounds developed and collected over more than 20 years. We refer to these technologies collectively as Pentad. We use 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's virtual screening facilitates more rapid identification of compounds that may be clinically viable 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 to have a greater likelihood of clinical success. We used Pentad to design or optimize AZD3480 (TC-1734), TC-5619, TC-2216 and TC-6499.

Inversine

Mecamylamine hydrochloride is the active ingredient in Inversine, which is currently our only approved product. Inversine is approved in the United States for the management of moderately severe to severe essential hypertension and uncomplicated cases of malignant hypertension, which are high blood pressure disorders. We believe that Inversine is prescribed predominantly for the treatment of neuropsychiatric disorders, including Tourette's syndrome, autism and bipolar disorder, in children and adolescents at a lower dose than is used for hypertension. Inversine has been approved for marketing since the 1950s. We acquired marketing rights to the product in August 2002 from Layton Bioscience, Inc., which had previously acquired the rights from Merck & Co., Inc. In connection with our acquisition, we assumed Layton's obligations under the agreement pursuant to which Layton acquired the rights from Merck. Pursuant to that agreement, we pay Merck an amount each year based on annual sales of Inversine, subject to a specified annual maximum. Our annual payment obligation to Merck expires in 2010. Sales of Inversine generated net revenues of $518,000 for the year ended December 31, 2007, $585,000 for the year ended December 31, 2006, and $681,000 for the year ended December 31, 2005.

Strategic Alliances and Collaborations

AstraZeneca AB

In December 2005, we entered into a collaborative research and license agreement with AstraZeneca AB under which we granted AstraZeneca exclusive development and worldwide commercialization rights to AZD3480 (TC-1734) as a treatment for specified indications. The agreement became effective in January 2006. Under the agreement, AstraZeneca is currently developing AZD3480 (TC-1734) as a treatment for Alzheimer's disease and cognitive dysfunction in schizophrenia. If AZD3480 (TC-1734) achieves clinical proof of concept in either Alzheimer's disease or cognitive dysfunction in schizophrenia, or if AstraZeneca initiates a Phase 3 clinical trial of AZD3480 (TC-1734) in either Alzheimer's disease or cognitive dysfunction in schizophrenia, AstraZeneca has agreed under the agreement to pursue development of AZD3480 (TC-1734) as a treatment for ADHD. In addition, AstraZeneca can develop and commercialize AZD3480 (TC-1734) for AAMI, MCI, any other indication that is deemed a cognitive disorder under the agreement and schizophrenia. We and AstraZeneca are also conducting a preclinical research collaboration under the agreement.

As a result of a process that we initiated under the agreement and a related election made by AstraZeneca in November 2007, TC-5619 is also subject to the agreement. We have agreed to develop TC-5619 independently through Phase 1 clinical development and a Phase 2 clinical proof of concept trial pursuant to an agreed development plan. Following our completion of the development plan, AstraZeneca has the right to license TC-5619 for any or all of schizophrenia and various conditions characterized by cognitive impairment on terms specified in the agreement.

Payment Terms. AstraZeneca paid us an initial fee of $10 million in February 2006 and an additional $20 million in January 2007 as a result of its December 2006 determination to proceed with further development of AZD3480 (TC-1734). We are eligible to receive other payments of up to $249 million, contingent upon the achievement of development, regulatory and first commercial sale milestones for AZD3480 (TC-1734) for Alzheimer's disease, cognitive dysfunction in schizophrenia and ADHD, and stepped double-digit royalties on any future AZD3480 (TC-1734) product sales. If AZD3480 (TC-1734) is developed under the agreement for an indication in addition to Alzheimer's disease, cognitive dysfunction in schizophrenia and ADHD, we would also be eligible to receive payments of up to $52 million, contingent upon the achievement of development, regulatory and first commercial sale milestones for AZD3480 (TC-1734) for each such indication. Under the terms of a sponsored research agreement and subsequent license agreement, we are required to pay the University of Kentucky Research Foundation a low single digit percentage of any of these payments, including royalties, that we receive from AstraZeneca relating to AZD3480 (TC-1734).

If TC-5619 achieves clinical proof of concept and AstraZeneca elects to license TC-5619, the agreement provides for AstraZeneca to make a $40 million payment to us and, in that event, we would be eligible to receive additional payments of up to $226 million, contingent upon the achievement of development, regulatory and first commercial sale milestones, as well as stepped double-digit royalties on any future product sales. If TC-5619 does not achieve clinical proof of concept but AstraZeneca remains interested in a potential license, the agreement provides for us and AstraZeneca to negotiate terms.

AstraZeneca's obligation to pay royalties to us for each compound subject to the collaboration expires on a country-by-country basis on the later of expiration of our patent rights that provide exclusivity for that compound in that country or twelve years after the first commercial sale in that country of either that compound or any related compound that meets specified criteria. If AstraZeneca obtains a patent covering the composition of a compound that is derived within a specified period from a compound that is subject to the collaboration, the term of AstraZeneca's patent would also be taken into account in determining the term of AstraZeneca's obligation to pay royalties to us for that derived compound. The U.S. patent rights to AZD3480 (TC-1734) expire between 2016 and 2018. We also have a pending U.S. patent application with respect to the particular salt form of AZD3480 (TC-1734) currently being developed that, if issued, would expire in 2025. The foreign patent rights corresponding to our issued U.S. patent rights expire between 2017 and 2019. We also have pending foreign

patent applications that, if issued, would expire between 2017 and 2025. The U.S. patent rights to the chemical genus that includes TC-5619 expire in 2019. We also have a pending U.S. patent application with respect to TC-5619 specifically and to a particular salt form of TC-5619 that, if issued, would expire in 2028. The foreign patent rights corresponding to our issued U.S. patent rights expire in 2024. Royalty rates are subject to reduction under the agreement in specified circumstances, including in any country if the licensed compound is no longer subject to adequate patent protection in that country or if AstraZeneca licenses patent rights from any third party under circumstances in which the product that we license to AstraZeneca might infringe the third party's patent rights.

Research Collaboration and Fees. The agreement provides for a research collaboration, which began in January 2006 and under which we and AstraZeneca are conducting research designed to discover and develop additional compounds that, like AZD3480 (TC-1734), act on the α4ß2 NNR as treatments for conditions characterized by cognitive impairment. Under the agreement, AstraZeneca has agreed to pay us research fees based on an agreed reimbursement rate for research services rendered by us in the collaboration, subject to specified limits. AstraZeneca has the right to exclusively license a specified number of these compounds, together with metabolites of these compounds and derivatives and other compounds related to these compounds that meet specified criteria for the same indications for which AstraZeneca has development and commercialization rights for AZD3480 (TC-1734). Under the agreement, we are eligible to receive additional payments of up to $145 million, contingent upon the achievement of development, regulatory and first commercial sale milestones for each compound discovered and developed as part of the research collaboration, and stepped royalties on any future product sales. The initial term of the research collaboration is four years and can be extended by mutual agreement. AstraZeneca can terminate the research collaboration effective three years after the research term began upon at least six months notice.

Development and Commercialization Costs. AstraZeneca is responsible for the clinical development and commercialization of AZD3480 (TC-1734) and any compounds that arise out of the research collaboration that it elects to advance and for substantially all development costs, except for costs that we incurred to complete the Phase 2 clinical trial of AZD3480 (TC-1734) in AAMI that we completed in March 2006 and costs associated with any work outside of the planned development programs that we agree to conduct. We have the option to co-promote AZD3480 (TC-1734) and any compounds that arise out of the research collaboration that are selected for advancement to specified classes of specialist physicians in the United States. If we exercise our co-promotion option, AstraZeneca is required to provide training to our sales force and compensate us for our detailing efforts following regulatory approval. If, following our completion of Phase 1 clinical development and a Phase 2 clinical proof of concept trial of TC-5619, AstraZeneca elects to license rights to TC-5619, AstraZeneca would assume responsibility for and fund all future development and commercialization.

Exclusivity Rights and Restrictions. Neither we nor AstraZeneca are permitted outside of the collaboration to develop or commercialize compounds that act on the α4ß2 NNR and meet pre-defined criteria for Alzheimer's disease, cognitive dysfunction in schizophrenia, other conditions characterized by cognitive impairment, schizophrenia or any indication for which AstraZeneca has development and commercialization rights under the agreement. This restriction on AstraZeneca lapses 30 months (or, if the research term is terminated by AstraZeneca prior to completion of the planned four-year term, 12 months) after the end of the research term. This restriction on us will lapse if AstraZeneca commences clinical development outside of the collaboration for a compound that acts on the α4ß2 NNR and meets pre-defined criteria.

We are entitled to offer to AstraZeneca the right to develop and commercialize any compound that acts on any NNR other than α4ß2 for any indication for which AstraZeneca has development and commercialization rights under the agreement. As an example, we made such an offer with respect to TC-5619, which led to AstraZeneca's future right to license TC-5619. If we do not offer this right to AstraZeneca for a compound that acts on any NNR other than the α4ß2 NNR, we are generally not permitted to develop or commercialize the compound for any indication for which AstraZeneca has development and commercialization rights under the agreement.

If we offer a compound to AstraZeneca, AstraZeneca could license the compound from us, together with metabolites of the compound and derivatives and other compounds related to the compound that meet specified criteria, on terms specified in the agreement. Alternatively, as in the case of TC-5619, AstraZeneca could negotiate a development plan with us pursuant to which we would conduct development intended to provide a pre-defined indication of efficacy. AstraZeneca could license the compound from us after we complete the additional development. For each compound licensed by AstraZeneca through this process, we are eligible to receive an exercise fee and other payments contingent upon the achievement of development, regulatory and first commercial sale milestones, as well as stepped royalties on any future product sales. If AstraZeneca elects not to license the compound, we are permitted to develop and commercialize the compound for any indication, except that, if we had offered the compound to AstraZeneca for schizophrenia, we will not be able to develop or commercialize the compound for any cognitive disorder. The agreement limits the number of compounds that we are permitted to offer to AstraZeneca through this process. We are generally not permitted to develop or commercialize compounds that act on any NNR for any indication for which AstraZeneca has development and commercialization rights under the agreement except through this process.

We are also entitled to offer to AstraZeneca the right to develop and commercialize (1) any compound for which AstraZeneca has development and commercialization rights for specified indications under the agreement or (2) any other compound that meets pre-defined criteria for cognitive activity, is in the same chemical family and acts on the same NNR or NNRs as any compound for which AstraZeneca has development and commercialization rights for specified indications under the agreement for any indication for which AstraZeneca does not have development and commercialization rights under the agreement. If we do not offer this right to AstraZeneca, we are not permitted to develop or commercialize the compound.

If AstraZeneca commences clinical development outside of the collaboration of a compound that acts on any NNR other than the $\alpha 7$ NNR and meets other pre-defined criteria, the restriction on our right to develop and commercialize compounds that act on any NNR, other than the $\alpha 4\beta 2$ NNR, for any indication for which AstraZeneca has development and commercialization rights under the agreement will lapse.

If we seek a strategic collaborator to develop or commercialize compounds that act by binding to NNRs for depression, anxiety or bipolar disorder, AstraZeneca may under certain circumstances have a right of first negotiation with us. If AstraZeneca is interested in such a collaboration but we and AstraZeneca do not agree on terms on which we would collaborate, for the following three years we would only be permitted to enter into a collaboration for the applicable compounds and indications on more favorable terms than the terms offered by AstraZeneca.

Termination. AstraZeneca can terminate the agreement without cause upon 90 days notice given any time after the earlier of the end of the research term or four years after the research term began. Either we or AstraZeneca can terminate the agreement in the event of the bankruptcy or uncured material breach of the other party. However, if a breach by AstraZeneca is limited to any specific compound or specified key market, we can terminate the agreement only with respect to that compound or key market. If a competitor of AstraZeneca acquires control of us, AstraZeneca can terminate the agreement or specified provisions of the agreement, including our right to participate on the committee overseeing development under the agreement and our co-promotion rights.

GlaxoSmithKline

On July 27, 2007, we entered into a product development and commercialization agreement with GlaxoSmithKline that sets forth the terms of an alliance designed to discover, develop and market product candidates that selectively target specified NNR subtypes in five therapeutic focus areas—pain, smoking cessation, addiction, obesity and Parkinson's disease. Our product candidate TC-6499, our neuropathic pain candidate currently in Phase 1 clinical development, is subject to the alliance. GlaxoSmithKline is participating in the alliance through its Center of Excellence for External Drug Discovery, or CEEDD.

Research and Early Development. Under the agreement, we have agreed, for specified periods of time and at our sole expense, to use diligent efforts to conduct research activities designed to discover product candidates that target specified NNR subtypes, to develop the product candidate identified as the lead for each therapeutic focus area through a Phase 2 clinical proof of concept trial and to develop up to two other product candidates for each therapeutic focus area to a specified stage of preclinical development. We are eligible to receive success-based milestone payments from GlaxoSmithKline if we successfully advance product candidates in each therapeutic focus area through preclinical and clinical development. Our research and development activities in the alliance are being overseen by a joint steering committee comprised of representatives of both us and GlaxoSmithKline.

Options; Later-Stage Development and Commercialization. With respect to each therapeutic focus area in the alliance, if we achieve clinical proof of concept with a lead product candidate, GlaxoSmithKline would have an exclusive option for an exclusive license to that lead product candidate and up to two other product candidates in development in the alliance for the same therapeutic focus area on a worldwide basis. If GlaxoSmithKline exercises its option and pays a non-refundable exercise fee, GlaxoSmithKline would become responsible for using diligent efforts to conduct later-stage development and commercialization of the lead product candidate at its sole expense. GlaxoSmithKline's exclusive license would include all fields of use other than those indications for which AstraZeneca has development and commercialization rights under our agreement with AstraZeneca.

If GlaxoSmithKline's option were to be triggered with respect to TC-6499 and exercised, we would retain an option to co-promote TC-6499 for pain to specialists and hospital-based physicians in the United States.

Payment Terms. Upon execution of the agreement, GlaxoSmithKline made payments to us of $35 million, which included a non-refundable initial payment of $20 million and the purchase of 1,275,502 shares of our common stock for an aggregate purchase price of $15 million pursuant to a stock purchase agreement between us and Glaxo Group Limited entered into in conjunction with the product development and commercialization agreement. We are also eligible to receive other payments of up to $1.5 billion, contingent on the achievement of specified discovery, development, regulatory and commercial milestones in five therapeutic focus areas of the alliance, as well as stepped double-digit royalties on any sales achieved for products licensed by GlaxoSmithKline.

With respect to each product licensed from us by GlaxoSmithKline that, at the time of first commercial sale in a particular country, is covered by an issued Targacept patent with adequate scope under the agreement, GlaxoSmithKline's royalty obligation with respect to sales of the product in the country generally would terminate upon the later of the expiration of the last Targacept patent with adequate scope or fifteen years after the first commercial sale of the product in the country. The royalty rate payable to us would be subject to reduction in specified circumstances under the agreement, including in any country if the product is no longer covered by a patent with adequate scope under the agreement in that country or if GlaxoSmithKline licenses patent rights from any third party in circumstances in which such license is reasonably considered necessary to avoid the infringement of the third-party patent rights.

Exclusivity. We have agreed that, with respect to each of the therapeutic focus areas of the alliance, for so long as we are required under the agreement to conduct research activities in the therapeutic focus area or for so long thereafter as there are any product candidates in development or being commercialized in the alliance in the therapeutic focus area, we will work in the therapeutic focus area exclusively with GlaxoSmithKline with respect to product candidates with NNR-derived activity. We have also agreed to work exclusively with GlaxoSmithKline with respect to product candidates that target the NNR subtypes specified for each therapeutic focus area under the agreement and with respect to product candidates with substantially the same mechanism of action, as defined in the agreement, as product candidates being developed or commercialized in the alliance, in each case for a specified period of time. Some or all of our exclusivity obligations would expire if GlaxoSmithKline were to in-license from a third party a product candidate with NNR-derived activity for a therapeutic focus area of the alliance. GlaxoSmithKline has agreed for a specified period of time not to conduct internal activities for any of the alliance's therapeutic focus areas with respect to product candidates that target the NNR subtypes specified under the agreement for such therapeutic focus area.

Expiration and Termination. If GlaxoSmithKline does not exercise any of its options, or if we do not achieve clinical proof of concept in any of the therapeutic focus areas of the alliance within a specified period, the agreement would expire. Otherwise, the agreement would expire with respect to each licensed product and country upon the expiration of the payment obligations of GlaxoSmithKline for that licensed product in that country and would expire in its entirety upon the expiration of the last payment obligation of GlaxoSmithKline for the last licensed product in the last country.

Either we or GlaxoSmithKline have the right to terminate the agreement if the other party becomes insolvent or commits an uncured material breach of the agreement, except that, if the uncured material breach is of a party's diligence obligations with respect to a product candidate for a particular therapeutic focus area under the agreement, the other party's right is only to terminate the agreement as applied to that therapeutic focus area. GlaxoSmithKline also has the right to terminate the agreement without cause upon 90 days notice, either in its entirety or as to any particular therapeutic focus area. We also have the right to terminate the agreement as to any particular therapeutic focus area, if GlaxoSmithKline challenges the scope, validity or enforceability of certain patents that cover compounds in development in the alliance for that therapeutic focus area. In addition, the agreement can be terminated by us or any successor following a change of control of us that meets specified conditions, upon payment of a specified sum to GlaxoSmithKline and the grant to GlaxoSmithKline of a license to a specified number of product candidates then in development in each of the therapeutic focus areas of the alliance. The rights and obligations of each of us and GlaxoSmithKline that survive termination of the agreement, including license grants, product candidates to which the license grants would apply and payment obligations, vary depending on the basis of the termination.

Patents and Proprietary Rights

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

As of February 29, 2008, our patent estate included 67 patents issued in the United States, one patent application allowed but not yet issued in the United States, 38 patent applications pending in the United States and numerous issued patents and pending patent applications in countries other than the United States. Our issued patents and pending patent applications in the United States include composition of matter coverage on a number of different structural families of compounds. The actual protection afforded by a patent varies from country to country and depends upon many factors, including the type of patent, the scope of its coverage and the availability of legal remedies in a particular country.

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

Product Candidate	Patent Scope	Patent Expiration
AZD3480 (TC-1734) . . .	Composition of matter for AZD3480 (TC-1734)	July 2018
	Composition of matter for a family of compounds that includes AZD3480 (TC-1734)	April 2016
	Methods of use of a family of compounds that includes AZD3480 (TC-1734) for treatment and prevention of CNS disorders	February 2017
TC-5619	Composition of matter for a family of compounds that includes TC-5619	August 2019
TC-5214	Pharmaceutical composition of S-mecamylamine	January 2020
	Methods of use of S-mecamylamine for neuropsychiatric disorders, including depression	January 2020
TC-2216	Composition of matter for TC-2216 as well as a family of compounds that includes TC-2216	June 2023
TC-6499	Composition of matter for TC-6499	February 2024

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

The patent expiration dates referenced above do not reflect any potential patent term extension that we may receive under The United States Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act. The Hatch-Waxman Act generally permits a patent extension term of up to five years as compensation for patent term lost during the FDA regulatory review process. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years. The patent term restoration period is generally one-half the time between the effective date of an investigational new drug application, or IND, and the submission date of a new drug application, or NDA, plus the time between the submission date and approval of an NDA. Only one patent applicable to an approved drug is eligible for the extension, and the extension must be applied for prior to expiration of the patent. The United States Patent and Trademark Office, in consultation with the FDA, reviews and approves applications for patent term extension.

License Agreements

We consider the following license agreements to be 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 TC-5214, mecamylamine hydrochloride and other specified compounds. The licensed patents and patent applications include issued patents covering the composition of TC-5214 and the other enantiomer of mecamylamine hydrochloride for use as a pharmaceutical and covering methods of use for the treatment of depression, ADHD, Tourette's syndrome and nicotine-responsive neuropsychiatric disorders. Under the agreement, we are obligated to pay to USFRF:

- an annual license fee until an NDA 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 right 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, if less, 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. USF may terminate the agreement if we fail to make a required royalty payment when due, or commit a material breach of the agreement, and do not cure the failure or breach within specified cure periods. If not earlier terminated, the agreement will terminate upon expiration of the last to expire of the licensed patent rights.

Yale University

Pursuant to an exclusive license agreement with Yale University, we hold an exclusive worldwide license to pending patent applications owned by Yale. The licensed patent applications include a pending U.S. application that, if issued in the future as a patent, could potentially cover the use of TC-5214 and mecamylamine hydrochloride, or other compounds classified as nicotinic antagonists, as an augmentation to other treatments for mood disorders. Under the agreement, we paid Yale a non-refundable license initiation fee and reimbursed Yale for its prior expenses with respect to the filing and prosecution of the licensed patent rights. In addition, we agreed to pay to Yale:

- an issuance fee that is conditional upon the issuance of a licensed patent in the United States that meets specified conditions;
- aggregate payments of up to $1,500,000 for each product subject to the license for which specified regulatory and first commercial sale milestones are achieved;
- royalties on any net sales of products subject to the license, subject, following the first launch of a product subject to the license, to specified annual minimum amounts; and
- a percentage of certain amounts received from a sublicensee of the licensed patent rights if the sublicense is not combined with a license to other patent rights of ours or with an agreement by us to collaborate to discover, research, develop or commercialize compounds or products for therapeutic use.

We are required to use reasonable commercial efforts to develop at least one product subject to the license for commercialization in the United States. We may terminate the agreement upon 30 days notice to Yale. Yale may terminate the agreement if we fail to make a required payment when due, or commit a material breach of the agreement, and do not cure the failure or breach within a specified cure period or if we notify Yale that we are finally abandoning our exploitation and intended exploitation of products covered by the agreement. If not earlier terminated, the agreement will expire 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, as well as the right to convert the license into an exclusive license upon payment of a fee. 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, if less, a percentage of that amount 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 through diligent efforts. We may terminate the agreement at any time with 90 days notice. VCUIPF may terminate the agreement if we fail to make a required payment or provide a required report when due. 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 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. WFUHS may terminate the agreement if we fail to make a required payment when due, or commit a material breach of the agreement, and do not cure the failure or breach within specified cure periods. In addition, WFUHS may terminate the license if we oppose any patent application or challenge the validity of any patent licensed under the agreement. If not earlier terminated, the agreement will terminate upon expiration of the last to expire of the licensed patent rights.

University of Kentucky Research Foundation

Pursuant to a sponsored research agreement, the University of Kentucky Research Foundation, or UKRF, agreed to assign to R.J. Reynolds Tobacco Company UKRF's rights to inventions that resulted in patents related to AZD3480 (TC-1734), TC-2696 and other earlier-stage compounds in our portfolio. These patents were subsequently assigned by RJR to us in August 2000. Under the sponsored research agreement and a subsequent license agreement with UKRF, we are obligated to pay royalties to UKRF based on amounts received from any licensee of these patents, including AstraZeneca.

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.

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 seek alliances and collaborations 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 alliances and collaborations, our goal will generally be to maintain co-promotion or co-commercialization rights in the United States and, in some cases, other markets. In order to implement our strategy successfully, we must develop a specialized sales and marketing organization with sufficient technical expertise. Our product currently available in the market, Inversine, is distributed by Cord Logistics, Inc., a Cardinal Health company, pursuant to an exclusive distribution agreement. Our agreement with Cord Logistics is terminable by either party at the end of each contract year upon 90 days prior notice or at any time upon 180 days notice. We paid Cord Logistics approximately $180,000 in 2007 and $150,000 in 2006.

Manufacturing

All of our current product candidates are compounds of low molecular weight, commonly referred to as small molecules, that can be manufactured in a simple synthetic process from readily available starting materials. We expect to continue to develop product candidates that can be produced cost-effectively by third-party contract manufacturers. Third parties currently manufacture both Inversine and its active ingredient for us.

We are able to manufacture the quantities of our product candidates necessary for relatively short preclinical toxicology studies ourselves. 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.

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.

We also face substantial competition from therapies designed to target NNRs. Pfizer's product Chantix, which is known outside of the United States as Champix, targets NNRs as an aid for smoking cessation. In addition, we believe that several prominent pharmaceutical companies have product candidates that target NNRs in development, including as examples Sanofi-Aventis, with a compound in Phase 2 for Alzheimer's disease, and Abbott Laboratories, with one compound in Phase 2 for Alzheimer's disease and ADHD, a second compound in Phase 2 for neuropathic pain and ADHD and two other compounds in Phase 1 for cognitive disorders or pain indications. Other companies that we believe have active NNR-based programs include AstraZeneca, Eli Lilly, Wyeth, Memory Pharmaceuticals, Critical Therapeutics, NeuroSearch A/S, CoMentis and EnVivo Pharmaceuticals. We expect that we will face increased competition in the future if therapies that target NNRs are further validated and if companies initiate or expand programs focused on NNRs or otherwise enter the CNS market, whether independently or by alliance or acquisition.

In addition, there are several pharmaceutical companies in the United States and globally that currently market and sell drugs for indications that we are targeting. There is currently no approved product for cognitive dysfunction in schizophrenia. We believe that the primary competitive products for use in indications that we are currently targeting with our most advanced product candidates include:

- for mild to moderate Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer/ Eisai, Razadyne from Johnson & Johnson and Exelon from Novartis; in addition, Namenda from Forest Laboratories, which acts by regulating the neurotransmitter glutamate, is marketed for moderate to severe Alzheimer's disease;
- for depression, selective serotonin reuptake inhibitors such as Prozac from Eli Lilly, Paxil/Seroxar from GlaxoSmithKline, Zoloft from Pfizer, Celexa and Lexapro from Forest Laboratories, dual uptake inhibitors such as Effexor from Wyeth and Cymbalta from Eli Lilly, and, as an adjunctive treatment, the atypical antipsychotic Abilify from Bristol-Myers Squibb/Otsuka;
- for anxiety disorders, benzodiazepines such as Pfizer's Xanax and Biovail's Ativan, as well as anti-depressants; and
- for neuropathic pain, Pfizer's Lyrica, which is indicated for, among other things, neuropathic pain associated with diabetic peripheral neuropathy and fibromyalgia, and Eli Lilly's Cymbalta, a selective serotonin and norepinephrine reuptake inhibitor indicated for, among other things, diabetic peripheral neuropathic pain.

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.

Regulatory Matters

Government Regulation and Product Approval

Government authorities in the United States, at the federal, state and local level, and in other countries extensively regulate, among other things, the research, development, testing, manufacture, quality control, approval, labeling, packaging, storage, record-keeping, promotion, advertising, distribution, marketing and export and import of drugs such as those we are developing. Our product candidates must be approved by FDA through the NDA process before they may be legally marketed in the United States.

United States Drug Development Process

In the United States, the FDA regulates drugs under the Federal Food, Drug, and Cosmetic Act, or FDCA, and implementing regulations. The process of obtaining regulatory approvals and the subsequent compliance with appropriate federal, state, local and foreign laws and regulations require the expenditure of substantial time and financial resources. Failure to comply with the applicable United States requirements at any time during the product development process, the approval process or after approval may subject an applicant to administrative

or judicial sanctions. These sanctions could include the FDA's refusal to approve pending applications, withdrawal of an approval, a clinical hold, warning letters, product recalls, product seizures, total or partial suspension of production or distribution injunctions, fines, refusals of government contracts, restitution, disgorgement, or civil or criminal penalties.

The process required by the FDA before a drug may be marketed in the United States generally involves the following:

- completion of preclinical laboratory tests, animal studies and formulation studies according to Good Laboratory Practices or other applicable regulations;
- submission to the FDA of an IND, which must become effective before human clinical trials may begin;
- performance of adequate and well-controlled human clinical trials according to Good Clinical Practices to establish the safety and efficacy of the drug for its intended use;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP to assure that the facilities, methods and controls are adequate to preserve the drug's identity, strength, quality and purity; and
- FDA review and approval of the NDA.

The testing and approval process requires substantial time, effort and financial resources.

Once a drug is identified for development it enters the preclinical testing stage. Preclinical tests include laboratory evaluations of chemistry, toxicity and formulation, as well as animal studies. An IND sponsor must submit the results of the preclinical tests, together with manufacturing information and analytical data, to the FDA as part of the IND. The sponsor also includes a protocol detailing, among other things, the objectives of the first clinical trial, the parameters to be used in monitoring safety and, if the first trial lends itself to an efficacy evaluation, the effectiveness criteria to be evaluated. Some non-clinical testing may continue even after the IND is submitted. The IND automatically becomes effective 30 days after receipt by the FDA, unless the FDA, within the 30-day time period, places the clinical trial on a clinical hold. In such a case, the sponsor and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during studies due to safety concerns or non-compliance with applicable law or regulation.

All clinical trials must be conducted under the supervision of one or more qualified investigators in accordance with good clinical practice regulations. These regulations include the requirement that all research subjects provide informed consent. Further, an institutional review board, or IRB, must review and approve the plan for any clinical trial before it commences at any institution. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and are reasonable in relation to the anticipated benefits. The IRB also approves the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative and must monitor the study until completed.

Each new clinical protocol must be submitted to the IND for FDA review and to the applicable IRBs for approval. Protocols detail, among other things, the objectives of the study, dosing procedures, subject selection and exclusion criteria, and the parameters to be used to monitor subject safety.

Human clinical trials are typically conducted in three sequential phases that may overlap or be combined:

- *Phase 1:* Involves one or more clinical trials in healthy human subjects to evaluate safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some drugs for severe or life-threatening diseases, the initial human testing may be conducted in patients, particularly where the drug may be too inherently toxic to administer ethically to healthy volunteers.

- *Phase 2:* Involves one or more clinical trials in a limited patient population to identify possible adverse effects and safety risks, to evaluate preliminarily the efficacy of the drug for specific targeted diseases and to determine dosage tolerance and optimal dosage.
- *Phase 3:* Involves one or more clinical trials to further evaluate dosage, clinical efficacy and safety in an expanded patient population at geographically dispersed study sites. These trials are intended to establish the overall risk-benefit ratio of the drug and provide, if appropriate, an adequate basis for product labeling.

Progress reports detailing the results of the clinical trials must be submitted at least annually to the FDA and safety reports must be submitted to the FDA and the investigators for serious and unexpected adverse events. Phase 1, Phase 2 and Phase 3 trials may not be completed successfully within any specified period, if at all. The FDA or the sponsor may suspend a clinical trial at any time on various grounds, including a finding that the research subjects or patients are being exposed to an unacceptable health risk. Similarly, an IRB can suspend or terminate approval of a clinical trial at its institution if the clinical trial is not being conducted in accordance with the IRB's requirements or if the drug has been associated with unexpected serious harm to patients.

Concurrent with clinical trials, companies usually complete additional animal studies and must also develop additional information about the chemistry and physical characteristics of the drug and finalize a process for manufacturing the drug as a product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the drug, and, among other things, the manufacturer must develop methods for testing the identity, strength, quality and purity of the final product. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product does not undergo unacceptable deterioration over its shelf life.

U.S. Review and Approval Processes

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical chemistry tests, proposed labeling, and other relevant information, are submitted to the FDA as part of an NDA requesting approval to market the product. The submission of an NDA is subject to the payment of user fees. A waiver of such fees may be obtained under certain limited circumstances.

In addition, under the Pediatric Research Equity Act, or PREA, an NDA or supplement to an NDA must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant deferrals for submission of data or full or partial waivers. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

The FDA reviews all NDAs submitted to ensure that they are sufficiently complete for substantive review before it accepts them for filing. The FDA has 60 days from its receipt of an NDA to determine if it will accept the submission for a substantive review, which is referred to as accepting it for filing. The FDA may request additional information rather than accept a NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. The FDA may refuse to file the NDA. If the submission is accepted for filing, the FDA begins an in-depth substantive review to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. In that regard, the FDA will inspect the facility or facilities where the product is manufactured before approving an NDA.

Under current performance goals, the FDA has either six or ten months to review and act on the NDA, depending upon whether the NDA is classified by the FDA as eligible for priority or standard review. The FDA often extends the review timeline by requesting additional information or clarification. The FDA may refer the NDA to an advisory committee for review, evaluation and a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendation of an advisory committee, but often follows such recommendation.

The FDA approval process is lengthy and difficult and the FDA may refuse to approve an NDA if the applicable regulatory criteria are not satisfied or may require additional clinical or other data and information. Even if such data and information is submitted, the FDA may ultimately decide that the NDA does not satisfy the criteria for approval. Data obtained from clinical trials are not always conclusive and the FDA may interpret data differently than we do. The FDA may issue an approvable letter, which may require additional clinical or other data or impose other conditions that must be met in order to secure final approval of the NDA.

NDAs receive either standard or priority review. A drug representing a significant improvement in treatment, prevention or diagnosis of disease may receive priority review. In addition, products studied for their safety and effectiveness in treating serious or life-threatening illnesses and that provide meaningful therapeutic benefit over existing treatments may receive accelerated approval and may be approved on the basis of adequate and well-controlled clinical trials establishing that the drug has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on the basis of an effect on a clinical endpoint other than survival or irreversible morbidity. As a condition of approval, the FDA may require that a sponsor of a drug receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. Priority review and accelerated approval do not change the standards for approval, but may expedite the approval process.

If a product receives regulatory approval, the approval may be limited to specific diseases and dosages, or the indications for use may otherwise be limited, which could restrict the commercial value of the product. In addition, the FDA may require Phase 4 testing, which involves clinical trials designed to further assess a drug's safety and effectiveness after NDA approval, and may require testing and surveillance programs to monitor the safety of approved products which have been commercialized.

If a drug product is the subject of an approved NDA, it may become 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 listed drug. This means, among other things, that it has the same active ingredient(s), route of administration, dosage form and strength, as well as the same labeling, with certain exceptions, and the labeling must prescribe conditions of use that have been previously approved for the listed drug. If the generic drug product has a different route of administration, dosage form, or strength, the FDA must grant a suitability petition approving the difference(s) from the listed drug before the ANDA may be filed. The ANDA must also contain data and information demonstrating that the generic drug is bioequivalent to the listed drug or, if the application is submitted pursuant to an approved suitability petition, information to show that the listed drug and the generic drug can be expected to have the same therapeutic effect as the listed drug when administered to patients for a proposed condition of use. There is generally no requirement, other than the requirement for evidence of bioequivalence, for an ANDA applicant to conduct or submit results of preclinical tests or clinical trials to establish the safety or efficacy of its drug product. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, are listed as such by the FDA and can typically be substituted by pharmacists under prescriptions written for the original listed drug.

Marketing Exclusivity

Market exclusivity provisions under the FDCA also can delay the submission or the approval of certain applications. The FDCA provides a five-year period of non-patent marketing exclusivity within the United States to the first applicant to gain approval of an NDA for a new chemical entity. A drug is a new chemical entity if the

FDA has not previously approved any other drug containing the same active moiety, which is the molecule or ion responsible for the action of the drug. During the exclusivity period, the FDA may not accept for review an ANDA or a Section 505(b)(2) NDA submitted by another company for another version of such drug where the applicant does not own or have a legal right of reference to all the data required for approval. However, an application may be submitted after four years if it contains a certification of patent invalidity or non-infringement. The FDCA also provides three years of marketing exclusivity for an NDA, Section 505(b)(2) NDA or supplement to an existing NDA if new clinical investigations, other than bioavailability studies, conducted or sponsored by the applicant are deemed by FDA to be essential to the approval of the application, for example, for new indications, dosages, or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

Pediatric exclusivity is another type of exclusivity in the United States. Pediatric exclusivity, if granted, provides an additional six months to an existing exclusivity or statutory delay in approval resulting from a patent certification. This six-month exclusivity, which runs from the end of other exclusivity protection or patent delay, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for such a study.

Orphan Drug Designation

Under the Orphan Drug Act, the FDA may grant orphan drug designation to a drug intended to treat a rare disease or condition, which is generally a disease or condition that either affects fewer than 200,000 individuals in the United States or affects more than 200,000 individuals in the United States but for which there is no reasonable expectation that the cost of developing and making available in the United States a drug for the disease or condition will be recovered from sales in the United States for that drug. Orphan drug designation must be requested before submitting an NDA. After the FDA grants orphan drug designation, the identity of the therapeutic agent and its potential orphan use are disclosed publicly by the FDA. Orphan drug designation does not convey any advantage in or shorten the duration of the regulatory review and approval process.

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication, except in very limited circumstances, for seven years.

The FDA also administers a clinical research grants program, whereby researchers may compete for funding to conduct clinical trials to support the approval of drugs, biologics, medical devices, and medical foods for rare diseases and conditions. A drug does not have to be designated as an orphan drug to be eligible for the grant program. An application for an orphan grant should propose one discrete clinical study to facilitate FDA approval of the product for a rare disease or condition. The study may address an unapproved new product or an unapproved new use for a product already on the market.

Post-Approval Requirements

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory standards is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product may result in restrictions on the product or even complete withdrawal of the product from the market. After approval, some types of changes to the approved product, such as adding new indications, manufacturing changes and additional labeling claims, are subject to further FDA review and approval. Drug manufacturers and other entities involved in the manufacture and distribution of approved drugs are required to

register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with cGMP and other laws.

Any products manufactured or distributed by us pursuant to FDA approvals are subject to continuing regulation by the FDA, including, among other things, record-keeping requirements, reporting of adverse experiences with the drug, providing the FDA with updated safety and efficacy information, drug sampling and distribution requirements, complying with certain electronic records and signature requirements, and complying with FDA promotion and advertising requirements. The FDA strictly regulates labeling, advertising, promotion and other types of information on products that are placed on the market. Drugs may be promoted only for the approved indications and in accordance with the provisions of the approved label.

From time to time, legislation is drafted, introduced and passed by the U.S. Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA. For example, on September 27, 2007, the Food and Drug Administration Amendments Act of 2007 was enacted, giving the FDA enhanced post-market authority, including the authority to require post-market studies and clinical trials, labeling changes based on new safety information, and compliance with a risk evaluation and mitigation strategy approved by the FDA. FDA's post-market authority takes effect 180 days after the enactment of the law. Failure to comply with any requirements under the new law may result in significant penalties. The new law also authorizes significant civil money penalties for the dissemination of false or misleading direct-to-consumer advertisements, and allows the FDA to require companies to submit direct-to-consumer television drug advertisements for FDA review prior to public dissemination. Additionally, the new law expands the clinical trial registry so that sponsors of all clinical trials, except for Phase 1 trials, are required to submit certain clinical trial information for inclusion in the clinical trial registry data bank. In addition to the impact of new legislation, FDA regulations and guidance are often revised or reinterpreted in ways that may significantly affect our business and our product candidates.

Foreign Regulation

In addition to regulations in the United States, we are subject to a variety of foreign regulations governing clinical trials of our product candidates and commercial sales and distribution of any products. Whether or not we obtain FDA approval for a product candidate or product, we must obtain approval by the comparable regulatory authorities of foreign countries before we can commence clinical trials of the product candidate 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 authorization applications either under a centralized or decentralized procedure. The centralized procedure, which is compulsory for medicines produced by certain biotechnological processes and optional for those which are highly innovative, provides for the grant of a single marketing authorization that is valid for all European Union member states. For drugs without approval in any member state, the decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state, known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials (draft summary of product characteristics, draft labeling and package leaflet) to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, the disputed points may eventually be referred to the European Commission, whose decision is binding on all member states.

Reimbursement

Sales of pharmaceutical products depend in significant part on the availability of third-party reimbursement. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. These third-party payors are increasingly challenging the price and examining the cost-effectiveness of medical products and services. In addition, significant uncertainty exists as to the reimbursement status of newly approved healthcare products. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of any of our products for which we receive marketing approval. Our product candidates may not be considered cost-effective. It is time consuming and expensive for us to seek reimbursement from third-party payors. Reimbursement may not be available or sufficient to allow us to sell any of our products for which we receive marketing approval on a competitive and profitable basis.

The passage of the Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposes new requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries, and includes a major expansion of the prescription drug benefit under a new Medicare Part D. Medicare Part D went into effect on January 1, 2006. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities which will provide coverage of outpatient prescription drugs. Part D plans include both stand-alone prescription drug benefit plans and prescription drug coverage as a supplement to Medicare Advantage plans. Unlike Medicare Part A and B, Part D coverage is not standardized. Part D prescription drug plan sponsors are not required to pay for all covered Part D drugs, and each drug plan can develop its own drug formulary that identifies which drugs it will cover and at what tier or level. However, Part D prescription drug formularies must include drugs within each therapeutic category and class of covered Part D drugs, though not necessarily all the drugs in each category or class. Any formulary used by a Part D prescription drug plan must be developed and reviewed by a pharmacy and therapeutic committee.

It is not clear what effect the MMA will have on the prices paid for currently approved drugs and the pricing options for drugs approved after January 1, 2006. Government payment for some of the costs of prescription drugs may increase demand for any of our products for which we receive marketing approval. However, any negotiated prices for our products covered by a Part D prescription drug plan will likely be lower than the prices we might otherwise obtain. Moreover, while the MMA applies only to drug benefits for Medicare beneficiaries, private payors often follow Medicare coverage policy and payment limitations in setting their own payment rates. Any reduction in payment that results from the MMA may result in a similar reduction in payments from non-governmental payors.

We expect that there will continue to be a number of federal and state proposals to implement governmental pricing controls and limit the growth of healthcare costs, including the cost of prescription drugs. Currently, Medicare is prohibited from negotiating directly with pharmaceutical companies for drugs. However, the U.S. Congress may consider legislation that would lift the ban on federal negotiations.

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 provides options for its member states to restrict the range of medicinal products for which their national health insurance systems provide reimbursement and 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. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products for which we receive marketing approval.

Employees

As of February 29, 2008, we had 102 full-time employees, 40 of whom are Ph.D.s, M.D.s or both, and two part-time employees. Our management believes that relations with our employees are good. None of our employees is represented under a collective bargaining agreement.

Our Corporate Information

We were incorporated in Delaware in 1997 as a wholly owned subsidiary of R.J. Reynolds Tobacco Company. In August 2000, we became an independent company when we issued and sold stock to venture capital investors. Our principal 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 internet address is www.targacept.com. The information contained on, or that can be accessed through, our website is not incorporated by reference into this annual report. We have included our website address as a factual reference and do not intend it as an active link to our website. Our annual reports on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K, and all amendments to those reports, are available to you free of charge through the Investor Relations page of our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the SEC.

Our trademarks include Targacept®, Inversine®, Pentad™, NNR Therapeutics™, TRIDMAC™ and Amplixa™. Other service marks, trademarks and trade names appearing in this annual report are the property of their respective owners.

Item 1A. Risk Factors.

Risks Related to Our Financial Results and Need for Additional Financing

We have a substantial accumulated deficit and anticipate that we will incur substantial losses for the foreseeable future. We may never 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. As of December 31, 2007, we had an accumulated deficit of $164.2 million. We had net loss of $28.1 million for the year ended December 31, 2007, net income of $2.1 million for the year ended December 31, 2006, and net loss of $29.0 million for the year ended December 31, 2005. Our losses have historically 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 incur substantial losses for the foreseeable future as we expand our clinical trial activity, as our clinical-stage and preclinical product candidates advance through the development cycle, as we progress our programs in the therapeutic focus areas of our alliance with GlaxoSmithKline and our preclinical research collaboration with AstraZeneca and as we invest in additional product opportunities and research programs and expand our research and development infrastructure. As a result, we will need to generate significant revenues to pay these expenses.

We derived a substantial portion of our revenue for 2007 and 2006 from our collaboration with AstraZeneca and we derived a substantial portion of our revenue for 2007 from our alliance with GlaxoSmithKline. We expect that a substantial portion of our revenue in the future will depend on the conduct of research and the successful achievement of milestone events in the development of AZD3480 (TC-1734) under our agreement with AstraZeneca and on the successful achievement of research and development-related milestone events under our agreement with GlaxoSmithKline, any or all of which may not occur.

Inversine is our only current source of product revenue. We acquired the rights to Inversine in August 2002. Sales of Inversine generated net revenue of only $518,000 for the year ended December 31, 2007, $585,000 for

the year ended December 31, 2006, and $681,000 for the year ended December 31, 2005. Inversine is approved in the United States for the management of moderately severe to severe essential hypertension and uncomplicated cases of malignant hypertension, which are high blood pressure disorders. However, we believe that the substantial majority of Inversine sales are derived from prescriptions written by a very limited number of physicians for the treatment of neuropsychiatric disorders, such as Tourette's syndrome, autism and bipolar disorder, in children and adolescents. If any of these physicians were to change their prescribing habits, Inversine sales would suffer. We do not expect that sales of Inversine will increase substantially in the future.

If we are unable to develop and commercialize any of our product candidates, if development is delayed or if sales revenue from any product candidate that receives marketing approval is insufficient, we may not be profitable. Even if we are profitable for any particular period, 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, duration, results and cost of clinical trials, as well as non-clinical studies and assessments, of our product candidates;
- the timing, receipt and amount of milestone and other payments from AstraZeneca, GlaxoSmithKline and potential future collaborators;
- the extent to which our research and development activities in the programs that are the therapeutic focus areas of our alliance with GlaxoSmithKline result in the achievement of milestone events under our alliance agreement;
- the duration of our preclinical research collaboration with AstraZeneca;
- 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 alliances, collaborations and licensing or other arrangements on terms favorable to us;
- the costs to satisfy our obligations under existing and potential future alliances and 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, the ownership interests of our stockholders will be diluted and the terms may include liquidation or other preferences that adversely affect the rights of our

stockholders. 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 alliance, collaboration or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates or grant licenses on terms that are not favorable to us.

Our current operating plan provides for us to continue, either alone or with a collaborator, to advance our product candidates through the development process. We do not expect our existing capital resources to be sufficient to enable us to fund the completion of the development of any of our product candidates. We currently expect that our existing capital resources will enable us to fund our operations at least through the first half of 2010. 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. 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.

AstraZeneca has the right to terminate our preclinical research collaboration prior to the completion of the planned four-year term, which would adversely affect our revenue.

We and AstraZeneca are conducting a preclinical research collaboration under our agreement that is designed to discover and develop additional compounds that, like AZD3480 (TC-1734), act on the α4ß2 NNR as treatments for conditions characterized by cognitive impairment. Under the agreement, AstraZeneca pays us research fees based on an agreed reimbursement rate for research services rendered by us in the preclinical research collaboration, subject to specified limits. The agreement provides for a four-year research term, which began in January 2006. AstraZeneca has the right to terminate the preclinical research collaboration, effective three years after the research term began, upon at least six months notice. If AstraZeneca terminates the preclinical research collaboration prior to completion of the planned four-year term, our revenue would be adversely affected.

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 or royalty revenue and our likelihood of success will be harmed.

AstraZeneca has two ongoing Phase 2b clinical trials of AZD3480 (TC-1734), one in mild to moderate Alzheimer's disease and one in cognitive dysfunction in schizophrenia. Prior to these trials, AZD3480 (TC-1734) had not been evaluated in any clinical trial in patients suffering from Alzheimer's disease or cognitive dysfunction in schizophrenia. In March 2006, we independently completed a Phase 2 clinical trial of AZD3480 (TC-1734) in age associated memory impairment, commonly referred to as AAMI, that was designed to further assess the effects of AZD3480 (TC-1734) on cognition in a cognitively impaired older adult population. Our ability to generate product or royalty revenue in the future will depend heavily on the successful development and commercialization of AZD3480 (TC-1734).

We are currently conducting Phase 1 single rising dose clinical trials of TC-5214, TC-5619 and TC-6499. We have completed a Phase 1 single rising dose clinical trial of TC-2216. Our other product candidates are in various stages of preclinical development.

Any of our product candidates could be unsuccessful if it:

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

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

If AstraZeneca does not have success in clinical trials of AZD3480 (TC-1734) in mild to moderate Alzheimer's disease or cognitive dysfunction in schizophrenia, we and AstraZeneca will not in the future obtain the regulatory approvals required to market AZD3480 (TC-1734) for Alzheimer's disease or cognitive dysfunction in schizophrenia notwithstanding favorable results in clinical trials of AZD3480 (TC-1734) in other indications.

Successful results in clinical trials of AZD3480 (TC-1734) in a condition characterized by one degree of cognitive impairment may not be predictive of successful results in clinical trials of AZD3480 (TC-1734) in a condition characterized by more severe cognitive impairment or in cognitive impairment resulting from a different condition. We have completed two Phase 2 clinical trials of AZD3480 (TC-1734) in AAMI and a third Phase 2 clinical trial of AZD3480 (TC-1734) in mild cognitive impairment, commonly referred to as MCI. In those trials, AZD3480 (TC-1734) demonstrated positive effects on some measures of cognition. AstraZeneca has ongoing separate Phase 2b clinical trials of AZD3480 (TC-1734) in mild to moderate Alzheimer's disease and in cognitive dysfunction in schizophrenia. The findings in any of our completed Phase 2 trials of AZD3480 (TC-1734) in AAMI or MCI may not be predictive of the effect of AZD3480 (TC-1734) in Alzheimer's disease or cognitive dysfunction in schizophrenia. Neither we nor AstraZeneca has previously conducted any clinical trial of AZD3480 (TC-1734) in Alzheimer's disease or cognitive dysfunction in schizophrenia.

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

AZD3480 (TC-1734) is metabolized at a different rate by extensive metabolizers through its primary metabolic pathway than it is by intermediate or poor metabolizers. In its ongoing clinical trials in mild to moderate Alzheimer's disease and cognitive dysfunction in schizophrenia, AstraZeneca has limited the highest dose evaluated in some of the trial subjects based on their individual metabolisms. Because neither we nor AstraZeneca has previously conducted any clinical trial of AZD3480 (TC-1734) in Alzheimer's disease or cognitive dysfunction in schizophrenia, neither we nor AstraZeneca has determined the dose range in which positive medical effects, if any, are achieved with AZD3480 (TC-1734) in persons with Alzheimer's disease or schizophrenia. If the doses at which AZD3480 (TC-1734) is evaluated are not within the dose range in which positive medical effects could be achieved with AZD3480 (TC-1734) in persons with Alzheimer's disease or schizophrenia, the ongoing clinical trials in these indications will not be successful. Moreover, it is possible that, even if the trials are successful and we or AstraZeneca receive in the future the regulatory approvals required to

market and sell AZD3480 (TC-1734), the regulatory authorities could limit the patient population for which AZD3480 (TC-1734) is approved to those who are extensive or intermediate metabolizers through the primary metabolic pathway of AZD3480 (TC-1734). If regulatory authorities limit the patient population for which AZD3480 (TC-1734) is approved in this manner, it would have an adverse effect on the commercial potential of AZD3480 (TC-1734).

The CDR test battery that we have used in our clinical trials of AZD3480 (TC-1734) is different from the Alzheimer's Disease Assessment Scale-cognitive subscale, or ADAS-Cog, the test battery that is most often used to assess the efficacy of drugs for Alzheimer's disease. ADAS-Cog is designed to measure improvement in persons who are severely impaired and is generally less sensitive than the CDR test battery in measuring improvement in persons who are less impaired. ADAS-Cog, and not the CDR test battery, is the primary endpoint in AstraZeneca's ongoing Phase 2b clinical trial of AZD3480 (TC-1734) in mild to moderate Alzheimer's disease. The findings in our completed trials as to the effect of AZD3480 (TC-1734) on various aspects of cognition as measured by the CDR test battery may not be predictive of the effect of AZD3480 (TC-1734) on cognition as measured by ADAS-Cog. If clinical trials of AZD3480 (TC-1734) in Alzheimer's disease are not successful, we and AstraZeneca will not obtain the regulatory approvals required to market AZD3480 (TC-1734) for Alzheimer's disease.

If the combination of AZD3480 (TC-1734) administered together with other drugs that are commonly prescribed for schizophrenia is not considered to be safe, the commercial potential of AZD3480 (TC-1734) would be adversely affected.

A drug that is generally safe when taken alone may not be safe or may not be as safe when taken together with other drugs. Our product candidate AZD3480 (TC-1734) is in development for cognitive dysfunction in schizophrenia. Many schizophrenic patients take one or more medications from the drug class known as anti-psychotics to treat some of the other symptoms of the disease. If the interaction of AZD3480 (TC-1734) and any or all of the anti-psychotics is determined to be unsafe or not tolerated, the commercial potential of AZD3480 (TC-1734) as a treatment for cognitive dysfunction in schizophrenia could be limited. Moreover, AstraZeneca could decide not to advance AZD3480 (TC-1734) as a treatment for cognitive dysfunction in schizophrenia, which would limit the overall commercial potential of AZD3480 (TC-1734).

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

The preclinical laboratory testing, development, manufacturing and clinical trials of product candidates that we develop, whether independently or in collaboration with a third party, as well as their distribution, sale and marketing, are regulated by the FDA and other federal, state and local governmental authorities in the United States and by similar agencies in other countries. We must receive regulatory approval of each product candidate before we can market and sell it. We have only limited experience in pursuing regulatory approvals. Securing FDA approval requires the submission of extensive preclinical and clinical data and information about the chemistry and manufacture of, and control procedures for, each potential product. In addition, the supporting information submitted to the FDA must establish the safety and efficacy of the product candidate for each indicated use. The drug development and 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 or 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.

A Phase 1 clinical trial program typically takes several months to complete, a Phase 2 clinical trial program typically takes several months to two years to complete and a Phase 3 clinical trial program typically takes one to four years to complete. Moreover, Phase 3 clinical trials may not follow successful completion of Phase 2 clinical trials directly, as additional non-clinical assessments or clinical trials may first be required. Industry sources have reported that the preparation and submission of an 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. However, additional clinical trials may be required by the FDA or foreign regulatory authorities following completion of a pivotal clinical trial and prior to seeking approval. The Pharmaceutical Research and Manufacturers of America has reported 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 or our collaborators interpret the results differently; or
- the FDA may deem the processes and facilities that we, our collaborators or our third-party manufacturers propose to use in connection with the manufacture of the product candidate to be unacceptable.

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 revenue.

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 approval and could adversely impact our revenue and results of operations.

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

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

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

If we do not prove in clinical trials that our product candidates are safe and effective, we will not obtain marketing approvals from the FDA and other applicable regulatory authorities. In particular, one or more of our product candidates may not exhibit the expected medical benefits in humans, may cause harmful side effects or may have other unexpected characteristics that preclude regulatory approval for any or all indications of use or limit commercial use if approved. For example, we had previously been developing TC-2696 as a treatment for acute post-operative pain. In December 2007, we announced that TC-2696 did not meet the primary endpoints in a Phase 2 clinical trial in third molar extraction patients. We have no current plans to conduct further development of TC-2696.

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

If positive results of completed clinical trials of our product candidates are not replicated in any future clinical trials, we will not obtain the regulatory approvals required to market and sell them.

Positive findings in preclinical studies of a product candidate may not be predictive of similar results in clinical trials in humans. In addition, positive results in early clinical trials of a product candidate may not be replicated in later clinical trials.

We completed a Phase 2 clinical trial of AZD3480 (TC-1734) in AAMI in March 2006. We previously completed two other Phase 2 clinical trials of AZD3480 (TC-1734), one in AAMI and one in MCI. In those trials, AZD3480 (TC-1734) demonstrated positive effects on some measures of cognition. However, our findings in those trials on cognition may not be replicated in clinical trials of AZD3480 (TC-1734) conducted in Alzheimer's disease, cognitive dysfunction in schizophrenia or other indications. In particular, the results of the Phase 2 clinical trial of AZD3480 (TC-1734) in AAMI that we completed in March 2006 were most favorable in the 50mg dose group. There is no 50mg dose group in AstraZeneca's ongoing Phase 2 clinical trials of AZD3480 (TC-1734) in mild to moderate Alzheimer's disease and cognitive dysfunction in schizophrenia. Also, although AZD3480 (TC-1734) demonstrated positive effects at some dose levels with respect to some measures of cognition tested in the first Phase 2 clinical trial in AAMI that we conducted, AZD3480 (TC-1734) did not demonstrate positive effects as to all measures at all dose levels and placebo showed superior effects to AZD3480 (TC-1734) as to some measures at some dose levels in that trial.

If favorable results of our completed clinical trial of mecamylamine hydrochloride as an augmentation treatment for major depression are not replicated in any future clinical trials of TC-5214, we will not obtain the regulatory approvals required to market and sell TC-5214.

TRIDMAC is a treatment combination comprised of mecamylamine hydrochloride as an augmentation therapy to citalopram hydrobromide. In our Phase 2 clinical trial of TRIDMAC in major depression, we observed

a statistically significant result in favor of TRIDMAC on one of two co-primary endpoints in the trial, group mean change from baseline on the Hamilton Depression Rating Scale, on an intent to treat basis and a strong trend in favor of TRIDMAC on a per protocol basis. The result on the other co-primary endpoint, achievement of remission, favored the TRIDMAC group over the placebo group, although this result was not statistically significant.

We are currently developing TC-5214 as an augmentation treatment for major depression in lieu of further development of mecamylamine hydrochloride. Mecamylamine hydrochloride is a racemate and TC-5214 is one of the enantiomers of mecamylamine. A racemate is a mixture of two different enantiomers that are mirror images of each other and have the same chemical but potentially different biological properties. Single enantiomers may cause a different biological response, have different pharmacokinetic properties or have different degrees of toxicity, in each case as compared to each other or to the racemate that is comprised of both enantiomers. Consequently, the favorable results that we observed with mecamylamine in our completed Phase 2 clinical trial may not be replicated in any clinical trials of TC-5214 that we conduct.

If we elect to pursue development of one of the enantiomers of TC-2216 in lieu of further development of TC-2216, our future development costs would be greater, our overall development timelines would be extended and our receipt of revenue from potential product sales may be delayed.

Our depression and anxiety program includes TC-2216, which is a racemate. We completed a Phase 1 single rising dose clinical trial of this product candidate in the first quarter of 2008. We may in the future elect to develop one of the enantiomers of TC-2216 in lieu of further development of TC-2216. However, based on our anticipated development of TC-5214 and our current budget management plans, we do not expect that we will conduct further clinical development of TC-2216 or its enantiomers in 2008.

Current FDA policy provides that, assuming that it is technologically feasible to separate a racemate into its component enantiomers, the pharmacokinetic activity of each enantiomer and, if evaluation of the racemate indicates unexpected toxicity, the toxicity of each enantiomer should be independently characterized and compared to each other and to the racemate. The FDA's policy also suggests that, where characterization of the separate enantiomers shows that one enantiomer has undesirable effects or that both enantiomers are pharmacologically active as opposed to one being inert, consideration should be given to developing a single enantiomer rather than the racemate. We have determined in preliminary animal testing that both enantiomers of TC-2216 have pharmacological activity. Accordingly, it is possible that regulatory considerations could discourage further development of TC-2216 in favor of one of its enantiomers.

If we elect to pursue development of one of the enantiomers of TC-2216 in lieu of further development of TC-2216, whether based on feedback from regulatory authorities or for any other reason, we may be required to conduct animal safety studies with the selected enantiomer that we have already conducted with TC-2216, as well as, potentially, one or more Phase 1 clinical trials of the selected enantiomer. As a result, our future development costs may be greater, our overall development timelines may be extended and our receipt of revenue from potential product sales may be delayed.

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 revenue 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 subjects 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 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 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 subject 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 subject enrollment can result in increased costs and longer development times. The failure to enroll subjects in a clinical trial could delay the completion of the clinical trial beyond our current expectations. In addition, the FDA could require us or AstraZeneca or GlaxoSmithKline to conduct clinical trials with a larger number of subjects than we have projected for any of our product candidates. We or AstraZeneca or GlaxoSmithKline may not be able to enroll a sufficient number of subjects in a timely or cost-effective manner. Furthermore, enrolled subjects may drop out of clinical trials, which could impair the validity or statistical significance of those clinical trials.

Prior to commencing clinical trials in the United States, we must submit an IND to the FDA and the IND must become effective. We are conducting our ongoing Phase 1 clinical trials of our product candidate TC-5619 and TC-6499 outside the United States. We have not submitted an IND to enable us to conduct clinical trials of any of TC-5619, TC-6499 or TC-2216 in the United States.

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

Our product candidates will remain subject to ongoing regulatory review even if they receive marketing approval. If we fail to comply with continuing regulations or if patients taking our products experience adverse health effects, we could lose these approvals or the sale of our products could be suspended or otherwise adversely affected.

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 or commercial potential, force us to withdraw it from the market or impede or delay our ability to obtain regulatory approvals in additional countries. For example, in February 2008, the FDA issued a public health advisory with regard to Pfizer's product Chantix, which targets NNRs and is approved as an aid for smoking cessation. The advisory noted an increasing likelihood of an association between Chantix and serious neuropsychiatric symptoms and described symptoms as including anxiety, nervousness, tension, depressed mood, unusual behaviors and thinking about or attempting suicide. The advisory also noted that the FDA had requested that Pfizer elevate the prominence of this safety information to the warnings and precautions section of the Chantix prescribing information, or labeling. All of our products currently in development also target NNRs.

In addition, the manufacturer of the product and its facilities will continue to be subject to FDA review and periodic inspections to ensure adherence to applicable regulations. After receiving marketing approval, the manufacturing, labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping related to the product will remain subject to extensive regulatory requirements. We may be slow to adapt, or we may never adapt, to changes in existing regulatory requirements or adoption of new regulatory requirements.

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

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

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

Because we have limited financial and managerial resources, we must focus on research programs and product candidates for the specific indications that we believe are the most promising. As a result, we may forego or delay pursuit of opportunities with other product candidates or other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Through 2007, we spent managerial and financial resources on clinical trials for TC-2696, a product candidate for pain. In December 2007, we announced that TC-2696 did not meet the primary endpoints in a Phase 2 clinical trial in third molar extraction patients. We have no current plans to conduct further development of TC-2696. We may in the future spend our resources on other research programs and product candidates for specific indications that ultimately do not yield any commercially viable products. Furthermore, if we do not accurately evaluate the commercial potential or target market for a particular product candidate, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights.

If we do not achieve specified discovery and development events in our alliance with GlaxoSmithKline for which we would be entitled to receive milestone payments, our research and development activities in the alliance may not be self-funding and we may need to utilize other financial resources to conduct the activities, which could adversely affect our ability to advance the development of our other product candidates.

We have an ongoing alliance with GlaxoSmithKline that is designed to discover, develop and market product candidates that selectively target specified NNR subtypes in five therapeutic focus areas—pain, smoking cessation, addiction, obesity and Parkinson's disease. Under the alliance agreement, we have agreed, at our sole expense, to seek to discover product candidates that target specified NNR subtypes for each therapeutic focus area of the alliance and to develop the most promising product candidate for each therapeutic focus area through a Phase 2 clinical proof of concept trial. We are eligible to receive milestone payments from GlaxoSmithKline upon the achievement of specified discovery, development, regulatory and commercial events with respect to TC-6499, our product candidate in development for neuropathic pain, and other product candidates that are discovered and developed in the alliance. If we do not achieve the specified milestone events, we will not receive payments sufficient to fund our research and development obligations in the alliance or otherwise to realize the expected benefit from the alliance. If that occurs, we may have to allocate available financial resources to our obligations in the alliance in lieu of employing those resources to advance the development of our product candidates outside of the alliance that may ultimately prove to have greater commercial potential.

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.

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

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

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

Risks Related to Our Dependence on Third Parties

The successful development and commercialization of our lead product candidate, AZD3480 (TC-1734), depends substantially on our collaboration with AstraZeneca. If AstraZeneca is unable to further develop or commercialize AZD3480 (TC-1734), experiences significant delays in doing so or terminates our agreement, our business will be materially harmed.

We entered into our collaborative research and license agreement with AstraZeneca for the development and worldwide commercialization of AZD3480 (TC-1734) for the treatment of Alzheimer's disease, cognitive dysfunction in schizophrenia and potentially other indications characterized by cognitive impairment in December 2005. We have a limited history of working together with AstraZeneca and we cannot predict the success of the

collaboration. The collaboration involves a complex allocation of rights, provides for milestone payments to us based on the achievement of specified development, regulatory and first commercial sale milestones and provides us with royalty-based revenue if AZD3480 (TC-1734) or another product candidate is successfully commercialized. AstraZeneca has decision-making authority for most matters in our collaboration. In addition, AstraZeneca has the right to assume control of patent matters with respect to AZD3480 (TC-1734) and has exercised its right with respect to the prosecution of some of our patents with respect to AZD3480 (TC-1734).

AstraZeneca is generally responsible for conducting and funding substantially all future development and regulatory approval activities for AZD3480 (TC-1734), except for costs associated with any work outside of the planned development programs that we agree to conduct, and has significant control over the conduct and timing of development efforts with respect to AZD3480 (TC-1734). Although we have had discussions with AstraZeneca regarding its current plans and intentions, AstraZeneca may change its development plans for AZD3480 (TC-1734). We have little control over the amount and timing of resources that AstraZeneca devotes to the development of AZD3480 (TC-1734). If AstraZeneca fails to devote sufficient financial and other resources to the development plan for AZD3480 (TC-1734), the development and potential commercialization of AZD3480 (TC-1734) would be delayed. This would result in a delay in milestone payments and, if regulatory approval to market and sell AZD3480 (TC-1734) is obtained, royalties that we could receive on commercial sales.

AstraZeneca has the right to terminate our agreement in its entirety upon 90 days notice after the earlier of the end of the term of the preclinical research collaboration that we are currently conducting, which began in January 2006, or four years after the research term began. AstraZeneca has the right to terminate the $\alpha4\beta2$ research collaboration effective three years after the research term began upon at least six months notice. If AstraZeneca terminates our agreement at any time, for any reason, it would delay our development of AZD3480 (TC-1734) and materially harm our business and could accelerate our need for additional capital. In particular, we would have to fund the clinical development and commercialization of AZD3480 (TC-1734) on our own, seek another collaborator or licensee for clinical development and commercialization or abandon the development and commercialization of AZD3480 (TC-1734).

If AstraZeneca were to exercise its future right to license TC-5619 but fail to devote sufficient financial and other resources to its development, our ability to derive revenue based on TC-5619 would be adversely affected.

We have agreed to develop TC-5619 independently through Phase 1 clinical development and a Phase 2 clinical proof of concept trial pursuant to an agreed development plan. Following our completion of the development plan, AstraZeneca has the right to license TC-5619 for any or all of schizophrenia and various conditions characterized by cognitive impairment on terms specified in our collaboration agreement. If AstraZeneca elects to license TC-5619, AstraZeneca would become generally responsible for conducting and funding substantially all future development and regulatory approval activities for TC-5619 and have significant control over the conduct and timing of development efforts with respect to TC-5619. AstraZeneca has an internal product candidate that, like TC-5619, acts on the $\alpha7$ NNR and that we believe is currently at a similar stage of development to TC-5619. If AstraZeneca were to fail to devote sufficient financial and other resources to the development of TC-5619, whether in favor of its own product candidate or for any other reason, the development and potential commercialization of TC-5619 would be delayed. This would result in a delay in milestone payments and, if regulatory approval to market and sell TC-5619 is obtained, royalties that we could receive on commercial sales.

If GlaxoSmithKline exercises any of the exclusive options that may be triggered under our alliance agreement, the successful development and commercialization of the licensed product candidates will depend substantially on GlaxoSmithKline.

We entered into our agreement with GlaxoSmithKline in July 2007. Prior to entering into the agreement, we did not have a history of working together with GlaxoSmithKline and we cannot predict the success of the

alliance. Under the agreement, if we achieve clinical proof of concept for a lead product candidate for any of the therapeutic focus areas of the alliance, GlaxoSmithKline would have an exclusive option for an exclusive license to the lead product candidate and up to two other product candidates in development in the alliance for the same therapeutic focus area on a worldwide basis. If GlaxoSmithKline were to exercise its option and pay the applicable exercise fee, GlaxoSmithKline would become responsible for using diligent efforts to conduct later-stage development and commercialization of the lead product candidate at its sole expense. In that event, we would have limited control over the amount and timing of resources that GlaxoSmithKline dedicates to the development of our licensed product candidates. Our ability to generate further revenue from the alliance would depend on GlaxoSmithKline's abilities to establish the safety and efficacy of our product candidates, to obtain regulatory approvals and to achieve market acceptance.

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

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

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

- collaborators have significant discretion in determining the efforts and resources that they will apply to these alliances and 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, that result in costly litigation or arbitration that diverts management attention and resources or that, if resolved unfavorably to us, result in adverse financial consequences for us under the terms of the applicable agreements; and
- alliances 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.

Alliances and collaborations may not lead to development of product candidates in the most efficient manner or at all.

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

If we do not establish additional alliances and 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 seeking alliances and collaborations 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 with respect to 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.

We have the right to offer to AstraZeneca the right to license any compound that acts on any NNR other than the $\alpha4\beta2$ NNR that we may in the future seek to exploit for Alzheimer's disease, cognitive dysfunction in schizophrenia, other conditions characterized by cognitive impairment or schizophrenia. We made such an offer with respect to TC-5619, which following a process under our agreement led to AstraZeneca's future right to license TC-5619. However, if we do not offer a compound that acts on any NNR other than the $\alpha4\beta2$ NNR to AstraZeneca, we are generally not permitted to develop or commercialize the compound for any of these indications. As a result, our ability to seek additional alliances and collaborations for these indications is substantially limited during the term of our collaboration with AstraZeneca. In addition, under our agreement with AstraZeneca, AstraZeneca may under certain circumstances have a right of first negotiation for the development and commercialization of compounds that act by binding to NNRs for depression, anxiety and bipolar disorder.

Similarly, we have agreed in our alliance agreement with GlaxoSmithKline that, with respect to each of the therapeutic focus areas of the alliance, for so long as we are required under the agreement to conduct research activities in the therapeutic focus area or for so long thereafter as there are any product candidates in development or being commercialized in the alliance in the therapeutic focus area, we will work in the therapeutic focus area exclusively with GlaxoSmithKline with respect to product candidates with NNR-derived activity. As a result, our ability to seek additional alliances for any of these areas is substantially limited during the term of our alliance with GlaxoSmithKline. The therapeutic focus areas of our alliance with GlaxoSmithKline are pain, smoking cessation, addiction, obesity and Parkinson's disease.

We face significant competition in seeking appropriate alliances and collaborations. Alliances and collaborations are complex and time-consuming to negotiate and document. We may not be able to negotiate them on acceptable terms, or at all. If we cannot, 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 any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to increase our expenditures to fund development or commercialization activities on our own, we may need to obtain additional capital, which may not be available to us on acceptable terms or at all. If we do not have sufficient funds, we will not be able to bring our product candidates to market and generate product revenue.

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

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

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

- could encounter difficulties in achieving volume production, quality control and quality assurance and suffer shortages of qualified personnel, which could result in its inability to manufacture sufficient quantities of drugs to meet our clinical timelines or to commercialize our product candidate;
- could terminate or choose not to renew its manufacturing agreement with us, based on its 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 its 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, its manufacturing agreement with us.

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

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 impair the credibility or reliability of the data generated in clinical trials of our product candidates, delay or prevent the development, approval and commercialization of our product candidates or result in enforcement action against us.

In particular, we have ongoing Phase 1 clinical trials of our product candidates TC-5619 and TC-6499. We have contracted with Forenap Pharma EURL, a contract research organization located in France, to conduct each of these trials, as well as the Phase 1 trial of TC-2216 completed in the first quarter of 2008. As a result, we are heavily reliant on Forenap Pharma for successful execution of Phase 1 development for multiple clinical-stage product candidates. If Forenap Pharma does not execute and complete any of the Phase 1 trials as expected, whether as a result of an unforeseen event affecting its business generally or for any other reason, our development of the affected product candidates would likely be adversely affected. In particular, we could have to contract with another contract research organization to execute or complete the affected trial. In addition, our clinical development program for the affected product candidate could be made more costly, the applicable development timeline could be delayed or extended and our receipt of revenue from potential product sales could be delayed. If multiple product candidates were to be affected, it could have a material adverse effect on our overall business and prospects.

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, or our present or future collaborators' 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. 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. Moreover, the U.S. Supreme Court's 2007 decision in *KSR International Co. vs. Teleflex, Inc.* may in some cases make it more difficult to obtain a patent, or to withstand a validity challenge to any issued

patent, for pharmaceutical products that have a relationship to other pharmaceutical products, such as combination products, specific salt forms or single enantiomers. 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. If we are unable to obtain, enforce or defend the patents with respect to our product candidates, our ability to commercialize our product candidates would be adversely affected and our business would suffer.

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 invent 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 or enforcement 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. For example, we generally do not seek patent protection for the computer-based molecular design technologies that form part of Pentad and instead seek to maintain those technologies as trade secrets.

To maintain the confidentiality of trade secrets and proprietary information, we generally enter into confidentiality agreements with our employees, consultants, contractors and collaborators 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 that 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 covering the pharmaceutical composition and methods of use of TC-5214. We may enter into additional licenses in the future. Our existing licenses impose, and we expect future licenses will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, the licensor may have the right to terminate the license, in which event we might not be able to market any product that is covered by the licensed patents.

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

Although we generally seek the broadest patent protection available for our 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. If we are unable to obtain patent protection for the actual composition of any compound that we seek to develop and commercialize and must rely on method of use patent coverage, we would likely be unable to prevent others from manufacturing or marketing that compound for any use that is not protected by our patent rights. If a third party were to receive marketing approval for any compound for which we rely on method of use patent coverage for another use, physicians could nevertheless prescribe it for indications that are not described in the product's labeling or approved by the FDA or other regulatory authorities. Even if we have patent protection for the prescribed indication, as a practical matter, we would have little recourse as a result of this off-label use. In that event, our revenue from the commercialization of the compound would likely be adversely affected.

If a third party were to obtain approval to market and sell mecamylamine hydrochloride, TC-5214 could be subject to competition arising from off-label use.

We have licensed patent rights in the United States covering the pharmaceutical composition and methods of use of TC-5214, one of the enantiomers of mecamylamine hydrochloride. We have licensed method of use patent rights, but do not have pharmaceutical composition patent coverage, for mecamylamine hydrochloride. As a result, we may be limited in our ability to prevent others from exploiting mecamylamine, which could have a negative impact on the commercial potential of TC-5214. We believe there are at least three companies that are currently developing mecamylamine: CoMentis, Inc., which we believe is developing mecamylamine in an eye drop formulation as a treatment for age-related macular degeneration, a condition characterized by degeneration of the retina in the eye; AGI Therapeutics Ltd., which we believe is developing mecamylamine for chemotherapy-induced diarrhea; and Cary Pharmaceuticals Inc., which we believe is developing mecamylamine in a fixed dose combination with bupropion as a smoking cessation aid. In addition, mecamylamine is the active ingredient in our approved product Inversine, and a third party could in the future pursue marketing approval of mecamylamine for the forms of hypertension for which Inversine is approved using the abbreviated new drug application process. If any third party were to receive marketing approval for mecamylamine for any indication, physicians could prescribe it for other indications that are not described in the product's labeling or approved by the FDA or foreign regulatory authorities. In particular, in light of its relationship to TC-5214, physicians could potentially prescribe mecamylamine as a treatment for major depression. In that event, if TC-5214 is in the future approved for marketing and sale by the FDA or foreign regulatory authorities, our revenue from the commercialization of TC-5214 would likely be adversely affected.

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

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

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

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

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

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

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

Risks Related to Commercialization

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

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

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

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

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

We currently have limited sales, marketing and distribution experience and no internal sales or distribution capabilities. If we are unable to enter into alliances and 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 focus any future internal sales and marketing resources 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 strategic alliances and collaborations with respect to product candidates for 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 would 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 cannot yet assess the impact of price regulations. As a result, we or our current or potential future collaborators 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 revenue 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 or our current or potential future collaborators 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 cannot yet 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 yet know the level of reimbursement, if any, for any products that we or our current or potential future collaborators 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 or sustain profitability could be affected.

We believe that the efforts of governments and third-party payors to contain or reduce the cost of healthcare will continue to affect the business and financial condition of pharmaceutical and biopharmaceutical companies. A number of legislative and regulatory proposals to change the healthcare system in the United States and other major healthcare markets have been proposed and adopted in recent years. For example, the U.S. Congress has enacted a limited outpatient prescription drug benefit for Medicare recipients as part of the Medicare Prescription Drug, Improvement and Modernization Act of 2003, or the MMA. While the drug benefit established by the MMA may increase demand for any of our products that are successfully developed, if our approved drugs or the approved drugs of any of our current or potential future collaborators are offered as a benefit under any Medicare drug plan, the prices for these drugs will be negotiated with non-governmental organizations and are likely to be lower than prices we might otherwise obtain. If successfully developed, AZD3480 (TC-1734), our product candidate for Alzheimer's disease, cognitive dysfunction in schizophrenia and other conditions characterized by cognitive impairment, could be particularly affected by this law because Alzheimer's disease is a disease that primarily affects the elderly. Non-Medicare third-party payors may also base the price they are willing to pay on the price paid 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 revenue 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 revenue.

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 foreign 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. Pfizer's product Chantix, which is known outside of the United States as Champix, targets NNRs as an aid for smoking cessation. In addition, we believe that several prominent pharmaceutical companies have product candidates that target NNRs in development, including as examples Sanofi-Aventis, with a compound in Phase 2 for Alzheimer's disease, and Abbott Laboratories, with one compound in Phase 2 for Alzheimer's disease and ADHD, a second compound in Phase 2 for neuropathic pain and ADHD and two other compounds in Phase 1 for cognitive disorders or pain indications. Other companies that we believe have active NNR-based programs include AstraZeneca, Eli Lilly, Wyeth, Memory Pharmaceuticals, Critical Therapeutics, NeuroSearch A/S, CoMentis and EnVivo Pharmaceuticals. We expect that we will face increased competition in the future if therapies that target NNRs are further validated and if companies initiate or expand programs focused on NNRs or otherwise enter the CNS market, whether independently or by alliance, collaboration or acquisition.

Any products that we are able to successfully develop and commercialize in the future could be subject to competition from lower priced generic drugs. The manufacturer of a generic product could challenge our patents as invalid or not infringed and subject us to expensive litigation. We do not know if we would prevail in litigation and succeed in keeping the generic product out of the market until our patent protection expires.

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

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

- for mild to moderate Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer/ Eisai, Razadyne from Johnson & Johnson and Exelon from Novartis; in addition, Namenda from Forest Laboratories, which acts by regulating the neurotransmitter glutamate, is marketed for moderate to severe Alzheimer's disease;
- for depression, selective serotonin reuptake inhibitors such as Prozac from Eli Lilly, Paxil from GlaxoSmithKline, Zoloft from Pfizer, Celexa and Lexapro from Forest Laboratories, dual uptake inhibitors such as Effexor from Wyeth and Cymbalta from Eli Lilly and, as an adjunctive treatment, the atypical antipsychotic Abilify from Bristol-Myers Squibb/Otsuka;
- for anxiety disorders, benzodiazepines such as Pfizer's Xanax and Biovail's Ativan, as well as anti-depressants; and
- for neuropathic pain, Pfizer's Lyrica, which is indicated for, among other things, neuropathic pain associated with diabetic peripheral neuropathy and fibromyalgia, and Eli Lilly's Cymbalta, a selective serotonin and norepinephrine reuptake inhibitor indicated for, among other things, diabetic peripheral neuropathic pain.

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 $10 million per occurrence and $10 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 specifically for 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 may in some jurisdictions disseminate under specified conditions articles published in peer-reviewed journals that discuss off-label uses of approved products to physicians. To the extent allowed, we may in the future disseminate peer-reviewed articles on our products to physicians. We do not currently promote Inversine for off-label use in the treatment of any neuropsychiatric disorder. However, if we undertake any promotional activities in the future for Inversine or any other product candidate that we are able to commercialize and our activities fail to comply with these regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities.

Risks Related to Employees and Managing Growth

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

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

The number of our employees and the scope of our operations have grown since we became a public company in 2006 and we expect to continue to grow over the next several years. 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 experience 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

The market price of our common stock may be highly volatile.

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

If our operating results fluctuate significantly, our stock price may decline.

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:

- the timing, receipt and amount of milestone payments from AstraZeneca, GlaxoSmithKline or any of our potential future collaborators;
- the extent to which our research and development activities in the programs that are the therapeutic focus areas of our alliance with GlaxoSmithKline result in the achievement of milestone events under our alliance agreement;
- the duration of our preclinical research collaboration with AstraZeneca;
- our inability, or the inability of AstraZeneca, GlaxoSmithKline or any of our potential future collaborators, to successfully complete clinical trials, or non-clinical studies and assessments, in a timely manner or at all, resulting in a delay in receiving, or a failure to receive, the required regulatory approvals to commercialize our product candidates;
- the timing of regulatory approvals or other regulatory actions;
- general and industry-specific economic conditions that may affect the research and development expenditures of AstraZeneca, GlaxoSmithKline or any of our potential future collaborators; and
- the expiration or termination of agreements with AstraZeneca, GlaxoSmithKline or any of our potential future collaborators, or the execution of new agreements.

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

If our 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 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. 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 owned by our stockholders and available for sale in the public market is limited only to the extent provided under applicable federal securities laws. In addition, we may, in the future, issue additional shares of our common stock to our employees, directors or consultants as compensation, in connection with strategic alliances, collaborations 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.

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

Our executive officers, directors and their affiliates and principal stockholders beneficially own or control approximately 35% of the outstanding shares of our common stock, based on the shares outstanding as of February 29, 2008. Accordingly, our current executive officers, directors and their affiliates and principal stockholders have substantial control over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transactions, as well as our management and affairs. The concentration of ownership may also delay or prevent a change of control of us at a premium price if these stockholders oppose it, even if it would benefit our other stockholders.

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

Provisions of our certificate of incorporation and bylaws could discourage, delay or prevent a merger, acquisition or other change in control that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their 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 66⅔% 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.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We lease approximately 58,000 square feet of laboratory and office space located in the Piedmont Triad Research Park in Winston-Salem, North Carolina. We also have rights exercisable at any time during the

remaining term of the lease to lease additional space in this facility. The term of our lease expires July 31, 2012, and we have a renewal option for an additional five-year term at a rental rate to be mutually determined. The current monthly payment under our lease is approximately $180,000. We believe that our leased facilities, together with our right to lease additional space, are adequate to satisfy our current needs.

Item 3. Legal Proceedings

We are not currently a party to any material pending legal proceedings or aware of any contemplated proceeding against us by any governmental authority.

Item 4. Submission of Matters to a Vote of Security Holders

No matters were submitted to a vote of security holders during the fourth quarter of the fiscal year ended December 31, 2007.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

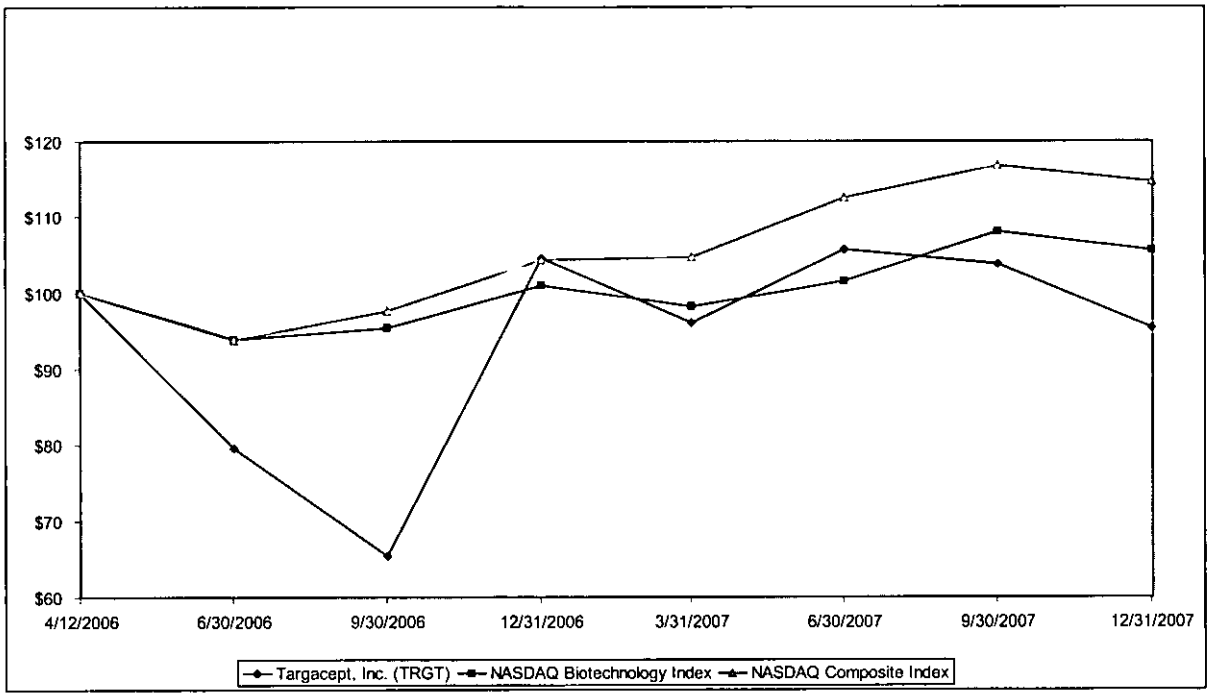
Our common stock began trading on the NASDAQ Global Market (formerly known as the NASDAQ National Market) on April 12, 2006 under the symbol "TRGT." The following table sets forth, for the periods indicated, the high and low sales prices for our common stock, as reported on the NASDAQ Global Market:

	Common Stock	
	High	*Low*
2006:		
Second Quarter	$ 9.00	$6.63
Third Quarter	$ 7.30	$5.26
Fourth Quarter	$ 9.80	$5.50
2007:		
First Quarter	$ 9.91	$7.97
Second Quarter	$10.30	$8.10
Third Quarter	$12.35	$8.71
Fourth Quarter	$10.10	$6.80

Comparative Stock Performance Graph

The following graph compares the cumulative total stockholder return for our common stock with the cumulative total return of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The comparison assumes the investment of $100.00 on April 12, 2006 (the date our common stock was first publicly traded) in each of our common stock, the NASDAQ Composite Index and the NASDAQ Biotechnology Index, assuming the reinvestment of any dividends. We have not paid any dividends on our common stock, and we do not include dividends in the representation of our performance. The stock price performance on the graph below does not necessarily indicate future price performance.

Comparison of Cumulative Total Return
Among Targacept, Inc., the NASDAQ Composite Index
and the NASDAQ Biotechnology Index



	Cumulative Total Return							
	4/12/06	6/30/06	9/30/06	12/31/06	3/31/07	6/30/07	9/30/07	12/31/07
TARGACEPT, INC.	100.00	80.00	65.00	105.00	96.00	106.00	104.00	95.00
NASDAQ COMPOSITE INDEX	100.00	94.00	98.00	104.00	105.00	112.00	117.00	115.00
NASDAQ BIOTECHNOLOGY INDEX	100.00	94.00	95.00	101.00	98.00	101.00	108.00	106.00

Stockholders

As of February 29, 2008, there were approximately 95 holders of record of our common stock.

Dividends

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 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.

Calculation of Aggregate Market Value of Non-Affiliate Shares

For purposes of calculating the aggregate market value of shares of our common stock held by non-affiliates as set forth on the cover page of this annual report, we have assumed that all outstanding shares are held by non-affiliates, except for shares held by our executive officers, directors and 10% or greater stockholders, in each case as of the determination date. This assumption is not intended to constitute an admission that all executive officers, directors and 10% or greater stockholders are, in fact, our affiliates, or that there are not other persons who may be deemed to be our affiliates.

Unregistered Sales of Securities; Issuer Purchases of Equity Securities

None.

Use of Proceeds from Sales of Registered Securities

On April 18, 2006, we sold 5,000,000 shares of our common stock in our initial public offering at a price to the public of $9.00 per share. As part of the offering, we granted the underwriters an over-allotment option to purchase up to an additional 750,000 shares of our common stock from us, which was not exercised. The offer and sale of all of the shares in the offering were registered under the Securities Act of 1933, as amended, pursuant to a registration statement on Form S-1 (File No. 333-131050), which was declared effective by the SEC on April 11, 2006.

After deducting underwriting discounts and commissions of $3.2 million and expenses of $1.1 million payable by us in connection with the offering, our net proceeds from the offering were $40.8 million. Between April 11, 2006 and December 31, 2007, we used approximately $39.4 million of the net proceeds to fund our operating activities, including activities relating to the development of our clinical and preclinical product candidates, and other general corporate purposes. During this period, our research and development expenses comprised approximately 79% of our operating expenses. The remaining approximately $1.4 million in net proceeds have been deposited in highly rated financial institutions in the United States. We have not used any of the net proceeds of the offering to make payments, directly or indirectly, to any of our directors or officers, to any of their associates, to any person owning ten percent or more of any class of our equity securities, or to any of our affiliates.

As noted in Item 1 of Part I of this annual report, we have no current plans to conduct further development of our product candidate TC-2696 and, based on our anticipated development of TC-5214 and our current budget management plans, we do not expect that we will conduct further clinical development of either our product candidate TC-2216 or one of its enantiomers in 2008. As a result, we do not expect that we will use any of the remaining proceeds from our initial public offering to further the development of those product candidates. We expect that we will instead use the proceeds that had been allocated to those product candidates to conduct Phase 1 and Phase 2 clinical development of TC-5214 and TC-6499 and to conduct clinical development of TC-5619 through a Phase 2 clinical proof of concept trial. This represents a change from our planned use of proceeds as described in our final prospectus filed with the SEC pursuant to Rule 424(b).

Item 6. Selected Financial Data.

You should read the following selected financial data together with our financial statements and the related notes included in this annual report and the "Management's Discussion and Analysis of Financial Condition and Results of Operations" section of this annual report. The selected financial data in this section are not intended to replace our financial statements.

We derived the statements of operations data for the years ended December 31, 2007, 2006 and 2005 and the balance sheet data as of December 31, 2007 and 2006 from our audited financial statements, which are included in this annual report. We derived the statements of operations data for the years ended December 31, 2004 and 2003 and the balance sheet data as of December 31, 2005, 2004 and 2003 from our audited financial statements not included in this report. Our historical results for any prior period are not necessarily indicative of the results to be expected for any future period. You should read the notes to our financial statements for an explanation of the method used to determine the number of shares used in computing basic and diluted net loss per share.

	Year Ended December 31,				
	2007	2006	2005	2004	2003
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Net operating revenues	$ 11,576	$ 27,538	$ 1,180	$ 3,738	$ 2,458
Operating expenses:					
Research and development	34,620	21,788	24,252	22,771	18,179
General and administrative	8,013	5,696	4,753	5,163	3,600
Transaction charges	—	—	1,635	—	—
Cost of product sales	715	457	481	198	743
Total operating expenses	43,348	27,941	31,121	28,132	22,522
Loss from operations	(31,772)	(403)	(29,941)	(24,394)	(20,064)
Interest and dividend income	3,837	2,584	1,174	505	791
Interest expense	(138)	(84)	(225)	(132)	(122)
Loss on disposal of fixed assets	—	—	—	(4)	—
Net (loss) income	(28,073)	2,097	(28,992)	(24,025)	(19,395)
Deemed dividend-beneficial conversion feature for Series C redeemable convertible preferred stock issued December 2004	—	—	—	(10,312)	—
Preferred stock accretion	—	(3,333)	(11,238)	(8,744)	(8,341)
Net loss attributable to common stockholders	$ (28,073)	$ (1,236)	$ (40,230)	$ (43,081)	$ (27,736)
Basic and diluted net loss per share applicable to common stockholders	(1.42)	$ (0.09)	$ (153.54)	$ (196.53)	$ (254.33)
Shares used to compute basic and diluted net loss per share	19,720,732	13,595,523	262,013	219,213	109,053

Item 7. 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 included in this annual report. In addition to historical information, the following discussion contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results, performance or experience could differ materially from those indicated by the forward-looking statements due to important factors, risks and uncertainties, including, but not limited to, those set forth under "Cautionary Note Regarding Forward-Looking Statements" in this annual report and under "Risk Factors" in Item 1A of Part I of this annual report.

Overview

Background

We are a biopharmaceutical company engaged in the design, discovery and development of NNR Therapeutics, a new class of drugs for the treatment of multiple diseases and disorders of the central nervous system. Our NNR Therapeutics selectively target a class of receptors known as neuronal nicotinic receptors, or NNRs. We currently have clinical-stage product candidates for target indications generally in three therapeutic areas: cognitive impairment, depression and anxiety, and pain. We also have preclinical programs focused in smoking cessation, addiction, obesity, pain, Parkinson's disease and inflammation. We have a collaboration with AstraZeneca and a strategic alliance with GlaxoSmithKline. We received over $73.0 million in aggregate upfront fees and milestone payments from AstraZeneca and GlaxoSmithKline during 2006 and 2007 and earned an additional $12.3 million in collaboration research and development revenue from our collaboration with AstraZeneca.

Our lead product candidate is a novel small molecule that we have historically referred to as TC-1734 and that our strategic collaborator, AstraZeneca, refers to as AZD3480. AZD3480 (TC-1734) modulates the activity of the α4ß2 NNR. In December 2005, we entered into a collaborative research and license agreement with AstraZeneca AB for the development and worldwide commercialization of AZD3480 (TC-1734) as a treatment for Alzheimer's disease, cognitive dysfunction in schizophrenia and potentially other conditions characterized by cognitive impairment such as ADHD, AAMI and MCI. AstraZeneca is currently conducting two Phase 2b clinical trials of AZD3480 (TC-1734), one in mild to moderate Alzheimer's disease, which is referred to as the "Sirocco" trial, and one in cognitive dysfunction in schizophrenia, which is referred to as the "HALO" trial. Based on information provided to us by AstraZeneca, we expect that both trials will be completed by the end of 2008.

We and AstraZeneca are also conducting a preclinical research collaboration under the agreement that is designed to discover and develop additional compounds that, like AZD3480 (TC-1734), act on the α4ß2 NNR as treatments for conditions characterized by cognitive impairment. AstraZeneca pays us research fees, based on a reimbursement rate specified under the agreement, for research services rendered in the preclinical research collaboration, subject to specified limits. The research term began in January 2006 and has a planned term of four years.

In July 2007, we entered into a product development and commercialization agreement with GlaxoSmithKline. The agreement sets forth the terms of an alliance designed to discover, develop and market product candidates that selectively target specified NNR subtypes in five therapeutic focus areas: pain, smoking cessation, addiction, obesity and Parkinson's disease.

Our other clinical-stage product candidates, in addition to AZD3480 (TC-1734), are described below.

- *TC-5619.* TC-5619 is a novel small molecule that we plan to develop for cognitive dysfunction in schizophrenia and potentially one or more other conditions characterized by cognitive impairment. TC-5619 modulates the activity of the α7 NNR. We are currently conducting a Phase 1 single rising dose clinical trial of TC-5619 and plan to initiate a Phase 1 multiple rising dose clinical trial of

TC-5619 in the second quarter of 2008. Following our completion of Phase 1 clinical development and a Phase 2 clinical proof of concept trial of TC-5619, AstraZeneca has the right to license TC-5619 for any or all of schizophrenia and various conditions characterized by cognitive impairment on terms specified in our agreement.

- *TC-5214.* TC-5214 is one of the two enantiomers of mecamylamine hydrochloride. Enantiomers are mirror images of each other that have the same chemical but potentially different biological properties and together form a chemical mixture known as a racemate. TC-5214 inhibits the activity of various NNR subtypes, including the α4ß2 NNR. We are currently developing TC-5214 as an augmentation treatment for major depression. We initiated a Phase 1 single rising dose clinical trial of TC-5214 in healthy volunteers in the first quarter of 2008.

  In 2006, we completed a Phase 2 clinical trial of the racemate mecamylamine hydrochloride as an augmentation treatment to citalopram hydrobromide, a commonly prescribed treatment for depression marketed as Celexa in the United States, in patients who did not respond adequately to first-line treatment with citalopram. We refer to this treatment combination as TRIDMAC. In our preclinical evaluation, TC-5214 has exhibited a more favorable overall safety and efficacy profile than mecamylamine. We have no current plans to conduct further clinical development of mecamylamine and intend instead to pursue the development of TC-5214.

- *TC-2216.* Our depression and anxiety program also includes the novel small molecule TC-2216. TC-2216 inhibits the activity of the α4ß2 NNR. We completed a Phase 1 single rising dose clinical trial of this product candidate in the first quarter of 2008. We may in the future elect to develop one of the enantiomers of TC-2216 in lieu of further development of TC-2216. However, based on our anticipated development of TC-5214 and our current budget management plans, we do not expect that we will conduct further clinical development of TC-2216 or either of its enantiomers in 2008.

- *TC-6499.* TC-6499 is novel small molecule that we plan to develop as a treatment for neuropathic pain. TC-6499 modulates the activity of the α4ß2 NNR. We initiated a Phase 1 single rising dose clinical trial of TC-6499 in the fourth quarter of 2007. TC-6499 is subject to a contingent future option of GlaxoSmithKline under the terms of our alliance.

We trace our scientific lineage to a research program initiated by R.J. Reynolds Tobacco Company in 1982 to study the activity and effects of nicotine in the body and the function of nicotinic receptors. We were incorporated in 1997 as a wholly owned subsidiary of RJR. In August 2000, we became an independent company when we issued and sold stock to venture capital investors. Since our inception, we have had limited revenue from product sales and have funded our operations principally through the sale of equity securities, revenue from collaboration agreements and grants and equipment and building lease incentive financing. 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, as well as intellectual property prosecution.

We generated net income for the fourth quarter and year ended December 31, 2006 due primarily to the recognition of revenue under our agreement with AstraZeneca upon achievement of a milestone event related to AZD3480 (TC-1734). Except for these periods, we have never been profitable. As of December 31, 2007, we had an accumulated deficit of $164.2 million. We expect to incur substantial losses for the foreseeable future as we expand our clinical trial activity, as our clinical-stage and preclinical product candidates advance through the development cycle, as we progress our programs in the therapeutic focus areas of our alliance with GlaxoSmithKline and our preclinical research collaboration with AstraZeneca and as we invest in additional product opportunities and research programs and expand our research and development infrastructure. Clinical trials and preclinical studies are time-consuming, expensive and may never yield a product that will generate revenue.

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.

Revenue

As of December 31, 2007, we had received $32.0 million in aggregate upfront fees and milestone payments from AstraZeneca under our collaboration agreement, which include a $10.0 million initial fee, a $20.0 million payment upon achievement of a milestone event related to AZD3480 (TC-1734) and a $2.0 million payment to secure the future right to license TC-5619. In addition, as of December 31, 2007, we had recognized $12.3 million in collaboration research and development revenue for research services that we provided in our preclinical research collaboration. We are eligible to receive other payments of up to $249.0 million, contingent upon the achievement of development, regulatory and first commercial sale milestones for AZD3480 (TC-1734) for Alzheimer's disease, cognitive dysfunction in schizophrenia and ADHD, and stepped double-digit royalties on any future product sales. If AZD3480 (TC-1734) is developed under the agreement for other indications characterized by cognitive impairment, we would also be eligible to receive payments contingent upon the achievement of development, regulatory and first commercial sale milestones for AZD3480 (TC-1734) for those indications. Under the terms of a sponsored research agreement and a subsequent license agreement between us and the University of Kentucky Research Foundation, or UKRF, we are required to pay to UKRF a low single digit percentage of any of these amounts that we receive from AstraZeneca. As a result, we paid UKRF $758,000 in January 2007.

In addition, if TC-5619 achieves clinical proof of concept and AstraZeneca elects to license TC-5619, the agreement provides for AstraZeneca to make a $40.0 million payment to us and to assume responsibility for and fund all future development and commercialization. In that event, we would be eligible to receive additional payments of up to $226.0 million, contingent upon the achievement of development, regulatory and first commercial sale milestones, as well as stepped double-digit royalties on any future product sales.

As of December 31, 2007, we had received $41.0 million in aggregate payments from GlaxoSmithKline under our alliance agreement. These payments include a $20.0 million initial payment, the purchase of 1,275,502 shares of our common stock for an aggregate purchase price of $15.0 million and a $6.0 million payment upon our initiation of a Phase 1 clinical trial of TC-6499. We are also eligible to receive other payments of up to $1.5 billion, contingent on the achievement of specified discovery, development, regulatory and commercial milestones in the five therapeutic focus areas of the alliance, as well as stepped double-digit royalties on any future sales of products licensed by GlaxoSmithKline.

Our collaboration agreement with AstraZeneca can be terminated by AstraZeneca if we breach the agreement and do not cure the breach or without cause upon 90 days notice given any time after the earlier of the end of the term of the preclinical research collaboration or four years after the research term began. Our alliance agreement with GlaxoSmithKline can be terminated by GlaxoSmithKline if we breach the agreement in certain respects and do not cure the breach or without cause upon 90 days notice.

We acquired rights to Inversine, which is our only product approved by the U.S. Food and Drug Administration, or FDA, for marketing, in August 2002. Inversine is approved for the management of moderately severe to severe essential hypertension and uncomplicated cases of malignant hypertension, which are high blood pressure disorders. However, we believe that Inversine is prescribed predominantly for the treatment of neuropsychiatric disorders, such as Tourette's syndrome, autism and bipolar disorder. Sales of Inversine generated net revenue of $518,000 for the year ended December 31, 2007, $585,000 for the year ended December 31, 2006 and $681,000 for the year ended December 31, 2005. We do not have or use a sales force or promote Inversine.

From time to time we seek and are awarded grants or work to be performed under grants awarded to third-party collaborators from which we derive revenue. As of December 31, 2007, we are a named subcontractor under a grant awarded to The California Institute of Technology by the National Institute on Drug Abuse, or NIDA, part of the National Institutes of Health, to fund research on innovative NNR-based approaches to the

development of therapies for smoking cessation. We expect to receive approximately $1.1 million in the aggregate over a five-year period that began in July 2006 in connection with the NIDA grant. Funding for awards under federal grant programs is subject to the availability of funds as determined annually in the federal appropriations process.

A substantial portion of our revenue depends on the conduct of research and the successful achievement of milestone events in the development of AZD3480 (TC-1734) under our agreement with AstraZeneca and on the successful achievement of research and development-related milestone events under our agreement with GlaxoSmithKline. Our revenue may vary substantially from quarter to quarter and year to year.

Research and Development Expenses

Since our inception, we have focused our activities on our drug discovery and development programs. We record research and development expenses as they are incurred. Research and development expenses represented approximately 80% of our total operating expenses for the year ended December 31, 2007 and 78% of our total operating expenses for each of the years ended December 31, 2006 and 2005. Research and development expenses include costs associated with:

- the employment of personnel involved in our drug discovery and development activities;
- research and development facilities and equipment;
- costs to conduct research activities under the α4ß2 research collaboration with AstraZeneca;
- the screening, identification and optimization of product candidates;
- the development and enhancement of our proprietary databases and computer-based molecular design technologies, which we refer to collectively as Pentad;
- formulation and chemical development;
- production of clinical materials, including fees paid to contract manufacturers;
- preclinical animal studies, including the costs to engage third-party research organizations;
- clinical trials, including fees paid to contract research organizations to monitor and oversee some of our trials;
- quality assurance activities;
- compliance with FDA regulatory requirements;
- consulting, license and sponsored research fees paid to third parties;
- depreciation of capital assets used to develop our products; and
- stock options or other stock-based compensation granted to personnel in research and development functions.

Under the terms of our collaboration agreement, beginning in January 2006, AstraZeneca assumed substantially all development costs for AZD3480 (TC-1734), except for costs that we incurred to complete the Phase 2 clinical trial of AZD3480 (TC-1734) in AAMI that we completed in March 2006 and costs associated with any work outside of the planned development program that we agree to conduct. For the year ended December 31 2005, we incurred $6.7 million for third-party services in connection with the development of AZD3480 (TC-1734). The following table shows, for the periods presented, total amounts that we incurred for third-party services in connection with preclinical studies, pharmaceutical development, clinical supplies and clinical trials, as applicable for our other most advanced product candidates:

Product Candidate	Year ended December 31, 2007	2006	2005
		(in thousands)	
TC-5619	$2,937	$ 903	$ —
TC-5214	3,926	—	—
Mecamylamine hydrochloride	—	555	1,067
TC-2216	1,687	1,691	903
TC-6499	1,566	—	—

In December 2007, we announced that TC-2696, a product candidate for acute post-operative pain, did not meet the primary endpoints in a Phase 2 clinical trial in third molar extraction patients. We have no current plans to conduct further development of TC-2696. We incurred total amounts for third party-services in connection with TC-2696 of $1.1 million for the year ended December 31, 2007, $891,000 for the year ended December 31, 2006 and $879,000 for the year ended December 31, 2005.

We use our research and development personnel and other resources across several programs. We currently have clinical, preclinical and early research programs ongoing, and many of our costs are not specifically attributable to a single program. Instead, these costs are directed to broadly applicable research efforts. Accordingly, we do not account for internal research and development costs on a program-by-program basis.

We have not received FDA or foreign regulatory marketing approval for any of our product candidates that are in development. Our current and future expenditures on 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 an alliance or collaboration in which our collaborator assumes responsibility for funding 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 program as a result of a variety of factors, including:

- the number of subjects who participate in the trials;
- the number and locations of sites included in the trials;
- the length of time required to enroll trial subjects;
- the patient populations for the trials;
- the duration of the trials and subject follow-up;
- the costs of producing supplies of the product candidates needed for 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.

In addition, our strategy includes entering into alliances and collaborations with third parties to participate in the development and commercialization of some of our product candidates. In situations in which third parties have responsibility for or authority 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 alliances or collaborations or how such arrangements would affect our development plans or capital requirements. Because of this uncertainty, and because of the uncertainties related to clinical trials and related activities as described above, we are unable to determine the duration and completion costs of our research and development programs or whether or when we will generate revenue from the commercialization and sale of any of our product candidates in development.

General and Administrative Expenses

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

Income Taxes

We generated net income for the year ended December 31, 2006 due primarily to the recognition of milestone-based revenue derived under our agreement with AstraZeneca. We incurred net operating losses for 2007 and for each other year since inception and consequently have not paid federal, state or foreign income taxes in any period. As of December 31, 2007, we had net operating loss carryforwards of $113.1 million for each of federal and state income tax purposes. We also had $3.9 million in research and development federal income tax credits as of December 31, 2007. The federal net operating loss carryforwards begin to expire in 2020. The state net operating loss carryforwards begin to expire in 2015. The research and development tax credits begin to expire in 2021. Utilization of the net operating loss carryforwards and credits may be subject to a substantial annual limitation due to ownership change limitations provided by Section 382 of the Internal Revenue Code of 1986, as amended, and similar state provisions. When an ownership change, as defined by Section 382, occurs, an annual limitation is imposed on a company's use of net operating loss and credit carryforwards attributable to periods before the change. As a result of a series of stock issuances, we had such an ownership change in November 2002. Consequently, an annual limitation is imposed on our use of net operating loss and credit carryforwards that are attributable to periods before the change, and a portion of the net operating loss carryforwards described above may potentially not be usable by us. We could experience additional ownership changes in the future. 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 is uncertain.

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 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. In addition, our reported financial condition and results of operations could vary if new accounting standards are enacted that are applicable to our business.

Our significant accounting policies are described in Note 2 to our audited financial statements for the year ended December 31, 2007 included in this annual report. We believe that our accounting policies relating to revenue recognition, accrued expenses and stock-based compensation are the most critical to understanding and evaluating our reported financial results. We have identified these policies as critical because they both are important to the presentation of our financial condition and results of operations and require us to make judgments and estimates on matters that are inherently uncertain and may change in future periods. For more information regarding these policies, you should refer to Note 2 to our audited financial statements included in this annual report.

Revenue Recognition

We use revenue recognition criteria in Staff Accounting Bulletin No. 101, *Revenue Recognition in Financial Statements*, or SAB 101, as amended by Staff Accounting Bulletin No. 104, *Revision of Topic 13*, or SAB 104. We derive a substantial portion of our revenues from our collaboration with AstraZeneca and our alliance with GlaxoSmithKline and expect that we will continue to derive a substantial portion of our revenues from these relationships over at least the next several years.

Our collaboration and alliance agreements contain multiple elements, including: upfront fees, which may include initial payments upon commencement of the contractual relationship, payment representing a common stock purchase premium or payment to secure a right for a future license; research fees for ongoing research and development; payments associated with the achievement of discovery, development, regulatory and commercial milestones; and rights to receive royalties based on specified percentages of any net product sales. In determining the accounting for collaboration and alliance agreements, we follow the provisions of Emerging Issues Task Force, or EITF, Issue 00-21, *Revenue Arrangements with Multiple Deliverables,* or EITF 00-21. EITF 00-21 provides guidance on whether an arrangement involves a single unit of accounting or separate units of accounting for revenue recognition purposes and, if separate units, how to allocate amounts received in the arrangement. If a collaboration or alliance agreement involves separate units of accounting, we determine the revenue recognition applicable to each unit.

We defer recognition of non-refundable upfront fees and amortize them over the estimated term of our performance obligations or, where our collaborator has substantially all research and development responsibility, over the estimated research and development period. The estimated research and development period may be adjusted from time to time to take into account any delays or acceleration in the development of the applicable product candidate or any extension or shortening of the applicable performance period. Any such delay or acceleration in the development of a product candidate, or extension or shortening of a performance period, could result in further deferral of revenue or acceleration in the recognition of deferred revenue. As of December 31, 2007, all amounts that we have received from AstraZeneca and GlaxoSmithKline are non-refundable.

We recognize collaboration research and development revenue from research services performed under our collaboration agreements as research is performed and related expenses are incurred.

We recognize revenue for non-refundable payments that are based on the achievement of discovery, development, regulatory and commercial milestones upon achievement of the milestone event if all of the following conditions are met:

- achievement of the milestone event was not reasonably assured at the inception of the arrangement;
- substantive effort is involved to achieve the milestone event; and
- the amount of the milestone payment appears reasonable in relation to the effort expended, the other milestone payments in the arrangement and the related risk associated with achievement of the milestone event.

If any of these conditions are not met, we would defer recognition of the milestone payment and recognize the payment on a straight-line basis over the estimated term of our performance obligations or, where our collaborator has substantially all research and development responsibility, over the estimated research and development period.

We recognize revenue for specific research and development costs that are reimbursable under our agreement with AstraZeneca, such as third-party manufacturing costs for drug material, in accordance with EITF Issue 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent*, and EITF Issue 01-14, *Income Statement Characterization of Reimbursements Received for "Out-of-Pocket" Expenses Incurred*. We reflect the revenue associated with these reimbursable amounts as a component of collaboration revenue and we reflect the costs associated with these reimbursable amounts as a component of research and development expenses.

Under our collaboration agreement with AstraZeneca, we received an initial fee of $10.0 million in February 2006. Based on the agreement terms and consideration of fair value, we allocated $5.0 million of the initial fee to the α4ß2 research collaboration. Upon effectiveness of the agreement in January 2006, we commenced recognizing the $5.0 million as revenue over the planned four-year term of the research collaboration. We deferred recognition of the remaining $5.0 million of the initial fee, which we allocated to the AZD3480 (TC-1734) license grants, until AstraZeneca made its determination in December 2006 to proceed with further development of AZD3480 (TC-1734). Beginning in January 2007, we commenced recognizing the previously deferred $5.0 million of the initial fee ratably over the expected remaining five-year development period for AZD3480 (TC-1734).

AstraZeneca's December 2006 determination to proceed with further development of AZD3480 (TC-1734) triggered a $20.0 million milestone payment to us. Based on the criteria of SAB 101, we recognized this amount as revenue in the fourth quarter of 2006. We received the milestone payment in January 2007.

In November 2007, AstraZeneca made a $2.0 million payment to us to secure the right to license to TC-5619 following our completion of Phase 1 clinical development and a Phase 2 clinical proof of concept trial pursuant to an agreed development plan. Beginning in November 2007, we commenced recognizing the $2.0 million payment ratably over the expected development period to clinical proof of concept.

We recorded research fees that we received from AstraZeneca during 2006 while it conducted additional clinical and non-clinical studies of AZD3480 (TC-1734) as deferred revenue, as we could have been required to repay the amount received. Following AstraZeneca's determination in December 2006 to proceed with further development of AZD3480 (TC-1734), the research fees became non-refundable and we recognized as revenue all research fees that were previously deferred. In January 2007, we commenced recognizing all research fees under our agreement with AstraZeneca as the research is performed and related expenses are incurred.

Under our alliance agreement and related stock purchase agreement with GlaxoSmithKline, GlaxoSmithKline made an initial payment to us of $20.0 million. GlaxoSmithKline also purchased 1,275,502 shares of our common stock for an aggregate purchase price of $15.0 million, which resulted in an aggregate deemed premium of $3.5 million based on the closing price of our common stock on the trading day immediately preceding the date that the alliance was announced. In July 2007, we commenced recognizing the initial payment and deemed premium as revenue on a straight-line basis over the estimated term of our research and early development performance obligations under the agreement.

In December 2007, we initiated a Phase 1 clinical trial of TC-6499, triggering a $6.0 million milestone payment to us from GlaxoSmithKline. We determined the milestone payment did not meet all of the conditions required for immediate revenue recognition. Specifically, based on the status of development of TC-6499 as of the inception of the agreement, we determined that achievement of the milestone event was reasonably assured. Consequently, we recorded the $6.0 million payment as deferred revenue and, in December 2007, commenced recognizing such amount on a straight-line basis over the estimated term of our research and early development

performance obligations under the agreement. If in the future we achieve any event that gives rise to a milestone payment to us under our agreement with GlaxoSmithKline, we anticipate that we would determine the milestone payment to meet the necessary conditions for immediate revenue recognition.

Accrued Expenses

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of actual cost. The majority of our service providers invoice us monthly in arrears for services performed. We make estimates of our accrued expenses as of each balance sheet date in our financial statements based on facts and circumstances known to us. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. 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 or manage clinical trials on our behalf or with contract manufacturers that produce clinical trial material. 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 enrollment of subjects, the completion of clinical trial milestones and the production of drug substance or drug product. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we will adjust the accrual accordingly. If we do not identify costs that we have begun to incur or if we underestimate or overestimate the level of services performed or the costs of these services, our actual expenses could differ from our estimates.

Stock-Based Compensation

Effective January 1, 2005, we adopted Statement of Financial Accounting Standard No. 123(R), *Share-Based Payment*, or SFAS 123R. Under SFAS 123R, we recognize the grant-date fair value of stock options and other stock-based compensation issued to employees and non-employee directors over the requisite service periods, which are typically the vesting periods. We currently use the Black-Scholes-Merton formula to estimate grant-date fair value and expect to continue to use this valuation model in the future. We adopted SFAS 123R using the modified-prospective-transition method, which required us to record compensation expense for the non-vested portion of previously issued awards that were outstanding at January 1, 2005, and any awards issued or modified after January 1, 2005, taking into account projected forfeitures. We recorded stock-based compensation expense related to stock options granted to employees and directors of $2.7 million for the year ended December 31, 2007, $919,000 for the year ended December 31, 2006, and $690,000 for the year ended December 31, 2005. As of December 31, 2007, we had $5.1 million in total unrecognized compensation cost related to non-vested stock-based compensation arrangements, which we expect to recognize over a weighted average period of 1.7 years.

Because there was no established market for our common stock prior to our initial public offering in April 2006, the fair value of our common stock underlying stock options and other stock-based compensation granted

to employees and non-employee directors was determined by our board of directors based upon information available as of the grant dates. We engaged an independent valuation firm in January 2006 to perform a retrospective analysis to determine the deemed fair market value of our common stock as of March 31, 2005 for accounting purposes. This retrospective analysis relied on income-based and market-based valuation methodologies. The fair market value of our common stock as of March 31, 2005 determined by the independent valuation firm provided additional support for the determination that options granted on or about that date had an exercise price at or above fair market value.

Results of Operations

Years ended December 31, 2007 and December 31, 2006

Net Operating Revenues

Net operating revenues decreased by $15.9 million to $11.6 million for the year ended December 31, 2007, from $27.5 million for the year ended December 31, 2006. The decrease was primarily attributable to a reduction of $17.6 million in milestones and license fees from collaborations to $3.5 million for 2007, from $21.1 million for 2006. The lower milestones and license fees from collaborations for 2007 was attributable to our recognition of $20.0 million upon AstraZeneca's December 2006 determination to proceed with further development of AZD3480 (TC-1734), a milestone event under our agreement with AstraZeneca for which we received payment in January 2007, partially offset by a $2.4 million increase for 2007 in the recognition of deferred license fee revenue from payments received from AstraZeneca and GlaxoSmithKline. No milestone events related to AZD3480 (TC-1734) were achieved under the agreement during 2007.

The decrease in net operating revenues was also attributable to a reduction of $565,000 in grant revenue to $222,000 for 2007, from $787,000 for 2006. The lower grant revenue was attributable to the expiration on September 30, 2006 of the cooperative agreement awarded to us in 2003 by the National Institute of Standards and Technology, or NIST, through its Advanced Technology Program, or ATP, to fund the development of sophisticated molecular simulation software. The grant revenue for the 2007 period related solely to activities in connection with our work as a subcontractor under the NIDA grant awarded to The California Institute of Technology to fund research on innovative NNR-based approaches to the development of therapies for smoking cessation.

The reductions in milestones and license fees from collaborations and grant revenue were partially offset by an increase of $2.3 million in collaboration research and development revenues to $7.3 million for 2007, from $5.0 million for 2006. The increase in collaboration research and development revenues was primarily attributable to an increase of $2.2 million in research fees to $6.9 million for 2007, from $4.7 million for 2006, resulting from additional services rendered by us in the preclinical research collaboration that we and AstraZeneca are conducting as product candidates in the collaboration progressed into more advanced stages of research. Based on the objectives and budget for the preclinical research collaboration with AstraZeneca for 2008, we anticipate that our collaboration research and development revenue generated under the collaboration will increase in 2008 as compared to 2007. However, AstraZeneca has the right to terminate the preclinical research collaboration effective three years after the research term began, upon at least six months notice. The research term began in January 2006. If AstraZeneca terminates the preclinical research collaboration prior to completion of the planned four-year term, our collaboration research and development revenue for 2009 periods would likely be adversely affected.

In future periods, we are eligible to receive additional research fees, license fees and milestone payments under our agreements with AstraZeneca and GlaxoSmithKline. The amount of research fees, license fees and milestone fees will depend on the extent and success of our research and development activities, the timing and achievement of the discovery, development, regulatory and commercial milestone events, whether AstraZeneca exercises its future right to license TC-5619 and whether GlaxoSmithKline exercises any options to license product candidates that arise under the agreement. In particular, we expect that a development-related event for

each of AZD3480 (TC-1734) and TC-6499 may be completed during 2008 that, if resulting in a successful outcome, would give rise to milestone payments under our collaboration agreement with AstraZeneca or our alliance agreement with GlaxoSmithKline. If either or both of these milestone events are achieved, we anticipate that our net operating revenues for 2008 would increase substantially as compared to 2007.

Net sales of Inversine decreased by $67,000 to $518,000 for the year ended December 31, 2007, from $585,000 for the year ended December 31, 2006. The decrease resulted from a reduction in the volume of sales of Inversine. We believe that the substantial majority of Inversine sales are derived from prescriptions written by a very limited number of physicians. If any of these physicians were to change their prescribing habits, it would likely cause sales of Inversine to decrease further. We do not anticipate any significant increase in the volume of Inversine sales. In light of our increased cost of product sales as described below, we instituted a 62% price increase for Inversine effective at the beginning of 2008. As of December 31, 2007, the effect of the price increase on net sales of Inversine is not determinable.

Research and Development Expenses

Research and development expenses increased by $12.8 million to $34.6 million for the year ended December 31, 2007, from $21.8 million for the year ended December 31, 2006. The increase for 2007 in research and development expenses reflects additional contracted research and development services, including clinical trial activities, formulation and clinical trial material production activities and pharmacology and toxicology studies, for our product candidates TC-5214, TC-5619 and TC-6499 of $3.9 million, $2.0 million and $1.6 million, respectively, as well as increased research and development personnel-related expenses. The increase in contracted research and development services was partially offset by reduced spending on mecamylamine hydrochloride following our completion of a Phase 2 clinical trial in the second half of 2006. The increase in research and development expenses for 2007 also reflects an increase of $4.8 million to $21.2 million in salary and benefits, occupancy costs and third-party service, supply and infrastructure costs incurred in connection with activities under the AstraZeneca collaboration and our other preclinical programs, including those in the therapeutic focus areas of our alliance with GlaxoSmithKline.

We expect that our research and development expenses will increase for 2008 and future periods as we expand our clinical trial activity, as our clinical-stage and preclinical product candidates advance through the development cycle, as we progress our programs in the therapeutic focus areas of our alliance with GlaxoSmithKline and our preclinical research collaboration with AstraZeneca and as we invest in additional product opportunities and research programs and expand our research and development infrastructure. In particular, we expect that, for 2008, our research and development expenses will increase substantially as compared to 2007 as a result of the anticipated clinical development expenses associated with TC-5214, TC-5619 and TC-6499 and higher research and development personnel-related expenses as a result of our growth.

General and Administrative Expenses

General and administrative expenses increased by $2.3 million to $8.0 million for the year ended December 31, 2007, from $5.7 million for the year ended December 31, 2006. The increase was principally attributable to an increase in stock-based compensation expense, a non-cash item, of $1.6 million as a result of compensatory stock option grants and greater occupancy, salary and benefit expenses and recruitment costs associated with an increase in our number of employees for 2007 as compared to 2006.

Cost of Product Sales

Our cost of product sales are those costs related directly to the sale of Inversine. Cost of product sales increased by $258,000 to $715,000 for the year ended December 31, 2007, from $457,000 for the year ended December 31, 2006. The increase primarily reflects the denial of our request for a waiver of FDA establishment fees for Inversine.

The FDA assesses product and establishment fees for marketed products each year for the twelve-month period beginning October 1. Payment is required in advance, but companies can request a waiver after making payment. In assessing waiver requests, the FDA considers whether the company is pursuing innovative drug products or technology and whether the fees would present a significant barrier to the company's ability to develop, manufacture or market innovative drug products or technology. Prior to 2007, we had historically requested and received a waiver of the FDA fees with respect to Inversine.

The waiver of the FDA fees that we had historically received with respect to Inversine has in the past resulted in lower cost of product sales. In March 2007, we received notice that the FDA, citing our increased revenue and cash assets, had denied our request for a waiver of the $206,000 in product and establishment fees that were assessed by the FDA and paid by us in 2006. In contrast, in 2006 our request for a waiver of the product and establishment fees that were assessed by the FDA and paid by us in 2005 was granted by the FDA with respect to the establishment fees, although it was denied with respect to the product fees.

The increase in our cost of product sales for 2007 resulted in a negative gross margin for Inversine of $197,000. The amount of product and establishment fees for the twelve months beginning October 1, 2007 is $261,000. We have not applied for a waiver of these fees and do not expect that we will file for a waiver of product and establishment fees in future years. Accordingly, we expect that these fees will impact our cost of product sales for 2008 and future periods. Effective at the beginning of 2008, we instituted a 62% price increase for Inversine, with the objective of offsetting the impact of these fees for 2008 and subsequent periods.

Interest Income

Interest income increased by $1.2 million to $3.8 million for the year ended December 31, 2007, from $2.6 million for the year ended December 31, 2006. The increase was attributable to a substantially higher average cash balance during 2007 following receipt of a $20.0 million milestone payment from AstraZeneca in January 2007, $35.0 million in payments from GlaxoSmithKline upon entering into our alliance in July 2007, and $8.0 million in additional payments from AstraZeneca and GlaxoSmithKline in the fourth quarter of 2007, partially offset by lower short-term interest rates.

Interest Expense

Interest expense increased by $54,000 to $138,000 for the year ended December 31, 2007, from $84,000 for the year ended December 31, 2006. The increase was attributable to higher average principal balance under a loan facility used to finance laboratory equipment, furniture and other capital equipment purchases following $2.0 million in borrowings against the facility in June 2007, as well as the expiration in April 2007 of the grace period for interest under a loan from the City of Winston-Salem.

Accretion of Dividends on Preferred Stock

Accretion of dividends on our convertible preferred stock was $3.3 million for the year ended December 31, 2006. Upon completion of our initial public offering in April 2006, all of our outstanding shares of convertible preferred stock converted into shares of common stock and there was no further accretion of dividends to be recorded.

Years ended December 31, 2006 and December 31, 2005

Net Operating Revenues

Net operating revenues increased by $26.3 million to $27.5 million for the year ended December 31, 2006, from $1.2 million for the year ended December 31, 2005. The increase was primarily attributable to $26.2 million in revenue derived under our agreement with AstraZeneca. We had no collaboration-based revenue for 2005. The revenue derived under our AstraZeneca agreement and recognized in 2006 included the following components.

- We recognized milestone-based revenue of $20.0 million as a result of the determination communicated to us by AstraZeneca in December 2006 to proceed with further development of AZD3480 (TC-1734), which triggered a $20.0 million milestone payment that we received in January 2007.
- We recognized collaboration research and development revenue of $4.7 million for services rendered by us to AstraZeneca pursuant to an agreed research plan for the preclinical research collaboration that we and AstraZeneca are conducting.
- We recognized $1.1 million of the $10.0 million initial fee that we received in February 2006 from AstraZeneca. The remaining $8.9 million of the initial fee was recorded as deferred revenue at December 31, 2006.
- We recognized revenue of $347,000 in connection with payments that we made to third parties for research and manufacturing services that are reimbursable under the agreement.

Grant revenue increased by $288,000 to $787,000 for the year ended December 31, 2006, from $499,000 for the year ended December 31, 2005. The grant revenue for 2006 related to work performed under the cooperative agreement awarded to us in 2003 by NIST through the ATP, and to work performed in connection with our subcontract under the grant awarded to The California Institute of Technology by NIDA. In contrast, the grant revenue for 2005 related only to work performed in connection with the ATP award. The increase for 2006 reflects $98,000 in additional research activity by us under the cooperative agreement and revenue of $190,000 for work performed in connection with the NIDA grant.

Net sales of Inversine decreased by $96,000 to $585,000 for the year ended December 31, 2006, from $681,000 for the year ended December 31, 2005. The decrease resulted from a reduction in the volume of sales of Inversine.

Research and Development Expenses

Research and development expenses decreased by $2.5 million to $21.8 million for the year ended December 31, 2006, from $24.3 million for the year ended December 31, 2005. The reduction in research and development expenses was primarily attributable to a decrease of $6.7 million in research and development expenses relating to AZD3480 (TC-1734) for 2006 as a result of the assumption by AstraZeneca of development costs for that product candidate under our collaboration agreement, partially offset by an increase in research and development expenses relating to TC-2216 and TC-5619 of $788,000 and $903,000, respectively, for 2006 to conduct additional preclinical safety studies and formulation work. The decrease was also partially offset by increased salary and benefit expenses for research and development personnel for 2006 and increased third-party service, supply and infrastructure costs incurred in connection with our $\alpha 4\beta 2$ research collaboration with AstraZeneca that we initiated in January 2006.

General and Administrative Expenses

General and administrative expenses increased by $943,000 to $5.7 million for the year ended December 31, 2006, from $4.8 million for the year ended December 31, 2005. The increase was principally attributable to higher awards made in 2006 under our annual cash incentive bonus program.

Transaction Charge

During the year ended December 31, 2005 we recorded expense of $1.6 million in connection with a public offering that we terminated in March 2005. There were no similar expenses for the year ended December 31, 2006 as all costs that we incurred in connection with our initial public offering that we completed in April 2006 were recorded as prepaid expenses pending the completion of the offering and were offset against the proceeds from the offering upon completion.

Cost of Product Sales

For the year ended December 31, 2006, our cost of product sales decreased by $24,000 to $457,000 from $481,000 for the year ended December 31, 2005. All of these costs related to sales of Inversine.

Interest Income

Interest income increased by $1.4 million to $2.6 million for the year ended December 31, 2006, from $1.2 million for the year ended December 31, 2005. The increase was attributable to a substantially higher average cash balance during 2006 following completion of our initial public offering in April 2006 and, to a lesser extent, higher short-term interest rates.

Interest Expense

Interest expense decreased by $141,000 to $84,000 for the year ended December 31, 2006, from $225,000 for the year ended December 31, 2005. The decrease was attributable to reduced indebtedness in 2006 resulting from our payment in August 2005 of the outstanding balance on a $1.3 million convertible promissory note to The Stanley Medical Research Institute and a lower principal balance under a loan facility used to finance laboratory equipment, furniture and other capital equipment purchases.

Accretion of Dividends on Preferred Stock

Accretion of dividends on our convertible preferred stock was $3.3 million for the year ended December 31, 2006 as compared to $11.2 million for the year ended December 31, 2005. Upon completion of our initial public offering in April 2006, all of our outstanding shares of convertible preferred stock converted into shares of common stock and there was no further accretion of dividends to be recorded.

Liquidity and Capital Resources

Sources of Liquidity

From August 2000 when we became an independent company until completion of our initial public offering in April 2006, we financed our operations and internal growth primarily through private placements of convertible preferred stock. We derived aggregate net proceeds of $121.8 million from these private placements. In April 2006, we completed an initial public offering of our common stock, consisting of 5.0 million shares of our common stock at a price of $9.00 per share. After deducting underwriting discounts and commissions and offering expenses, our net proceeds from the offering were $40.8 million. We have also received funding from: upfront fees, payments for research and development services and payments upon achievement of milestone events under collaboration and alliance agreements; equipment and building lease incentive financing; government grants and interest income. We began generating revenue from product sales of Inversine in December 2002. To date, the net contribution from Inversine sales has not been a significant source of cash and we do not expect it to be a significant source in the future.

In July 2007, we entered into a product development and commercialization agreement and related stock purchase agreement with GlaxoSmithKline. Pursuant to these agreements, GlaxoSmithKline made an initial payment to us of $20.0 million and purchased 1,275,502 shares of our common stock for an aggregate purchase price of $15.0 million.

In December 2005, we entered into a collaboration agreement with AstraZeneca. In January 2006, the agreement became effective and we began conducting research for which we are eligible to receive research fees. AstraZeneca paid us an initial fee of $10.0 million in February 2006, $20.0 million in January 2007 upon achievement of a milestone event related to AZD3480 (TC-1734), $2.0 million in November 2007 to secure the future right to license TC-5619 and $8.3 million in aggregate research fees in the period from February 2006 through December 31, 2007.

We have a loan facility with R.J. Reynolds Tobacco Holdings, Inc. used to finance laboratory equipment, furniture and other capital equipment purchases. We entered into the loan facility in May 2002 and amended it in January 2004 to permit us borrow up to an additional $2.0 million in 2004 in up to three separate borrowings. We borrowed $1.0 million in April 2004 and $973,000 in December 2004 under the amended facility to finance equipment. The April 2004 borrowing bears a fixed interest rate of 5.87%, is payable in 48 equal monthly installments and matures in April 2008. The December 2004 borrowing bears a fixed interest rate of 6.89%, is payable in 48 monthly installments and matures in January 2009. In June 2006, we further amended the facility to permit us to borrow an additional $2.0 million on or before June 30, 2007 in up to three separate borrowings. We borrowed the additional $2.0 million in two tranches in June 2007. The first June 2007 tranche is in the amount of $1.6 million, accrues interest at 7.36% and is repayable in monthly payments of $39,000 through the maturity date of June 1, 2011. The second June 2007 tranche is in the amount of $400,000, accrues interest at 7.48% and is repayable in monthly payments of $10,000 through the maturity date of July 1, 2011. All borrowings under the facility are secured by specified tangible fixed assets determined sufficient by the lender at the time of disbursement. As of December 31, 2007, the outstanding principal balance under the loan facility was $2.2 million. There is no additional borrowing capacity available to us under the loan facility.

In April 2002, we received a $500,000 loan from the City of Winston-Salem. Under the terms of the loan, there was no interest accrual or payment due until the fifth anniversary. Following expiration of the five-year grace period in April 2007, the outstanding principal balance of the loan bears interest at an annual interest rate of 5% and is payable in 60 equal monthly installments of $9,000. As of December 31, 2007, the outstanding principal balance under the loan was $431,000.

Our cash, cash equivalents and short-term investments were $87.0 million as of December 31, 2007 and $54.2 million as of December 31, 2006.

Cash Flows

Net cash provided by operating activities was $24.8 million for the year ended December 31, 2007, as compared to net cash used in operating activities of $9.9 million for the year ended December 31, 2006, a difference of $34.7 million. Our net loss increased by $30.2 million to $28.1 million for the year ended December 31, 2007, from net income of $2.1 million for the year ended December 31, 2006. The increased net loss was more than offset by adjustments for changes in working capital and non-cash charges for 2007. The working capital adjustments that provided the largest source of cash for 2007 were an increase of $28.0 million in our deferred license fee revenue balance, a decrease of our collaboration revenue and accounts receivable balance of $19.2 million and an increase of $1.9 million in accounts payable and accrued expenses. The $28.0 million increase in deferred license fee revenue is comprised of our receipt of the $20.0 million initial payment from GlaxoSmithKline and the aggregate deemed premium of $3.5 million resulting from GlaxoSmithKline's purchase of 1,275,502 shares of our common stock in July 2007, the $6.0 million in deferred revenue received from GlaxoSmithKline upon our initiation of a Phase 1 clinical trial of TC-6499 and the $2.0 million payment received from AstraZeneca to secure the future right to license TC-5619, partially offset by recognition of $3.5 million of deferred license fee revenue during 2007. The $19.2 million reduction in collaboration revenue and accounts receivable is primarily due to our receipt in January 2007 of the $20.0 million development milestone triggered by AstraZeneca's December 2006 determination to proceed with further development of AZD3480 (TC-1734). The $1.9 million increase in accounts payable and accrued expenses is due to increased clinical trial activity and the advancement of our programs in the therapeutic focus areas of our alliance with

GlaxoSmithKline. The difference in net cash provided by operating activities also reflects an increase in stock-based compensation expense of $1.8 million to $2.7 million for 2007, from $919,000 for 2006.

Net cash used in operating activities decreased by $16.3 million to $9.9 million for the year ended December 31, 2006, from $26.2 million for the year ended December 31, 2005. We had net income of $2.1 million for the year ended December 31, 2006, as compared to a net loss of $29.0 million for the year ended December 31, 2005, a difference of $31.1 million. Our net income for 2006 was more than offset by adjustments for changes in working capital. These adjustments included a $23.2 million increase in our collaboration revenue and accounts receivable balance, partially offset by an $8.9 million increase in our deferred license fee revenue balance and a $1.8 million increase in accounts payable and accrued expenses. The $23.2 million increase in collaboration revenue and accounts receivable related to revenues generated under our collaboration agreement with AstraZeneca and recognized upon AstraZeneca's December 2006 determination to proceed with further development of AZD3480 (TC-1734). The $8.9 million increase in deferred license fee revenue represents the $10.0 million initial fee paid by AstraZeneca, net of $1.1 million of such initial fee recognized during 2006. The $1.8 million increase in accounts payable and accrued expenses is a result of higher accrued liability for awards under our annual cash incentive bonus program, a liability recorded for amounts due UKRF with respect to AZD3480 (TC-1734) and additional project-related payables.

Net cash used in investing activities increased by $13.0 million to $26.3 million for the year ended December 31, 2007, from $13.3 million for 2006. Cash used in investing activities primarily reflects the portion of our cash that we allocate to, and the timing of purchases and maturities of, our short-term investments. Additionally, we purchased $4.9 million of property and equipment for 2007, an increase of $3.8 million from $1.1 million in property and equipment purchases for 2006. The increased purchases were primarily for equipment required to support our research and development operations and furniture and equipment purchases in connection with the expansion of our leased facilities effective in January 2007. Net cash used in investing activities increased by $13.0 million to $13.3 million for the year ended December 31, 2006, from $250,000 for 2005. The increase was primarily attributable to the timing of purchases and maturities of short-term investments, as well as an increase of $826,000 to $1.1 million in property and equipment purchases for 2006, from $250,000 for 2005. The increased purchases were primarily to acquire equipment for use in expanding our internal research and development activities.

Net cash provided by financing activities decreased by $27.0 million to $13.1 million for the year ended December 31, 2007, from $40.1 million for the year ended December 31, 2006. The decrease was primarily attributable to our receipt of $40.8 million in net proceeds as a result of the completion in April 2006 of our initial public offering, partially offset by the receipt of $11.5 million from GlaxoSmithKline for the purchase of 1,275,502 shares of common stock in July 2007, excluding the effect of the $3.5 million deemed premium resulting from such purchase, and $2.0 million in incremental net borrowings under our loan facility in 2007. Net cash used in financing activities was $1.7 million for the year ended December 31, 2005. The $41.8 million increase for 2006 reflects the net proceeds of our initial public offering in April 2006 described above, as well as $1.6 million in decreased net borrowings in 2006 under our loan facility, partially offset by $612,000 in proceeds from the issuance of redeemable convertible preferred stock during 2005.

Funding Requirements

As of December 31, 2007, we had an accumulated deficit of $164.2 million. We expect 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, duration, results and cost of clinical trials, as well as non-clinical studies and assessments, of our product candidates;
- the timing, receipt and amount of milestone and other payments from AstraZeneca, GlaxoSmithKline and potential future collaborators;

- the extent to which our research and development activities in the programs that are the therapeutic focus areas of our alliance with GlaxoSmithKline result in the achievement of milestone events under our alliance agreement;
- the duration of our preclinical research collaboration with AstraZeneca;
- 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 alliances, collaborations and licensing or other arrangements on terms favorable to us;
- the costs to satisfy our obligations under existing and potential future alliances and collaborations;
- the timing, receipt and amount of sales or royalties, if any, from our potential products; and
- the extent and scope of our general and administrative expenses.

We anticipate that implementing our strategy will require substantial increases in our capital expenditures and other capital commitments as we expand our clinical trial activity, as our clinical-stage and preclinical product candidates advance through the development cycle, as we progress our programs in the therapeutic focus areas of our alliance with GlaxoSmithKline and our preclinical research collaboration with AstraZeneca and as we invest in additional product opportunities and research programs and expand our research and development infrastructure. We do not expect our existing capital resources to be sufficient to enable us to fund the completion of the development of any of our product candidates. We currently expect our existing capital resources, which include $29.1 million in net proceeds from our public offering of common stock in January 2008, to be sufficient to fund our operations at least through the first half of 2010. However, our operating plan may change as a result of many factors, including those described above. We may need additional funds sooner than planned to meet operational needs and capital requirements for product development.

We do not expect to generate sufficient cash from our operations to sustain our business for the foreseeable future. We expect our continuing operating losses to result in increases in our cash required to fund operations over the next several quarters and years. To the extent our capital resources are insufficient to meet future capital requirements, we will need to finance future cash needs through public or private equity offerings, debt financings, alliances, collaborations, or licensing arrangements. Additional equity or debt financing, alliances, collaborations or 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 or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently. Additionally, any future equity funding may dilute the ownership of our stockholders.

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 alliance 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 fixed contractual obligations as of December 31, 2007:

	Payments Due by Period				
Contractual Obligations	**Total**	**Less Than 1 Year**	**1-3 Years**	**3-5 Years**	**More Than 5 Years**
Long-term debt obligations	$ 2,604,470	$ 918,596	$1,258,831	$ 427,043	$—
Operating lease obligations	9,897,203	2,159,390	4,318,780	3,419,033	—
Other contractual obligations	7,914,697	7,856,105	53,828	4,764	—
Total	$20,416,370	$10,934,091	$5,631,439	$3,850,840	$—

The amounts of long-term debt obligations reflected in the above table do not include $4,811,000 of indebtedness under a loan agreement that we entered into with a bank in March 2008. The March 2008 loan is repayable in equal monthly installments of $112,000 over four years. The amounts of long-term debt obligations reflected in the above table include $1,788,000 of indebtedness outstanding as of December 31, 2007 under two of the tranches of a loan facility with R.J. Reynolds Tobacco Holdings, Inc. that were repaid in full in March 2008 with the proceeds of the initial loan from the bank.

The amounts of other contractual obligations reflected in the above table include obligations to purchase drug product or drug substance, to compensate clinical investigators, clinical trial sites and contract research organizations contingent on the performance of services in connection with clinical trials and to compensate contract research organizations contingent on the performance of non-clinical research and development services. The amount of other contractual obligations for 2008 reflected in the above table also includes annual maintenance fees or other fixed payments required under our technology license agreements. Our technology license agreements are generally terminable by us on short notice. As a result, the annual maintenance fees or other fixed payments under those agreements are not included in other contractual obligations in the above table after 2008. The amounts of other contractual obligations for all periods reflected in the above table exclude contingent royalty payments that we may be required to pay under our technology license agreements and other contingent payments that we may become required to make under our technology license agreements upon achievement of specified development, regulatory or commercial milestones.

Recent Developments

In March 2008, we entered into a loan agreement with a bank pursuant to which we initially borrowed $4.8 million and have up to an aggregate of $500,000 in additional borrowing capacity available to fund the purchase of equipment, furnishings, software and other fixed assets and enable the refinancing of our existing loan facility with R.J. Reynolds Tobacco Holdings, Inc. Under the terms of the agreement, borrowings under the loan facility may be made in up to four term loans and each loan bears interest, at our election, at either (1) the One Month LIBOR Rate plus 2.15% per annum, as adjusted monthly on the first day of each month, or (2) a fixed rate to be calculated by the bank at the closing of the loan equal to the bank's fixed rate cost of funds index corresponding to the term of the loan plus 2.15% per annum. The agreement provides for repayment of each loan over a period determined by us, not to exceed four years, in equal monthly installments of principal and interest and for a first priority security interest in favor of the bank in the assets acquired with the proceeds of the loan facility.

Our initial loan under the loan facility bears interest at a rate of 5.231% per annum and is repayable in equal monthly installments of $112,000 through the maturity date of March 1, 2012. We used $1.7 million of the proceeds from the loan to pay and satisfy in full the principal and interest outstanding on two of the tranches under our existing loan facility and granted a first priority security interest in favor of the bank in assets previously acquired with the proceeds of those tranches.

In January 2008, we completed a public stock offering, consisting of 4.4 million shares of our common stock sold at a price of $7.07, the closing bid price on the date of the offering. Our net proceeds from the offering were $29.1 million after deducting underwriting discounts and commissions and offering expenses.

As of December 31, 2007, we had $23.0 million of our short-term investment portfolio invested in AAA rated and government-guaranteed auction rate securities. Auction rate securities are designed to provide liquidity via an auction process that resets the applicable interest rate at predetermined calendar intervals, usually every 28 days. In January 2008, auctions for all of the auction rate securities that we owned as of December 31, 2007 were successful. We continued to maintain auction rate securities in our short-term investment portfolio after the successful auctions, and the credit concerns that currently exist in the capital markets led to failed auctions later in the first quarter of 2008. As of March 12, 2008, we owned $16.8 million of auction rate securities for which auctions failed. These securities may not be readily redeemable to cash unless and until a future auction is successful. Based on our ability to access our cash and other short-term investments, we do not anticipate that the current illiquidity of auction rate securities that we own will affect our ability to operate our business as planned in 2008.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Recent Accounting Pronouncements

In September 2006, the Financial Accounting Standards Board, or FASB, issued SFAS No. 157, *Fair Value Measurements*, or SFAS 157. SFAS 157 defines fair value, establishes a framework for measuring fair value in accordance with accounting principles generally accepted in the United States, or GAAP, and expands disclosures about fair value measurements. The provisions of SFAS 157 are effective for fiscal years beginning after November 15, 2007. We do not expect SFAS 157 to have a material impact on our financial results.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities*, or SFAS 159. SFAS 159 allows entities to choose voluntarily, at specified election dates, to measure many financial assets and liabilities (as well as certain non-financial instruments) at fair value. The election can be made only on an instrument-by-instrument basis and is irrevocable. The provisions of SFAS 159 are effective for fiscal years beginning after November 15, 2007. We do not expect SFAS 159 to have a material impact on our financial results.

In July 2007, the EITF reached consensus on Issue 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services to be Used in Future Research and Development Activities*, or EITF 07-3. EITF 07-3 concluded that non-refundable advance payments for goods or services to be received in the future for use in research and development activities should be deferred and capitalized and that the capitalized amounts should be expensed as the goods are delivered or the services are rendered. If an entity's expectations change such that it does not expect it will need the goods to be delivered or the services to be rendered, capitalized nonrefundable advance payments should be charged to expense. EITF 07-3 is effective for new contracts entered into during fiscal years beginning after December 15, 2007, including interim periods within those fiscal years. We do not expect EITF 07-3 to have a material impact on our financial results.

In November 2007, the EITF reached consensus on Issue 07-1, *Accounting for Collaboration Arrangements*, or EITF 07-1. The consensus requires collaborators to present the result of activities for which they act as the principal on a gross basis and report any payments received from or made to other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational and consistently applied accounting policy election. EITF 07-1 is effective for annual periods beginning after December 15, 2008 and will be applied retrospectively for collaborative arrangements existing at the effective date of the consensus as a change in accounting principle. We do not expect EITF 07-1 to have a material impact on our financial results.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

The primary objective of our investment activities is to preserve our capital to fund operations. We also seek to maximize income from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of cash equivalents and short-term investments in a variety of securities of high credit quality. As of December 31, 2007, we had cash, cash equivalents and short-term investments of $87.0 million. 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 estimate that an immediate and uniform 10% increase in market interest rates from levels as of December 31, 2007 would not have a material impact on the total fair value of our portfolio.

We contract for the conduct of some of our clinical trials and other research and development and manufacturing activities with contract research organizations, investigational sites and manufacturers in Europe and India. We may be subject to exposure to fluctuations in foreign currency exchange rates in connection with these agreements. If the average Euro/U.S. dollar or Indian Rupee/U.S. dollar exchange rate were to strengthen or weaken by 10% against the exchange rate as of December 31, 2007, we estimate that the impact on our financial position, results of operations and cash flows would not be material. We do not hedge our foreign currency exposures.

We have not used derivative financial instruments for speculation or trading purposes.

Item 8. Financial Statements and Supplementary Data.

INDEX TO THE FINANCIAL STATEMENTS

TARGACEPT, INC.

TARGACEPT, INC.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of
Targacept, Inc.

We have audited the accompanying balance sheets of Targacept, Inc. as of December 31, 2007 and 2006, 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, 2007. 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, 2007 and 2006, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2007, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), Targacept, Inc.'s internal control over financial reporting as of December 31, 2007, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated March 12, 2008 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Greensboro, North Carolina
March 12, 2008

TARGACEPT, INC.

BALANCE SHEETS

	December 31, 2007	December 31, 2006
ASSETS		
Current assets:		
Cash and cash equivalents	$ 53,403,092	$ 41,744,363
Short-term investments	33,636,687	12,445,193
Collaboration revenue and accounts receivable	4,197,479	23,367,959
Inventories	140,413	173,693
Prepaid expenses	1,035,324	1,121,698
Total current assets	92,412,995	78,852,906
Property and equipment, net	6,114,555	2,040,355
Intangible assets, net of accumulated amortization of $204,555 and $166,791 at December 31, 2007 and 2006, respectively	437,445	475,209
Total assets	$ 98,964,995	$ 81,368,470
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 2,295,912	$ 1,982,180
Accrued expenses	5,460,643	3,889,114
Current portion of long-term debt	918,596	593,330
Current portion of deferred rent incentive	42,068	234,877
Current portion of deferred license fee revenue	6,478,772	2,250,000
Total current liabilities	15,195,991	8,949,501
Long-term debt, net of current portion	1,685,874	816,072
Deferred rent incentive, net of current portion	150,742	—
Deferred license fee revenue, net of current portion	30,348,093	6,604,167
Total liabilities	47,380,700	16,369,740
Commitments and contingencies		
Stockholders' equity (deficit):		
Common stock, $0.001 par value, 100,000,000 shares authorized; 20,503,419 and 19,132,233 shares issued and outstanding at December 31, 2007 and 2006, respectively	20,504	19,132
Capital in excess of par value	215,798,337	201,141,257
Accumulated deficit	(164,234,546)	(136,161,659)
Total stockholders' equity (deficit)	51,584,295	64,998,730
Total liabilities and stockholders' equity (deficit)	$ 98,964,995	$ 81,368,470

See accompanying notes.

TARGACEPT, INC.

STATEMENTS OF OPERATIONS

	Year ended December 31,		
	2007	2006	2005
Operating revenues:			
Collaboration research and development	$ 7,288,196	$ 5,019,057	$ —
Milestones and license fees from collaborations	3,547,788	21,145,833	—
Product sales, net	518,295	585,318	681,285
Grant revenue	221,652	787,356	498,632
Net operating revenues	11,575,931	27,537,564	1,179,917
Operating expenses:			
Research and development (including stock-based compensation of $844,669, $643,373 and $457,670 in 2007, 2006 and 2005, respectively)	34,619,494	21,787,873	24,251,463
General and administrative (including stock-based compensation of $1,902,036, $275,147 and $232,784 in 2007, 2006 and 2005, respectively)	8,012,594	5,696,129	4,753,464
Transaction charges	—	—	1,634,973
Cost of product sales	715,424	457,254	480,933
Total operating expenses	43,347,512	27,941,256	31,120,833
Loss from operations	(31,771,581)	(403,692)	(29,940,916)
Other income (expense):			
Interest income	3,836,599	2,584,294	1,174,398
Interest expense	(137,905)	(84,073)	(225,005)
Total other income (expense)	3,698,694	2,500,221	949,393
Net (loss) income	(28,072,887)	2,096,529	(28,991,523)
Preferred stock accretion	—	(3,332,705)	(11,237,976)
Net loss attributable to common stockholders	$(28,072,887)	$(1,236,176)	$(40,229,499)
Basic and diluted net loss attributable to common stockholders per share	$ (1.42)	$ (0.09)	$ (153.54)
Weighted average common shares outstanding—basic and diluted	19,720,732	13,595,523	262,013

See accompanying notes.

TARGACEPT, INC.

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

	Redeemable Convertible Preferred Stock			Common Stock		Capital in Excess of Par Value	Common Stock Warrants	Accumulated Deficit	Total Stockholders' Equity (Deficit)
	Series A	Series B	Series C	Shares	Amount				
Balances at December 31, 2004	$ 30,166,741	$ 39,622,161	$ 101,988,994	256,816	$ 257	$ 11,573,677	$ 213,710	$(134,753,508)	$(122,965,864)
Issuance of 496,132 shares of Series C redeemable convertible preferred stock at $1.21 per share	—	—	612,281	—	—	—	—	—	—
Issuance of 13,611 shares of common stock related to exercise of stock options	—	—	—	13,611	13	23,773	—	—	23,786
Stock-based compensation	—	—	—	—	—	690,454	—	—	690,454
Accreted redemption value for common stock warrants attached to Series A redeemable convertible preferred stock	42,744	—	—	—	—	—	—	(42,744)	(42,744)
Accreted redemption value for Series A, Series B and Series C redeemable convertible preferred stock	1,627,500	2,137,744	7,429,988	—	—	—	—	(11,195,232)	(11,195,232)
Net loss and comprehensive loss	—	—	—	—	—	—	—	(28,991,523)	(28,991,523)
Balances at December 31, 2005	$ 31,836,985	$ 41,759,905	$ 110,031,263	270,427	$ 270	$ 12,287,904	$ 213,710	$(174,983,007)	$(162,481,123)
Issuance of 29,793 shares of common stock related to exercise of stock options	—	—	—	29,793	30	61,608	—	—	61,638
Stock-based compensation	—	—	—	—	—	918,520	—	—	918,520
Accreted redemption value for Series A, Series B, and Series C redeemable convertible preferred stock	483,729	635,385	2,213,591	—	—	—	—	(3,332,705)	(3,332,705)
Net proceeds from initial public offering	—	—	—	5,000,000	5,000	40,770,013	—	—	40,775,013
Conversion of redeemable convertible preferred stock	(32,320,714)	(42,395,290)	(112,244,854)	13,832,013	13,832	147,103,212	—	39,843,814	186,960,858
Expiration of common stock warrants	—	—	—	—	—	—	(213,710)	213,710	—
Net income and comprehensive income	—	—	—	—	—	—	—	2,096,529	2,096,529
Balances at December 31, 2006	—	—	—	19,132,233	$19,132	$201,141,257	—	$(136,161,659)	$ 64,998,730
Issuance of 95,684 shares of common stock related to exercise of stock options	—	—	—	95,684	96	432,137	—	—	432,233
Stock-based compensation	—	—	—	—	—	2,746,705	—	—	2,746,705
Net proceeds from sale of 1,275,502 shares of common stock to GlaxoSmithKline	—	—	—	1,275,502	1,276	11,478,238	—	—	11,479,514
Net loss and comprehensive loss	—	—	—	—	—	—	—	(28,072,887)	(28,072,887)
Balances at December 31, 2007	—	—	—	20,503,419	$20,504	$215,798,337	—	$(164,234,546)	$ 51,584,295

See accompanying notes.

TARGACEPT, INC.

STATEMENTS OF CASH FLOWS

	Year ended December 31,		
	2007	2006	2005
Operating activities			
Net (loss) income	$ (28,072,887)	$ 2,096,529	$(28,991,523)
Adjustments to reconcile net (loss) income to net cash provided by (used in) operating activities:			
Depreciation and amortization	907,162	820,920	803,185
Stock-based compensation expense	2,746,705	918,520	690,454
Recognition of deferred rent incentive	(42,067)	(402,647)	(402,647)
Changes in operating assets and liabilities, excluding the effects from acquired assets and liabilities:			
Collaboration revenue and accounts receivable	19,170,480	(23,249,796)	366,402
Inventories	33,280	(131,753)	60,700
Prepaid expenses and accrued interest receivable	237,444	(646,219)	998,595
Accounts payable and accrued expenses	1,885,261	1,848,002	228,318
Deferred license fee revenue	27,972,698	8,854,167	—
Net cash provided by (used in) operating activities	24,838,076	(9,892,277)	(26,246,516)
Investing activities			
Purchase of investments	(151,751,107)	(41,191,431)	(25,500,000)
Proceeds from sale of investments	130,408,543	29,000,000	25,500,000
Purchase of property and equipment	(4,943,598)	(1,075,987)	(250,247)
Net cash used in investing activities	(26,286,162)	(13,267,418)	(250,247)
Financing activities			
Proceeds from issuance of notes payable	2,000,000	406,967	—
Principal payments on notes payable and long-term debt	(804,932)	(1,190,862)	(2,363,350)
Proceeds from issuance of redeemable convertible preferred stock, net of transaction costs	—	—	612,281
Proceeds from issuance of common stock	11,911,747	40,836,651	23,786
Net cash provided by (used in) financing activities	13,106,815	40,052,756	(1,727,283)
Net increase (decrease) in cash and cash equivalents	11,658,729	16,893,061	(28,224,046)
Cash and cash equivalents at beginning of period	41,744,363	24,851,302	53,075,348
Cash and cash equivalents at end of period	$ 53,403,092	$ 41,744,363	$ 24,851,302

See accompanying notes.

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 NNR Therapeutics™, a new class of drugs for the treatment of multiple diseases and disorders of the central nervous system. The Company's NNR Therapeutics selectively target neuronal nicotinic receptors, or NNRs. Its facilities are located in Winston-Salem, North Carolina.

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 mature within three months from the date of purchase.

Short-Term Investments

In accordance with the Company's investment policy, surplus cash is invested with high credit quality financial institutions in money market accounts, certificates of deposit and student loan auction rate securities. The Company determines the appropriate classification of marketable securities at the time of purchase and reevaluates such designation as of each balance sheet date. All marketable securities entered into during 2007 and 2006 were classified as available-for-sale. Interest income on investments, as well as realized gains and losses, are included in "Interest income." The cost of securities sold is based on the specific identification method.

Student loan auction rate securities are variable rate debt instruments that have a contractual maturity of approximately 20 to 40 years. However, interest rates are reset and securities are re-auctioned after approximately 28 days. Even though the stated maturity dates of these investments may be more than one year beyond the balance sheet date, the Company has classified all student loan auction rate securities as short-term investments. In accordance with Accounting Research Bulletin No. 43, Chapter 31, *Working Capital – Current Assets and Current Liabilities*, the Company views its entire available-for-sale portfolio as available for use in its current operations. The student loan auction rate securities owned by the Company at December 31, 2007 were rated AAA by a major credit rating agency and guaranteed by the Federal Family Education Loan Program. Based upon the Company's history with the student loan auction rate securities market, the Company had a reasonable expectation as of December 31, 2007 that these investments could be redeemed at any of the regularly scheduled 28-day auctions. Accordingly, the Company believed as of December 31, 2007 that the risk that these investments could not be redeemed within a year was minimal. All of the $23,000,000 of student loan auction rate securities owned by the Company as of December 31, 2007 successfully re-auctioned in January 2008. See Note 18 for a discussion of events related to auction rate securities held by the Company that occurred after December 31, 2007.

Collaboration Revenue and Accounts Receivable

Substantially all of the Company's collaboration revenue is related to the collaboration and alliance agreements discussed in Note 15. Substantially all of the Company's accounts receivable are related to such collaboration and alliance agreements and trade sales of its approved product Inversine®. All of the Company's trade accounts receivable are due from customers located within the United States. The Company makes judgments with respect to the collectability of trade accounts receivable based on historical experience and current economic trends. Actual collections could differ from those estimates.

2. Summary of Significant Accounting Policies—(continued)

During 2007, 2006 and 2005, the Company recognized revenue of $10,836,000, $26,165,000 and $0, respectively, or 94%, 95% and 0% of net revenue, respectively, from the collaboration and alliance agreements discussed in Note 15.

Inventories

Inventories are stated at the lower of cost or market. Cost is determined by the weighted average method and consists of materials and manufacturing costs.

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 3-10 years. Lab equipment is typically depreciated over 3-5 years, office furniture and fixtures are typically depreciated over 5-10 years, and leasehold improvements are typically amortized over the lesser of the asset life or the lease term.

Intangible assets consist of licensed patent rights assigned from Layton Bioscience, Inc. The intangible assets are being amortized to research and development expense on a straight-line basis over the remaining useful life of the patents, or a period of 17 years from the date of acquisition.

The Company assesses the net realizable value of its long-lived assets and evaluates such assets for impairment whenever events or changes in business circumstances indicate that the carrying amount of an asset may not be recoverable. An impairment would be recognized when estimated undiscounted future cash flows expected to result from the use of the asset and its eventual disposition are less than its carrying amount. An impairment, if recognized, would be based on the excess of the carrying value of the impaired asset over its fair value. Through December 31, 2007, there has been no such impairment.

Patents

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

Research and Development Expense

Research and development costs are expensed as incurred and include salaries of, and stock-based compensation for, personnel involved in research and development activities, contractor fees, administrative expenses and allocations of research-related overhead costs. Administrative expenses and research-related overhead costs included in research and development expense 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 the cost-sharing agreements described in Note 15.

2. Summary of Significant Accounting Policies—(continued)

Accrued Expenses

The Company records accruals based on estimates of the services received, efforts expended and amounts owed pursuant to contracts with clinical trial centers, contract research organizations and other service providers. In the normal course of business, the Company contracts with third parties to perform various clinical trial and development 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 production of drug substance or drug product, the successful recruitment of subjects, the completion of portions of a 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 are recognized based on the Company's estimate of the degree of completion of the event or events specified in the specific contract.

Transaction Charges

In the first quarter of 2005, the Company recognized $1,635,000 for expenses incurred in connection with a terminated public offering.

Deferred Rent Incentive

In August 2002, the Company received $2,013,000 as an incentive to lease its current facility. Through December 31, 2006, the incentive was recognized on a straight-line basis over the initial five-year term of the lease as a reduction to the lease expense. In January 2007, the Company renewed its lease for its current facility through July 2012 and began recognizing the remaining incentive over the renewal term. The Company recognized $42,000 of the incentive during 2007 and $403,000 of the incentive during 2006 and 2005.

Fair Value of Financial Instruments

The carrying amounts of cash and cash equivalents, short-term investments, accounts receivable, accounts payable and accrued expenses are considered to be representative of their respective fair values. At December 31, 2006, the Company estimated the fair value of long-term debt using discounted cash flows based on its incremental borrowing rates for similar debt. The fair value of long-term debt was $1,402,000 at December 31, 2006, as compared to the book value of $1,409,000. The difference between fair value and book value was attributable to the benefit of the interest grace period for the Company's loan from the city of Winston-Salem. During 2007, the interest grace period for the loan from the City of Winston-Salem expired, and the Company began making interest payments consistent with market rates. Therefore, at December 31, 2007 the carrying value of long-term debt is representative of the fair value.

Credit Risk

Financial instruments that potentially subject the Company to credit risk consist principally of cash, short-term investments and collaboration revenue and accounts receivable. The Company places its cash and cash equivalents with high credit quality financial institutions. The Company has established guidelines for investment of its excess cash designed to emphasize safety, liquidity and preservation of capital. At December 31, 2007 and 2006, the Company had deposits with high credit quality financial institutions in excess of federally insured limits of approximately $53,200,000 and $41,588,000, respectively.

2. Summary of Significant Accounting Policies—(continued)

Revenue Recognition

The Company uses revenue recognition criteria in Staff Accounting Bulletin No. 101, *Revenue Recognition in Financial Statements*, or SAB 101, as amended by Staff Accounting Bulletin No. 104, *Revision of Topic 13*, or SAB 104.

In determining the accounting for collaboration agreements, the Company follows the provisions of Emerging Issues Task force, or EITF, Issue 00-21, *Revenue Arrangements with Multiple Deliverables*, or EITF 00-21, for multiple element revenue arrangements. EITF 00-21 provides guidance on whether an arrangement that involves multiple revenue-generating activities or deliverables should be divided into separate units of accounting for revenue recognition purposes and, if this division is required, how the arrangement consideration should be allocated among the separate units of accounting. If the arrangement constitutes separate units of accounting according to the EITF's separation criteria, a revenue recognition policy must be determined for each unit. If the arrangement constitutes a single unit of accounting, the revenue recognition policy must be determined for the entire arrangement.

Collaboration research and development revenue is earned and recognized as research is performed and related expenses are incurred. Non-refundable upfront fees, which may include initial payments upon commencement of the contractual relationship, payment representing a common stock purchase premium or payment to secure a right for a future license, are recorded as deferred licensed fee revenue and recognized into revenue as milestone and license fees from collaborations on a straight-line basis over the expected development period, to the extent such fees are attributable to a specific licensed product candidate, or otherwise over the expected period of the Company's performance obligations.

Revenue for non-refundable payments based on the achievement of collaboration milestones is recognized as revenue when the milestones are achieved if all of the following conditions are met: (1) achievement of the milestone event was not reasonably assured at the inception of the arrangement; (2) substantive effort is involved to achieve the milestone event; and (3) the amount of the milestone payment appears reasonable in relation to the effort expended, the other milestone payments in the arrangement and the related risk associated with achievement of the milestone event. If any of these conditions is not met, the milestone payment is deferred and recognized on a straight-line basis over the expected period of the Company's performance obligations.

Revenues for specific research and development costs that are reimbursable under collaboration agreements are recognized in accordance with EITF Issue 99-19, *Reporting Revenue Gross as a Principal Versus Net as an Agent*, and EITF Issue 01-14, *Income Statement Characterization of Reimbursements Received for "Out-of-Pocket" Expenses Incurred*. The revenue associated with these reimbursable amounts is reflected as a component of collaboration revenue and the costs associated with these reimbursable amounts is reflected as a component of research and development expense.

Product sales revenue is recorded when goods are shipped, at which point title has passed, net of allowances for returns and discounts. Revenues from grants are recognized as the Company performs the work and incurs reimbursable costs in accordance with the objectives of the award.

Shipping and Handling Costs

During 2007, 2006 and 2005, $215,000, $191,000 and $175,000 of shipping and handling costs, respectively, were included in cost of product sales.

2. Summary of Significant Accounting Policies—(continued)

Income Taxes

The liability method is used in accounting for income taxes as required by Statement of Financial Accounting Standards, or SFAS, No. 109, *Accounting for Income Taxes*, or SFAS 109. 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.

On January 1, 2007, the Company adopted Financial Accounting Standards Interpretation No. 48, *Accounting for Uncertainty in Income Taxes*, or FIN 48. FIN 48 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements in accordance with SFAS 109. FIN 48 prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. FIN 48 also provides guidance on de-recognition, classification, interest and penalties, accounting in interim periods, disclosures and transition. The Company's policy is to classify any interest recognized in accordance with FIN 48 as interest expense and to classify any penalties recognized in accordance with FIN 48 as an expense other than income tax expense. The adoption of FIN 48 did not have a material effect on the Company's financial statements.

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*, or SFAS 128. Under the provisions of SFAS 128, basic net loss per share attributable to common stockholders, or 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, or 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. The Company has excluded all common share equivalents from the calculation of net loss per share attributable to common stockholders because their effect is antidilutive for the periods presented. As a result, historical Diluted EPS is identical to historical Basic EPS for the periods presented.

Initial Public Offering and Pro Forma Information

On April 18, 2006, the Company completed an initial public offering, or IPO, of 5,000,000 shares of its common stock at a price of $9.00 per share. The Company's net proceeds from the IPO, after deducting underwriters' discounts and commissions and offering expenses payable by the Company, were $40,775,000. The Company's common stock began trading on the NASDAQ Global Market (formerly known as the NASDAQ National Market) on April 12, 2006.

2. Summary of Significant Accounting Policies—(continued)

Upon completion of the IPO, all outstanding shares of the Company's Series A, Series B, and Series C redeemable convertible preferred stock, discussed in Note 9, automatically converted into shares of common stock and all outstanding warrants expired unexercised. Unaudited pro forma Basic EPS and Diluted EPS is computed using the weighted average number of common shares outstanding, including the pro forma effects of the automatic conversion of all outstanding shares of redeemable convertible preferred stock into shares of the Company's common stock effective upon the completion of the IPO as if such conversion had occurred at the date of the original issuance.

The following table sets forth the computation of Basic EPS and Diluted EPS:

	Year ended December 31,		
	2007	2006	2005
Historical			
Numerator:			
Net loss attributable to common stockholders	$(28,072,887)	$(1,236,176)	$(40,229,499)
Denominator:			
Weighted-average common shares outstanding	19,720,732	13,595,523	262,013
Basic and diluted net loss per share attributable to common stockholders	$ (1.42)	$ (0.09)	$ (153.54)
Pro forma (unaudited)			
Numerator:			
Net (loss) income attributable to common stockholders	$(28,072,887)	$ 2,096,529	$(28,991,523)
Denominator:			
Shares used above	19,720,732	13,595,523	262,013
Pro forma adjustments to reflect assumed conversion of preferred stock and shares issued upon completion of IPO, on a weighted average basis	—	4,054,865	13,806,169
Shares used to compute pro forma basic net (loss) income per share attributable to common stockholders	19,720,732	17,650,388	14,068,182
Pro forma adjustments to reflect effects of dilutive stock options outstanding, on a weighted average basis	—	904,628	—
Shares used to compute pro forma diluted net (loss) income per share attributable to common stockholders	19,720,732	18,555,016	14,068,182
Pro forma basic and diluted net (loss) income per share attributable to common stockholders:			
Basic	$ (1.42)	$ 0.12	$ (2.06)
Diluted	$ (1.42)	$ 0.11	$ (2.06)

2. Summary of Significant Accounting Policies—(continued)

The Company has excluded all outstanding stock options and warrants from the unaudited pro forma calculation of net (loss) income per share attributable to common stockholders for 2007 and 2005 because such securities are antidilutive. For 2006, the dilutive effects of outstanding stock options have been included in the unaudited pro forma calculation. The potentially dilutive securities consist of the following on a weighted average basis:

	December 31,		
	2007	2006	2005
Outstanding stock options	2,628,087	1,924,628	1,466,715
Redeemable convertible preferred stock	—	4,054,865	13,806,169
Outstanding warrants	—	63,043	215,054
Total	2,628,087	6,042,536	15,487,938

Stock-Based Compensation

The Company has two stock-based incentive plans, the 2000 Equity Incentive Plan of Targacept, Inc., as amended and restated, or the 2000 Plan, and the Targacept, Inc. 2006 Stock Incentive Plan, as amended and restated, or the 2006 Plan. The 2000 Plan and the 2006 Plan, or the Plans, are described more fully in Note 12.

Effective January 1, 2005, the Company adopted the fair value recognition provisions of SFAS No. 123 (revised 2004), *Share-Based Payment,* or SFAS 123R, using the modified-prospective-transition method. Under that transition method, compensation cost recognized includes: (a) compensation cost for all stock-based payments granted prior to, but not yet vested as of, January 1, 2005, based on the grant date fair value estimated in accordance with the original provisions of SFAS No. 123; (b) compensation cost for all stock-based payments granted subsequent to January 1, 2005, based on the grant date fair value estimated in accordance with the provisions of SFAS 123R; and (c) compensation cost for awards modified on April 7, 2005, based on the modification provisions in accordance with SFAS 123R.

SFAS 123R also requires the benefits of tax deductions in excess of recognized compensation cost to be reported as a financing cash flow, rather than as an operating cash flow as required under pre-existing literature. This requirement reduces net operating cash flows and increases net financing cash flows for periods after adoption. While the Company cannot estimate what those amounts will be in the future (because they depend on, among other things, when employees exercise stock options and the tax deductions available to the Company at those times), no amount of operating cash flows have been recognized for prior periods for excess tax deductions because of net operating losses generated since inception. No financing cash flows have been recognized for periods since adoption for excess tax deductions because the related deferred tax assets are offset by a valuation allowance.

In November 2005, the Financial Accounting Standards Board, or FASB, issued FASB Staff Position, or FSP, No. FAS 123(R)-3, *Transition Election Related to Accounting for the Tax Effects of Share-Based Payment Awards.* This FSP provides an elective alternative transition method for calculating the pool of excess tax benefits available to absorb tax deficiencies recognized subsequent to the adoption of SFAS 123R and reported in the Statements of Cash Flows. This method includes simplified procedures to establish the beginning balance of the pool of excess tax benefits and to determine the subsequent effect on the pool and cash flows resulting from the tax effects of employee stock-based compensation awards that were outstanding upon adoption of SFAS 123R. The Company has elected to adopt the alternative transition method provided in the FSP.

2. Summary of Significant Accounting Policies—(continued)

Recent Accounting Pronouncements

In September 2006, the FASB issued SFAS No. 157, *Fair Value Measurements*, or SFAS 157. SFAS 157 defines fair value, establishes a framework for measuring fair value in accordance with accounting principles generally accepted in the United States, or GAAP, and expands disclosures about fair value measurements. The provisions of SFAS 157 are effective for fiscal years beginning after November 15, 2007. The Company does not expect SFAS 157 to have a material impact on its financial results.

In February 2007, the FASB issued SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities*, or SFAS 159. SFAS 159 allows entities to choose voluntarily, at specified election dates, to measure many financial assets and liabilities (as well as certain non-financial instruments) at fair value. The election can be made only on an instrument-by-instrument basis and is irrevocable. The provisions of SFAS 159 are effective for fiscal years beginning after November 15, 2007. The Company does not expect SFAS 159 to have a material impact on its financial results.

In July 2007, the EITF reached consensus on Issue 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services to be Used in Future Research and Development Activities*, or EITF 07-3. EITF 07-3 concluded that non-refundable advance payments for goods or services to be received in the future for use in research and development activities should be deferred and capitalized and that the capitalized amounts should be expensed as the goods are delivered or the services are rendered. If an entity's expectations change such that it does not expect it will need the goods to be delivered or the services to be rendered, capitalized nonrefundable advance payments should be charged to expense. EITF 07-3 is effective for new contracts entered into during fiscal years beginning after December 15, 2007, including interim periods within those fiscal years. The Company does not expect EITF 07-3 to have a material impact on its financial results.

In November 2007, the EITF reached consensus on Issue 07-1, *Accounting for Collaboration Arrangements*, or EITF 07-1. The consensus requires collaborators to present the result of activities for which they act as the principal on a gross basis and report any payments received from or made to other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational and consistently applied accounting policy election. EITF 07-1 is effective for annual periods beginning after December 15, 2008 and will be applied retrospectively for collaborative arrangements existing at the effective date of the consensus as a change in accounting principle. The Company does not expect EITF 07-1 to have a material impact on its financial results.

Use of Estimates

The preparation of financial statements in conformity with GAAP 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.

3. Short-term investments

The Company's short-term investments consisted of:

	December 31,	
	2007	2006
Student loan auction rate securities	$23,000,000	$ —
Certificates of deposit	10,533,995	12,191,430
Accrued interest	102,692	253,763
	$33,636,687	$12,445,193

4. Inventories

Inventories consisted of the following:

	December 31,	
	2007	2006
Raw materials	$ 51,877	$ —
Finished goods	88,536	3,600
Work-in-progress	—	170,093
	$140,413	$173,693

5. Property and equipment

Property and equipment consisted of the following:

	December 31,	
	2007	2006
Lab equipment	$ 8,941,265	$ 5,908,860
Office furniture and fixtures	2,658,750	1,593,486
Leasehold improvements	1,029,439	190,434
	12,629,454	7,692,780
Less: accumulated depreciation	(6,514,899)	(5,652,425)
Property and equipment, net	$ 6,114,555	$ 2,040,355

The Company recorded $869,000, $783,000 and $765,000 of depreciation expense for 2007, 2006 and 2005, respectively.

6. Intangible Assets

Intangible assets consisted of the following:

	December 31, 2007	December 31, 2006
Patents	$ 642,000	$ 642,000
Less: accumulated amortization	(204,555)	(166,791)
Total	$ 437,445	$ 475,209

The Company recognized amortization expense of $38,000 for each of 2007, 2006 and 2005. The Company expects to recognize $38,000 of amortization expense for each of the next five years.

7. Accrued Expenses

Accrued expenses consisted of the following:

	December 31, 2007	December 31, 2006
Clinical trial costs	$2,830,307	$1,793,538
Employee compensation	2,331,463	1,923,345
Other	298,873	172,231
Total	$5,460,643	$3,889,114

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 Holdings, Inc., or RJRT. The note payable to the City of Winston-Salem matures on April 19, 2012, was non-interest bearing until April 2007 and bears interest thereafter at an annual rate of 5% or 7% depending on the gross revenue of the Company until maturity. No payments were due on the City of Winston-Salem note until the 5-year anniversary of the loan. In April 2007, the Company began making monthly payments of $9,000 on the loan based on an interest rate of 5%.The note payable to RJRT was amended in January 2004 to allow for up to three additional tranches to be advanced to the Company for up to a total of $2,000,000. The Company was advanced an additional tranche on April 1, 2004 in the amount of $1,027,000. This additional tranche accrues interest at 5.87% and is repayable in monthly payments of $24,000 through the maturity date of April 1, 2008. The Company was advanced another additional tranche on December 23, 2004 in the amount of $973,000. This tranche accrues interest at 6.89% and is repayable in monthly payments of $23,000 through the maturity date of January 1, 2009. The original borrowing of $2,500,000 matured on May 1, 2006 and was paid and satisfied in full. In June 2006, the note payable to RJRT was further amended to permit the Company to borrow an additional $2,000,000 on or before June 30, 2007 in up to three separate borrowings. The Company borrowed the additional $2,000,000 in two tranches in June 2007. The first June 2007 tranche was in the amount of $1,600,000, accrues interest at 7.36% and is repayable in monthly payments of $39,000 through the maturity date of June 1, 2011. The second June 2007 tranche was in the amount of $400,000, accrues interest at 7.48% and is repayable in monthly payments of $10,000 through the maturity date of July 1, 2011. The Company paid $128,000, $81,000 and $146,000 in interest under the RJRT and City of Winston-Salem notes during 2007, 2006 and 2005, respectively.

8. Long-term debt—(continued)

The note payable to RJRT is secured by equipment owned by the Company with a book value of approximately $2,407,000, net of accumulated depreciation, at December 31, 2007.

Maturities of long-term debt were as follows at December 31, 2007:

2008	918,596
2009	619,442
2010	639,389
2011	401,601
2012	25,442
	$2,604,470

9. Redeemable Preferred Stock

In August 2000, the Company issued 5,000,000 shares of its Series A redeemable convertible preferred stock, or the Series A, to RJRT, and completed a private placement of 6,537,634 of its Series B redeemable convertible preferred stock, or the Series B, generating cash of $29,073,000, net of offering costs. In January 2001, the Company issued 29,333 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, or the Series C, and received cash of $45,488,000, net of offering costs.

In March 2003, the Company completed a private placement of an additional 11,404,958 shares of Series C and received cash of $13,767,000, net of offering costs. In December 2004, the Company completed a private placement of an additional 27,272,728 shares of Series C and received cash of $32,900,000, net of offering costs. In May 2005, the Company completed a private placement of an additional 496,132 shares of Series C and received cash of $612,000, net of offering costs.

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

Conversion

Each share of Series A, Series B and Series C was 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.

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 equaled or exceeded $11.00 (subject to certain adjustments) or such lesser amount as is approved by the holders of (a) a majority of then outstanding shares of Series A and Series B, considered together as a single class on an as-converted basis, and (b) at least sixty-five percent (65%) of the then outstanding shares of Series C, and (ii) the gross proceeds to the Company

9. Redeemable Preferred Stock—(continued)

were not less than $50,000,000 or such lesser amount approved by the holders of (a) a majority of then outstanding shares of Series A and Series B, considered together as a single class on an as-converted basis, and (b) at least sixty-five percent (65%) of the then outstanding shares of Series C.

Dividends

Each share of Series C accrued dividends daily on a cumulative basis at the rate of 8% per annum, which were recorded as an increase to Series C and an increase to accumulated deficit. At December 31, 2005, cumulative accrued dividends on the Series C stock totaled $17,264,000. The accrued but unpaid cumulative dividend on the Series C was forfeited upon conversion of the Series C.

Voting

Each holder of the Series A, Series B and Series C was entitled to the number of votes equal to the number of shares of common stock into which such holder's shares were convertible on the applicable record date.

All outstanding shares of the Company's redeemable convertible preferred stock automatically converted into shares of common stock upon completion of the IPO, as described more fully in Note 2. Based on the terms of the redeemable convertible preferred stock, accrued dividends totaling $39,830,000 were forfeited in connection with the conversion. Upon completion of the IPO, all outstanding warrants expired unexercised.

Common stock issued upon automatic conversion of the redeemable convertible preferred stock was as follows:

Series	Shares Outstanding	Carrying Amount	Conversion Ratio	Shares of Common Stock Issued
A	5,000,000	$ 32,320,714	0.133	666,666
B	6,567,567	42,395,290	0.318 or 0.133	2,082,623
C	76,937,998	112,244,854	0.144	11,082,724
	88,505,565	$186,960,858		13,832,013

These conversion ratios reflect a 1 for 7.5 share reverse stock split effected February 3, 2005.

10. Stockholders' Equity (Deficit)

On February 2, 2005 the Company's Board of Directors adopted and the stockholders approved a 1 for 7.5 share reverse stock split of the Company's common stock effective as of February 3, 2005. All common stock and per common share amounts for all periods presented in the accompanying financial statements have been restated to reflect the effect of this reverse stock split.

On April 18, 2006, the Company amended its Certificate of Incorporation to increase the number of authorized shares of common stock to 100,000,000 and to set the number of authorized shares of undesignated preferred stock at 5,000,000. As discussed in Note 9, all Series A, Series B and Series C stock converted into shares of common stock upon completion of the IPO.

10. Stockholders' Equity (Deficit)—(continued)

In conjunction with the issuance of Series A, the Company issued a warrant to purchase 215,054 shares of the Company's common stock at an original exercise price of $34.88 per share (subject to certain adjustments). In connection with the Company's issuance of Series C and price adjustment provisions of the warrant, the conversion price of the warrant was adjusted to $14.63.

The fair value of the warrant to purchase 215,054 shares of the Company's common stock was estimated at the grant date to be $213,710 or $0.99 per share. As discussed in Note 9, the warrant expired unexercised upon completion of the IPO.

The Company had 3,125,161 and 2,476,977 shares of common stock reserved for future issuance upon the exercise of outstanding stock options at December 31, 2007 and 2006, respectively.

11. Income Taxes

For the years ended December 31, 2007 and 2005, there was no provision (benefit) for federal or state income taxes, as the Company incurred operating losses from inception through 2005 and for 2007. For the year ended December 31, 2006, there is no provision (benefit) for federal or state income taxes because taxable income was offset by operating loss carryforwards.

The Company's effective tax rate differs from the federal income tax rate for the following reasons:

	Year Ended December 31,		
	2007	2006	2005
Expected federal income tax benefit/expense at statutory rate	34%	34%	34%
Increase (decrease) resulting from:			
Research and development credits	3	(32)	3
Stock-based compensation	(1)	11	(1)
State income tax expense, net of federal benefit	4	6	4
Change in valuation allowance	(40)	(20)	(41)
Other	—	1	1
	— %	— %	— %

At December 31, 2007, 2006 and 2005, the Company had net operating loss carryforwards for federal income tax purposes of approximately $113,093,000, $94,571,000 and $98,373,000, respectively, and for state income tax purposes of approximately $113,083,000, $94,566,000 and $98,368,000, respectively, and research and development federal income tax credits of approximately $3,910,000, $2,799,000 and $2,131,000, respectively. The federal net operating loss carryforwards begin to expire in 2020. The state net operating loss carryforwards begin to expire in 2015. The research and development tax credits begin to expire in 2021.

Utilization of the net operating loss carryforwards and credits may be subject to a substantial annual limitation due to ownership change limitations provided by Section 382 of the Internal Revenue Code of 1986, as amended, and similar state provisions. As a result of a series of stock issuances, the Company had such an ownership change on November 30, 2002. Consequently, an annual limitation is imposed on the Company's use of net operating loss and credit carryforwards attributable to periods before the change.

11. Income Taxes—(continued)

Deferred income taxes reflect the net tax effects of temporary differences between the carrying amount of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. The Company's net deferred tax assets relate primarily to its net operating loss carryforwards. A valuation allowance has been recognized to offset the deferred tax assets related primarily to the net operating loss 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, 2007, 2006 and 2005, the valuation allowance increased (decreased) approximately $10,619,000, $(410,000) and $11,750,000, respectively.

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

	December 31,	
	2007	2006
Deferred tax assets:		
Net operating loss carryforward	$ 40,830,045	$ 33,849,517
Research and development tax credit	3,127,603	2,798,861
Collaboration revenue	2,546,169	—
Patents	1,367,498	1,172,145
Stock-based compensation	791,326	160,356
Total gross deferred tax assets	48,662,641	37,980,879
Valuation allowance	(48,556,006)	(37,937,051)
Net deferred tax asset	106,635	43,828
Deferred tax liabilities		
Equipment and other	(106,635)	(43,828)
Net deferrred tax asset	$ —	$ —

On January 1, 2007, the Company adopted FIN 48. FIN 48 clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements in accordance with SFAS 109, *Accounting for Income Taxes*. FIN 48 prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. FIN 48 also provides guidance on de-recognition, classification, interest and penalties, accounting in interim periods, disclosures and transition. There was no cumulative effect adjustment upon adoption of FIN 48.

A reconciliation of beginning and ending unrecognized tax benefits is as follows:

Balance at January 1, 2007	$ 720,000
Additions based on tax positions related to the current year	222,000
Balance at December 31, 2007	$ 942,000

Because of the impact of deferred tax accounting, none of the unrecognized tax benefits would, if recognized, affect the effective tax rate. No interest or penalties with respect to unrecognized tax positions are recognized in the statement of operations. The Company believes it is reasonably possible unrecognized tax

11. Income Taxes—(continued)

benefits will increase $100,000 to $300,000 in the next 12 months as a result of claiming additional research and development credits. Since the Company has incurred cumulative operating losses since inception, all tax years remain open to examination by major jurisdictions.

12. Stock-Based Incentive Plans

On August 22, 2000, the Company established the 2000 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.

On April 7, 2005 the Company's Board of Directors authorized an amendment to each stock option agreement held by current employees that changed the exercise price per share for each unvested portion as of March 31, 2005 to $1.75. As of March 31, 2005, there were 354,672 shares issued to 75 employees subject to the unvested portions of employee options ranging from an original option price of $5.10 to $5.63 that were affected by the amendments. Each affected option was required to be accounted for as a modification of an award under SFAS 123R. The fair market value was calculated immediately prior to the modification and immediately after the modification to determine the incremental fair market value. This incremental value of $147,000 and the fair market value of each modified option will be expensed as compensation on a quarterly basis over the remaining vesting period.

The 2006 Plan became effective in April 2006 and is the successor equity incentive program to the 2000 Plan. All shares previously reserved under the 2000 Plan and not subject to outstanding awards under the 2000 Plan are now reserved for grant under the 2006 Plan. As of December 31, 2007, the number of shares authorized for issuance under the Plans is 4,362,078, of which 1,113,836 shares remain available for grant at December 31, 2007.

Awards may be made, with respect to the 2006 Plan, or may have been made, with respect to either of the Plans to participants under the Plans in the form of incentive and nonqualified stock options, restricted stock, stock appreciation rights, stock awards, and performance awards. Eligible participants under the Plans include employees, directors and certain independent contractors, consultants or advisors of the Company or a related corporation. Awards made under the Plans have vesting periods that are determined at the discretion of the administrator and range from 0 to 5 years and most commonly have 10-year contractual terms or, in some cases, shorter terms designed to comply with Section 409A of the Internal Revenue Code. The exercise price of incentive options granted under the Plans may not be less than 100% of the fair market value of the common stock on the date of grant, as determined by the administrator.

Beginning January 1, 2005, under SFAS 123R, the Company recognized the grant-date fair value of stock options and other stock-based compensation issued to employees and non-employee directors over the requisite service periods, which are typically the vesting periods. The Company uses the Black-Scholes-Merton formula to estimate the fair value of its stock-based payments. The volatility assumption used in the Black-Scholes-Merton formula is based on the calculated historical volatility of twelve benchmark biotechnology companies that have been identified as comparable public entities. The expected term of options granted during 2006 and 2005 is derived from the simplified method allowable under Staff Accounting Bulletin No. 107. Under this approach, the expected term would be the mid-point between the weighted average of vesting period and the contractual term. The expected term for options granted during 2007 is based on historical analysis. The risk-free rate for periods within the contractual life of the option is based on the U.S. Treasury yield curve in effect at the time of grant.

13. Commitments and Contingencies—(continued)

Employment Arrangements

The Company has entered into employment agreements with certain of its executive officers. Under the agreements, if the Company terminates the employment of the executive officer other than for just cause or if the executive officer terminates his employment for good reason, in each case as that term is defined in the agreement, the executive officer is entitled, among other things, to receive severance equal to his current base salary for nine to twelve months following termination or, if shorter, until he secures other employment. The executive officer would also be entitled to 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.

14. Retirement Savings Plan

The Company has a 401(k) retirement plan in which all of its employees are eligible to participate. The plan provides for the Company to make 100% matching contributions up to a maximum of 6% of employees' eligible compensation. The Company contributed $559,000, $539,000 and $412,000 to the plan for the years ended December 31, 2007, 2006 and 2005, respectively.

15. Strategic Alliance and Collaboration Agreements

AstraZeneca AB

In December 2005, the Company entered into a collaborative research and license agreement with AstraZeneca AB under which the Company granted AstraZeneca exclusive development and worldwide commercialization rights to the Company's product candidate known as AZD3480 (TC-1734) as a treatment for Alzheimer's disease, cognitive dysfunction in schizophrenia and potentially other conditions marked by cognitive impairment such as attention deficit hyperactivity disorder, age associated memory impairment and mild cognitive impairment. The collaboration agreement also provides for a multi-year preclinical research collaboration between the Company and AstraZeneca.

The Company is eligible to receive future research fees, license fees and milestone payments under its collaboration agreement with AstraZeneca. The amount of research fees, license fees and milestone payments will depend on the extent of the Company's research activities and the timing and achievement of development, regulatory and first commercial sale milestone events.

AstraZeneca paid the Company an initial fee of $10,000,000 in February 2006. Based on the collaboration agreement terms, the Company allocated $5,000,000 of the initial fee to the research collaboration, which the Company is recognizing as revenue on a straight-line basis over the planned four-year term of the research collaboration. The Company deferred recognition of the remaining $5,000,000 of the initial fee, which was allocated to the AZD3480 (TC-1734) license grants, until December 2006, when AstraZeneca made a determination to proceed with further development of AZD3480 (TC-1734) following the completion of additional clinical and non-clinical studies that AstraZeneca conducted during 2006. On December 27, 2006, AstraZeneca communicated its decision to proceed with further development of AZD3480 (TC-1734) to the Company. As a result, in the first quarter of 2007, the Company began recognizing the $5,000,000 of the initial fee that it had previously deferred as revenue on a straight-line basis over the estimated five-year development period for AZD3480 (TC-1734).

11. Income Taxes—(continued)

benefits will increase $100,000 to $300,000 in the next 12 months as a result of claiming additional research and development credits. Since the Company has incurred cumulative operating losses since inception, all tax years remain open to examination by major jurisdictions.

12. Stock-Based Incentive Plans

On August 22, 2000, the Company established the 2000 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.

On April 7, 2005 the Company's Board of Directors authorized an amendment to each stock option agreement held by current employees that changed the exercise price per share for each unvested portion as of March 31, 2005 to $1.75. As of March 31, 2005, there were 354,672 shares issued to 75 employees subject to the unvested portions of employee options ranging from an original option price of $5.10 to $5.63 that were affected by the amendments. Each affected option was required to be accounted for as a modification of an award under SFAS 123R. The fair market value was calculated immediately prior to the modification and immediately after the modification to determine the incremental fair market value. This incremental value of $147,000 and the fair market value of each modified option will be expensed as compensation on a quarterly basis over the remaining vesting period.

The 2006 Plan became effective in April 2006 and is the successor equity incentive program to the 2000 Plan. All shares previously reserved under the 2000 Plan and not subject to outstanding awards under the 2000 Plan are now reserved for grant under the 2006 Plan. As of December 31, 2007, the number of shares authorized for issuance under the Plans is 4,362,078, of which 1,113,836 shares remain available for grant at December 31, 2007.

Awards may be made, with respect to the 2006 Plan, or may have been made, with respect to either of the Plans to participants under the Plans in the form of incentive and nonqualified stock options, restricted stock, stock appreciation rights, stock awards, and performance awards. Eligible participants under the Plans include employees, directors and certain independent contractors, consultants or advisors of the Company or a related corporation. Awards made under the Plans have vesting periods that are determined at the discretion of the administrator and range from 0 to 5 years and most commonly have 10-year contractual terms or, in some cases, shorter terms designed to comply with Section 409A of the Internal Revenue Code. The exercise price of incentive options granted under the Plans may not be less than 100% of the fair market value of the common stock on the date of grant, as determined by the administrator.

Beginning January 1, 2005, under SFAS 123R, the Company recognized the grant-date fair value of stock options and other stock-based compensation issued to employees and non-employee directors over the requisite service periods, which are typically the vesting periods. The Company uses the Black-Scholes-Merton formula to estimate the fair value of its stock-based payments. The volatility assumption used in the Black-Scholes-Merton formula is based on the calculated historical volatility of twelve benchmark biotechnology companies that have been identified as comparable public entities. The expected term of options granted during 2006 and 2005 is derived from the simplified method allowable under Staff Accounting Bulletin No. 107. Under this approach, the expected term would be the mid-point between the weighted average of vesting period and the contractual term. The expected term for options granted during 2007 is based on historical analysis. The risk-free rate for periods within the contractual life of the option is based on the U.S. Treasury yield curve in effect at the time of grant.

12. Stock-Based Incentive Plans—(continued)

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

	Year ended December 31,		
	2007	2006	2005
Dividend yield	—	—	—
Risk-free interest rate	4.0%	4.7%	4.1%
Volatility	0.7	0.7	0.7
Expected life	6.55 years	6.25 years	6.25-6.50 years

A summary of option activity and changes during each of the years ended December 31, 2007, 2006 and 2005 is presented below:

	Options	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
Outstanding at January 1, 2005	987,800	$4.88		
Granted	653,743	1.76		
Forfeited	(17,923)	5.00		
Exercised	(13,611)	1.75		
Outstanding at December 31, 2005	1,610,009	2.88		
Granted	935,596	5.55		
Forfeited	(38,835)	3.07		
Exercised	(29,793)	2.07		
Outstanding at December 31, 2006	2,476,977	3.89		
Granted	789,386	8.83		
Forfeited	(45,518)	4.75		
Exercised	(95,684)	4.52		
Outstanding at December 31, 2007	3,125,161	5.11	7.69	$10,268,628
Vested and exercisable at December 31, 2007	1,886,303	4.16	6.79	$ 7,939,228

The weighted average grant date fair value of options granted during 2007, 2006 and 2005 was $6.02, $3.80 and $1.20, respectively. The total intrinsic value of options exercised during the years ended December 31, 2007, 2006 and 2005 was $461,000, $141,000 and $13,000, respectively.

12. Stock-Based Incentive Plans—(continued)

A summary of the status of non-vested stock options granted under the Plans as of December 31, 2007 and changes during the year ended December 31, 2007 is presented below:

	Options	Weighted Average Grant-Date Fair Value
Non-vested at January 1, 2007	1,160,761	$3.05
Granted	789,386	6.02
Vested	(670,912)	3.89
Forfeited	(40,377)	3.34
Non-vested at December 31, 2007	1,238,858	$4.48

As of December 31, 2007, there was $5,094,000 of total unrecognized compensation cost related to non-vested stock-based compensation arrangements granted under the Plans, considering estimated forfeitures. That cost is expected to be recognized over a weighted average period of 1.7 years. The total fair value of shares subject to stock-based compensation arrangements granted under the Plans that vested during the year ended December 31, 2007 was $2,612,000.

During 2005, the Company granted options to purchase 6,000 shares of common stock at an exercise price of $0.08, below the fair value of $1.75 per share of common stock. The fair value of these shares was recorded as compensation expense in the amount of $46,000 during the twelve months ended December 31, 2005.

13. Commitments and Contingencies

Operating Lease

On March 1, 2002, the Company entered into an agreement with Wake Forest University Health Sciences to lease an office and research facility in Winston-Salem, North Carolina with an initial term that extended through July 31, 2007. The lease contained a renewal option for up to one additional five-year term, with a lease rate similar to the initial term. In December 2004, the Company amended the terms of the lease to include an additional 1,000 square feet and an option on additional space in the leased facility. In January 2007, the Company amended the terms of the lease to include approximately 14,000 square feet of additional space beginning January 1, 2007 and approximately 3,000 square feet of additional space beginning August 1, 2007 and concurrently exercised its renewal option. Rent expense incurred by the Company under the lease was $2,176,000, $1,500,000 and $1,500,000 for the years ended December 31, 2007, 2006 and 2005, respectively. Rent expense is offset by the monthly recognition of the deferred rent incentive discussed in Note 2.

The following table illustrates expected future lease payments under the lease:

2008	$ 2,159,390
2009	2,159,390
2010	2,159,390
2011	2,159,390
2012	1,259,643
	$ 9,897,203

13. Commitments and Contingencies—(continued)

Employment Arrangements

The Company has entered into employment agreements with certain of its executive officers. Under the agreements, if the Company terminates the employment of the executive officer other than for just cause or if the executive officer terminates his employment for good reason, in each case as that term is defined in the agreement, the executive officer is entitled, among other things, to receive severance equal to his current base salary for nine to twelve months following termination or, if shorter, until he secures other employment. The executive officer would also be entitled to 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.

14. Retirement Savings Plan

The Company has a 401(k) retirement plan in which all of its employees are eligible to participate. The plan provides for the Company to make 100% matching contributions up to a maximum of 6% of employees' eligible compensation. The Company contributed $559,000, $539,000 and $412,000 to the plan for the years ended December 31, 2007, 2006 and 2005, respectively.

15. Strategic Alliance and Collaboration Agreements

AstraZeneca AB

In December 2005, the Company entered into a collaborative research and license agreement with AstraZeneca AB under which the Company granted AstraZeneca exclusive development and worldwide commercialization rights to the Company's product candidate known as AZD3480 (TC-1734) as a treatment for Alzheimer's disease, cognitive dysfunction in schizophrenia and potentially other conditions marked by cognitive impairment such as attention deficit hyperactivity disorder, age associated memory impairment and mild cognitive impairment. The collaboration agreement also provides for a multi-year preclinical research collaboration between the Company and AstraZeneca.

The Company is eligible to receive future research fees, license fees and milestone payments under its collaboration agreement with AstraZeneca. The amount of research fees, license fees and milestone payments will depend on the extent of the Company's research activities and the timing and achievement of development, regulatory and first commercial sale milestone events.

AstraZeneca paid the Company an initial fee of $10,000,000 in February 2006. Based on the collaboration agreement terms, the Company allocated $5,000,000 of the initial fee to the research collaboration, which the Company is recognizing as revenue on a straight-line basis over the planned four-year term of the research collaboration. The Company deferred recognition of the remaining $5,000,000 of the initial fee, which was allocated to the AZD3480 (TC-1734) license grants, until December 2006, when AstraZeneca made a determination to proceed with further development of AZD3480 (TC-1734) following the completion of additional clinical and non-clinical studies that AstraZeneca conducted during 2006. On December 27, 2006, AstraZeneca communicated its decision to proceed with further development of AZD3480 (TC-1734) to the Company. As a result, in the first quarter of 2007, the Company began recognizing the $5,000,000 of the initial fee that it had previously deferred as revenue on a straight-line basis over the estimated five-year development period for AZD3480 (TC-1734).

15. Strategic Alliance and Collaboration Agreements—(continued)

The Company expects to recognize any revenue based on the achievement of milestones under the collaboration agreement upon achievement of the milestone event, if the Company determines that the revenue satisfies the revenue recognition requirements of SAB 101, as amended by SAB 104.

AstraZeneca's determination to proceed with further development of AZD3480 (TC-1734) triggered a $20,000,000 payment in accordance with the agreement, and the Company recognized the full amount as revenue in December 2006. The payment was received in January 2007 in accordance with the terms of the agreement.

Under the agreement, the Company is also eligible to receive additional payments of up to $249,000,000, contingent upon the achievement of development, regulatory and first commercial sale milestones for AZD3480 (TC-1734) for three indications, as well as tiered double-digit royalties dependent on sales achieved following regulatory approval. Under the terms of a sponsored research agreement and a subsequent license agreement between the Company and the University of Kentucky Research Foundation, or UKRF, Targacept is required to pay UKRF a low single digit percentage of any payments that are received from AstraZeneca related to AZD3480 (TC-1734).

The Company recorded $758,000 in license fees to UKRF in 2006. No fees were paid to UKRF in 2007 or 2005.

In 2006, during the period that AstraZeneca conducted additional safety and product characterization studies, AstraZeneca agreed to pay the Company research fees equal to 50% of the Company's research expenses in the parties' preclinical research collaboration. The Company recorded these fees as deferred revenue pending AstraZeneca's decision whether to proceed with further development of AZD3480 (TC-1734). As a result of AstraZeneca's decision to proceed with further development of AZD3480 (TC-1734), in December 2006, the Company recognized as collaboration research and development revenue all previously deferred research fees, plus the other 50% of the Company's research expenses incurred in the research collaboration that had not previously been recorded, which totaled $4,672,000. Subsequently, the Company has recognized collaboration research and development revenue as the research is performed and related expenses are incurred. The Company recognized collaboration research and development revenue of $6,888,000 in 2007. The Company recognized additional collaboration research and development revenue of $400,000 and $347,000 in 2007 and 2006, respectively, for clinical trial material purchased by AstraZeneca from the Company.

In October 2007, the Company provided notice under its agreement with AstraZeneca offering AstraZeneca the right to license its product candidate TC-5619 for specified conditions characterized by cognitive impairment. Based on a subsequent election by AstraZeneca made under the terms of the agreement, AstraZeneca paid the Company $2,000,000 and the Company agreed to develop TC-5619 independently through completion of Phase 1 clinical development and a Phase 2 proof of concept clinical trial in accordance with a mutually acceptable development plan, following which AZ would have the right to license TC-5619. The Company is recognizing the $2,000,000 payment as revenue on a straight-line basis over the expected development period for TC-5619 to reach proof of concept.

GlaxoSmithKline

On July 27, 2007, the Company entered into a product development and commercialization agreement with SmithKline Beecham Corporation, doing business as GlaxoSmithKline, and Glaxo Group Limited, which are

15. Strategic Alliance and Collaboration Agreements—(continued)

referred to together as GlaxoSmithKline, that sets forth the terms of an alliance designed to discover, develop and market product candidates that selectively target specified NNR subtypes in five therapeutic focus areas: pain, smoking cessation, addiction, obesity and Parkinson's disease.

Under the product development and commercialization agreement, the Company has agreed, for specified periods of time, to use diligent efforts to conduct research activities designed to discover product candidates that target specified NNR subtypes, to develop the product candidate identified as the lead for each therapeutic focus area of the alliance through a Phase 2 proof of concept trial and to develop up to two other product candidates for each therapeutic focus area to a specified stage of preclinical development. With respect to each therapeutic focus area in the alliance, if the Company achieves clinical proof of concept with respect to a lead product candidate, GlaxoSmithKline would have an exclusive option for an exclusive license to that lead product candidate and up to two other product candidates in development in the alliance for the same therapeutic focus area on a worldwide basis. If GlaxoSmithKline exercises its option and pays the applicable exercise fee, GlaxoSmithKline would become responsible for using diligent efforts to conduct later-stage development and commercialization of the lead product candidate at its sole expense. GlaxoSmithKline's exclusive license would include all fields of use other than those indications for which the Company has granted development and commercialization rights for product candidates under its collaboration agreement with AstraZeneca AB.

The terms of the alliance provide for the Company to conduct its research and development activities under the product development and commercialization agreement at its sole expense. The Company is, however, eligible to receive milestone payments from GlaxoSmithKline if it successfully advances product candidates subject to the alliance through preclinical and clinical development.

Under the product development and commercialization agreement and a related stock purchase agreement, GlaxoSmithKline made an initial payment to the Company of $20,000,000 and purchased 1,275,502 shares of the Company's common stock for an aggregate purchase price of $15,000,000. The purchase price paid by GlaxoSmithKline reflected an aggregate deemed premium of $3,520,000, based on the closing price of the Company's common stock on the trading day immediately preceding the date that the agreements were signed and announced. The Company deferred both the initial payment made by GlaxoSmithKline and the deemed premium paid for the shares of the Company's common stock purchased by GlaxoSmithKline and is recognizing them as revenue on a straight-line basis over the estimated term of the Company's research and early development obligations under the agreement. Currently, the Company estimates the term of such obligations to be nine years. As of December 31, 2007, the Company had recognized $1,125,000 of the initial payment and deemed premium as revenue.

The Company is also eligible to receive up to $1,500,000,000 in additional payments from GlaxoSmithKline, contingent upon the achievement of specified discovery, development, regulatory and commercial milestones across the five therapeutic focus areas of the alliance, as well as tiered double-digit royalties dependent on sales achieved following regulatory approval for any product licensed by GlaxoSmithKline. The Company expects to recognize any revenue based on the achievement of milestones under the agreement upon achievement of the milestone event, if the Company determines that the revenue satisfies the revenue recognition requirements of SAB 101, as amended by SAB 104. The amounts that the Company may receive will depend on the success of the Company's research and development activities, the timing and achievement of the discovery, development, regulatory and commercial milestone events and whether GlaxoSmithKline exercises any options that are triggered under the agreement.

15. Strategic Alliance and Collaboration Agreements—(continued)

In December 2007, the Company received a $6,000,000 payment from GlaxoSmithKline upon the Company's initiation of a Phase 1 clinical trial of TC-6499, a milestone event under the agreement. The Company determined the payment did not meet each of the conditions of its revenue recognition policy (see Note 2) required for recognition of the full amount into revenue upon achievement of the milestone. Specifically, based on the progress of this product candidate as of inception of the agreement, achievement of this milestone was reasonably assured. Therefore, the Company has deferred recognition of the payment and is recognizing the payment as revenue on a straight-line basis over the estimated term of the Company's research and early development obligations under the agreement.

16. Related Party Transactions

Prior to completion of the IPO, RJRT was the holder of record of more than 5% of the Company's outstanding shares of common stock. However, upon the IPO, RJRT no longer beneficially owned more than 5% of the Company's outstanding 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 a loan facility with RJRT, which was amended in June 2006 as described in Note 8. As of December 31, 2007 and 2006, the Company owed RJRT $2,174,000 and $909,000, respectively, under the note payable. The Company paid $112,000, $81,000 and $146,000 in interest during 2007, 2006 and 2005, respectively.

A member of the Company's board of directors served as an officer of RJRT and its parent company, Reynolds American, Inc., until retiring from RJRT and Reynolds American effective as of August 31, 2006. Prior to his retirement, equity compensation for the director's service was made, at the director's request, directly to RJRT. The number of shares subject to stock options granted to RJRT in connection with the director's services was 1,000 shares per year. In connection with the issuance of the stock options, the Company recognized compensation expense of $0, $1,000 and $5,000 during the years ended December 31, 2007, 2006 and 2005, respectively.

17. Selected Quarterly Financial Data (unaudited)

	2007 Quarter			
	First	Second	Third	Fourth
Net Operating Revenues	$ 2,051,190	$ 2,842,049	$ 3,126,327	$ 3,556,365
Gross loss on product sales	(25,038)	(926)	(72,005)	(99,160)
Operating loss	(5,642,828)	(9,070,859)	(8,403,197)	(8,654,697)
Net loss	(4,793,382)	(8,262,594)	(7,370,544)	(7,646,367)
Net loss attributable to common stockholders	(4,793,382)	(8,262,594)	(7,370,544)	(7,646,367)
Basic and diluted net loss per share attributable to common stockholders(1)(2)	$ (0.25)	$ (0.43)	$ (0.37)	$ (0.37)
Weighted average common shares outstanding—basic and diluted(2)	19,136,796	19,147,011	20,096,528	20,483,664

17. Selected Quarterly Financial Data (unaudited)—(continued)

	2006 Quarter			
	First	Second	Third	Fourth
Net Revenue(3)	$ 606,124	$ 589,407	$ 998,293	$25,343,740
Gross (loss) profit on product sales	(14,028)	153,039	29,424	(40,371)
Operating (loss) income	(5,513,488)	(5,315,043)	(5,651,697)	16,076,536
Net (loss) income	(5,238,100)	(4,616,818)	(4,865,602)	16,817,049
Net (loss) income attributable to common stockholders	(8,041,310)	(5,146,313)	(4,865,602)	16,817,049
Basic net (loss) income per share attributable to common stockholders(1)	$ (29.42)	$ (0.33)	$ (0.25)	$ 0.88
Diluted net (loss) income per share attributable to common stockholders(1)	$ (29.42)	$ (0.33)	$ (0.25)	$ 0.83
Weighted average common shares outstanding—basic	273,368	15,595,020	19,118,854	19,126,972
Weighted average common shares outstanding—diluted	273,368	15,595,020	19,118,854	20,224,805

(1) Per common share amounts for the quarters and full years have been calculated separately. Accordingly, quarterly amounts do not add to the annual amount because of differences in the weighted average common shares outstanding during each period principally due to the effect of the Company's issuing shares of its common stock during the year.

(2) In 2007, diluted weighted average common shares outstanding is identical to basic weighted average common shares outstanding and diluted EPS is identical to Basic EPS since common share equivalents are excluded from the calculation of diluted weighted average common shares outstanding, as their effect is antidilutive.

(3) Net revenue for the fourth quarter of 2006 includes $20,000,000 in milestone revenue and $4,672,000 in collaboration research and development revenue under the AstraZeneca agreement recognized as a result of AstraZeneca's determination to proceed with further development of AZD3480 (TC-1734).

18. Subsequent Events

The Company entered into a loan agreement with a bank in March 2008 pursuant to which the Company initially borrowed $4,811,000 and has up to an aggregate of $489,000 in additional borrowing capacity available to fund the purchase of equipment, furnishings, software and other fixed assets and enable the refinancing of its existing loan facility with R.J. Reynolds Tobacco Holdings, Inc. Under the terms of the agreement, borrowings under the loan facility may be made in up to four term loans and each loan bears interest, at the Company's election, at either (1) the One Month LIBOR Rate plus 2.15% per annum, as adjusted monthly on the first day of each month, or (2) a fixed rate to be calculated by the bank at the closing of the loan equal to the bank's fixed rate cost of funds index corresponding to the term of the loan plus 2.15% per annum. The agreement provides for repayment of each loan over a period determined by the Company, not to exceed four years, in equal monthly installments of principal and interest and for a first priority security interest in favor of the bank in the assets acquired with the proceeds of the loan facility.

18. Subsequent Events—(continued)

The Company's March 2008 loan under the loan facility bears interest at a rate of 5.231% per annum and is repayable in equal monthly installments of $112,000 through the maturity date of March 1, 2012. The Company used $1,679,000 of the proceeds from the loan to pay and satisfy in full the principal and interest outstanding on two of the tranches under its existing loan facility and granted a first priority security interest in favor of the bank in assets previously acquired with the proceeds of those tranches.

In January 2008, the Company issued 4,370,000 shares of common stock in a public offering at $7.07 per share, the closing bid price on the offering date. The offering resulted in proceeds to the Company of $29,112,000 after underwriters' discounts and commissions and offering expenses payable by the Company.

During the first quarter of 2008, the Company continued to own student loan auction rate securities in its short-term investment portfolio, as described in Note 2. As of March 12, 2008, the Company had $16,750,000 invested in these securities for which auctions failed in the first quarter of 2008. All student loan auction rate securities owned by the Company as of March 12, 2008 are guaranteed by the Federal Family Educational Loan Program and carry AAA ratings. The Company earns interest on the investments that failed to settle at auction, at the maximum contractual rate. As of December 31, 2007, the carrying value of these investments was equal to the fair value based on successful auctions both preceding and subsequent to year end. The Company plans to continue to monitor the fair value of its auction rate securities for each reporting period for a possible other-than-temporary impairment.

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure.

Not applicable.

Item 9A. Controls and Procedures.

(a) *Evaluation of Disclosure Controls and Procedures.* Our management, with the participation of our chief executive officer and chief financial officer, evaluated the effectiveness of our disclosure controls and procedures in accordance with Rule 13a-15 under the Exchange Act as of the end of the period covered by this annual report. In designing and evaluating our disclosure controls and procedures, our management recognized that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives, and our management necessarily applied its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of the end of the period covered by this annual report, our chief executive officer and chief financial officer concluded that, as of such date, our disclosure controls and procedures were effective to provide reasonable assurance that information required to be disclosed by us in the reports that we file or submit under the Exchange Act is (a) accumulated and communicated to our management, including our chief executive officer and chief financial officer, as appropriate to allow timely decisions regarding required disclosure and (b) recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms.

(b) *Management's Report on Internal Control Over Financial Reporting.* Our management is responsible for establishing and maintaining adequate internal control over financial reporting. Internal control over financial reporting is defined in Rule 13a-15(f) or 15d-15(f) promulgated under the Exchange Act as a process designed by, or under the supervision of, the principal executive and principal financial officers and effected by the board of directors, management and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles and includes those policies and procedures that:

- pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;
- provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorizations of our management and directors; and
- provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of our assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions or that the degree of compliance with the policies or procedures may lessen. Our management, including our chief executive officer and chief financial officer, assessed the effectiveness of our internal control over financial reporting as of December 31, 2007 using the criteria established in a report entitled "Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission" and in accordance with the interpretive guidance issued by the SEC in Release No. 34-55929. Based on its assessment, our management concluded that, as of December 31, 2007, our internal control over financial reporting was effective.

Our independent registered public accounting firm has issued an audit report on the effectiveness of our internal control over financial reporting as of December 31, 2007. The report appears below.

REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders of
Targacept, Inc.

We have audited Targacept, Inc.'s internal control over financial reporting as of December 31, 2007, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Targacept, Inc.'s management is responsible for maintaining effective internal control over financial reporting, and for its assessment of the effectiveness of internal control over financial reporting included in the accompanying Management's Report on Internal Control Over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit.

We conducted our audit 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 effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, Targacept, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2007, based on the COSO criteria.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the accompanying balance sheets of Targacept, Inc. as of December 31, 2007 and 2006, 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, 2007 and our report dated March 12, 2008 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Greensboro, North Carolina
March 12, 2008

(c) *Changes in Internal Controls*. No change in our internal control over financial reporting (as defined in Rule 13a-15(f) under the Exchange Act) occurred during the quarter ended December 31, 2007 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Information called for by this Item may be found in our definitive Proxy Statement in connection with our 2008 Annual Meeting of Stockholders to be filed with the SEC under the headings "Board of Directors and Management," "Corporate Governance" and "Section 16(a) Beneficial Ownership Reporting Compliance" and is incorporated herein by reference.

Code of Business Conduct and Ethics

We have adopted a code of business conduct and ethics that applies to all of our directors and officers and other employees, including our principal executive officer, principal financial officer and principal accounting officer. This code is publicly available on our website at *www.targacept.com.* To the extent permissible under applicable law, the rules of the SEC or NASDAQ listing standards, we intend to post on our website any amendment to the code of business conduct and ethics, or any grant of a waiver from a provision of the code of business conduct and ethics, that requires disclosure under applicable law, the rules of the SEC or NASDAQ listing standards.

Item 11. Executive Compensation.

Information called for by this Item may be found in our definitive Proxy Statement in connection with our 2008 Annual Meeting of Stockholders to be filed with the SEC under the headings "Executive Compensation" and "Corporate Governance" and is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Information called for by this Item may be found in our definitive Proxy Statement in connection with our 2008 Annual Meeting of Stockholders to be filed with the SEC under the headings "Security Ownership of Certain Beneficial Owners and Management" and "Equity Compensation Plan Information" and is incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Information called for by this Item may be found in our definitive Proxy Statement in connection with our 2008 Annual Meeting of Stockholders to be filed with the SEC under the headings "Certain Relationships and Related Person Transactions" and "Corporate Governance" and is incorporated herein by reference.

Item 14. Principal Accounting Fees and Services.

Information called for by this Item may be found in our definitive Proxy Statement in connection with our 2008 Annual Meeting of Stockholders to be filed with the SEC under the headings "Independent Registered Public Accounting Firm Fee Information and Audit Committee Pre-Approval Policy" and is incorporated herein by reference.

PART IV

Item 15. Exhibits, Financial Statement Schedules

(a)(1) *Financial Statements.* For a list of the financial statements included herein, see "Index to the Financial Statements" on page 83 of this annual report.

(a)(2) *Financial Statement Schedules.* All schedules are omitted because they are not applicable or because the required information is shown under Item 8, "Financial Statements and Supplementary Data."

(a)(3) *Exhibits.* The list of exhibits filed as a part of this annual report is set forth on the Exhibit Index immediately preceding such exhibits and is incorporated herein by this reference.

(b) *Exhibits.* See Exhibit Index.

(c) *Separate Financial Statements and Schedules.* None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

Date: March 14, 2008

Targacept, Inc.

By: /s/ J. DONALD DEBETHIZY

J. Donald deBethizy
Chief Executive Officer and President

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated. Each person whose signature appears below hereby constitutes and appoints J. Donald deBethizy, Alan A. Musso and Peter A. Zorn, and each of them singly (with full power to each of them to act alone), as such person's true and lawful attorneys-in-fact and agents, with full power of substitution and re-substitution, to sign any and all amendments to this Annual Report on Form 10-K and to file the same, with all exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite or necessary to be done, as fully to all intents and purposes as such person might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents, or any of them or any of their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Signature	Title	Date
/s/ J. DONALD DEBETHIZY **J. Donald deBethizy**	Chief Executive Officer, President and Director (principal executive officer)	March 14, 2008
/s/ ALAN A. MUSSO **Alan A. Musso**	Vice President, Chief Financial Officer and Treasurer (principal financial officer and principal accounting officer)	March 14, 2008
/s/ MARK SKALETSKY **Mark Skaletsky**	Chairman of the Board of Directors	March 14, 2008
/s/ M. JAMES BARRETT **M. James Barrett**	Director	March 14, 2008
/s/ CHARLES A. BLIXT **Charles A. Blixt**	Director	March 14, 2008
/s/ JULIA R. BROWN **Julia R. Brown**	Director	March 14, 2008
/s/ G. STEVEN BURRILL **G. Steven Burrill**	Director	March 14, 2008
/s/ ERROL B. DE SOUZA **Errol B. De Souza**	Director	March 14, 2008
/s/ ALAN W. DUNTON **Alan W. Dunton**	Director	March 14, 2008
/s/ JOHN P. RICHARD **John P. Richard**	Director	March 14, 2008
/s/ RALPH SNYDERMAN **Ralph Snyderman**	Director	March 14, 2008

EXHIBIT INDEX

Exhibit Number	Description
3.1	Fourth Amended and Restated Certificate of Incorporation of the Company (incorporated by reference to Exhibit 4.1 to the Company's Registration Statement on Form S-8, as filed with the SEC on May 8, 2006 (Registration No. 333-133881))
3.2	Bylaws of the Company (incorporated by reference to Exhibit 4.2 to the Company's Registration Statement on Form S-8, as filed with the SEC on May 8, 2006 (Registration No. 333-133881))
4.1	Specimen common stock certificate (incorporated by reference to Exhibit 4.1 to Amendment No. 3 to the Company's Registration Statement on Form S-1/A, as filed with the SEC on March 16, 2006 (Registration No. 333-131050))
4.2(a)	Third Amended and Restated Investor Rights Agreement, dated as of May 12, 2004, by and among the Company and certain stockholders of the Company (incorporated by reference to Exhibit 4.2(a) to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
4.2(b)	Amendment No. 1, dated December 6, 2004, to Third Amended and Restated Investor Rights Agreement, dated May 12, 2004 (incorporated by reference to Exhibit 4.2(b) to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
4.2(c)	Amendment No. 2, dated March 16, 2006, to Third Amended and Restated Investor Rights Agreement, dated May 12, 2004 (incorporated by reference to Exhibit 4.2(c) to Amendment No. 4 to the Company's Registration Statement on Form S-1/A, as filed with the SEC on March 24, 2006 (Registration No. 333-131050)
10.1*	Form of Indemnification Agreement between the Company and each of its directors and officers (incorporated by reference to Exhibit 10.1 to Amendment No. 3 to the Company's Registration Statement on Form S-1/A, as filed with the SEC on March 16, 2006 (Registration No. 333-131050))
10.2(a)	Lease Agreement, effective August 1, 2002, by and between the Company and Wake Forest University Health Sciences (incorporated by reference to Exhibit 10.2(a) to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.2(b)	First Lease Amendment, effective as of January 1, 2005, to Lease Agreement effective August 1, 2002, by and between the Company and Wake Forest University Health Sciences (incorporated by reference to Exhibit 10.2(b) to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.2(c)	Second Lease Amendment, executed June 30, 2006 effective as of March 31, 2006, to Lease Agreement effective August 1, 2002, by and between the Company and Wake Forest University Health Sciences (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended June 30, 2006)
10.2(d)+	Third Lease Amendment, dated January 22, 2007 effective January 1, 2007, to Lease Agreement, effective August 1, 2002, by and between the Company and Wake Forest University Health Sciences (incorporated by reference to Exhibit 10.2(d) to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2006)
10.3	Loan Agreement, dated as of April 19, 2002, between the Company and the City of Winston-Salem (incorporated by reference to Exhibit 10.3 to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))

Exhibit Number	Description
10.4	Second Amended and Restated Note and Security Agreement, dated June 30, 2006, between the Company and R.J. Reynolds Tobacco Holdings, Inc. (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed July 7, 2006)
10.5(a)*	Amended and Restated Targacept, Inc. 2000 Equity Incentive Plan (incorporated by reference to Exhibit 99 to the Company's Registration Statement on Form S-8, as filed with the SEC on May 8, 2006 (Registration No. 333-133882))
10.5(b)*	Form of Incentive Stock Option Agreement under Targacept, Inc. 2000 Equity Incentive Plan (incorporated by reference to Exhibit 10.5(b) to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.5(c)*	Form of Non-employee Director Nonqualified Stock Option Agreement under Targacept, Inc. 2000 Equity Incentive Plan (incorporated by reference to Exhibit 10.5(c) to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.5(d)*	Form of Restricted Stock Award Agreement under Targacept, Inc. 2000 Equity Incentive Plan (incorporated by reference to Exhibit 10.5(d) to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.6(a)*	Targacept, Inc. 2006 Stock Incentive Plan, amended and restated as of November 28, 2007
10.6(b)*	Form of Incentive Stock Option Agreement under Targacept, Inc. 2006 Stock Incentive Plan (incorporated by reference to Exhibit 10.6(a) to Amendment No. 3 to the Company's Registration Statement on Form S-1/A, as filed with the SEC on March 16, 2006 (Registration No. 333-131050))
10.6(c)*	Form of Nonqualified Stock Option Agreement under Targacept, Inc. 2006 Stock Incentive Plan (incorporated by reference to Exhibit 10.6(b) to Amendment No. 3 to the Company's Registration Statement on Form S-1/A, as filed with the SEC on March 16, 2006 (Registration No. 333-131050))
10.6(d)*	Form of Non-employee Director Nonqualified Stock Option Agreement under Targacept, Inc. 2006 Stock Incentive Plan (incorporated by reference to Exhibit 10.6(c) to Amendment No. 3 to the Company's Registration Statement on Form S-1/A, as filed with the SEC on March 16, 2006 (Registration No. 333-131050))
10.6(e)*	Form of Restricted Stock Award Agreement under Targacept, Inc. 2006 Stock Incentive Plan (incorporated by reference to Exhibit 10.6(d) to Amendment No. 3 to the Company's Registration Statement on Form S-1/A, as filed with the SEC on March 16, 2006 (Registration No. 333-131050))
10.7*	Employment Agreement, dated as of August 22, 2000, by and between the Company and J. Donald deBethizy (incorporated by reference to Exhibit 10.7 to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.8*	Employment Agreement, dated as of August 22, 2000, by and between the Company and Merouane Bencherif (incorporated by reference to Exhibit 10.8 to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.9*	Employment Agreement, dated as of August 22, 2000, by and between the Company and William S. Caldwell (incorporated by reference to Exhibit 10.9 to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.10*	Employment Agreement, dated as of April 24, 2001, by and between the Company and Geoffrey C. Dunbar (incorporated by reference to Exhibit 10.10 to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.11*	Employment Agreement, dated as of February 8, 2002, by and between the Company and Alan A. Musso (incorporated by reference to Exhibit 10.11 to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))

Exhibit Number	Description
10.12(a)*	Employment Agreement, dated as of September 1, 2003, by and between the Company and Jeffrey P. Brennan (incorporated by reference to Exhibit 10.12 to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.12(b)*	Amendment No. 1, dated December 3, 2007, to Employment Agreement, dated as of September 1, 2003, by and between the Company and Jeffrey P. Brennan
10.13	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.
10.14+	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. (incorporated by reference to Exhibit 10.16 to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.15(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 (incorporated by reference to Exhibit 10.17(a) to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.15(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 (incorporated by reference to Exhibit 10.17(b) to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.16(a)+	License Agreement, dated May 26, 1999, by and between the Company and the University of Kentucky Research Foundation (incorporated by reference to Exhibit 10.18(a) to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.16(b)+	Amendment No. 1, dated August 16, 2005, to License Agreement, dated May 26, 1999, by and between the Company and the University of Kentucky Research Foundation (incorporated by reference to Exhibit 10.18(b) to Amendment No. 5 to the Company's Registration Statement on Form S-1/A, as filed with the SEC on April 6, 2006 (Registration No. 333-131050))
10.17+	License Agreement, effective as of August 12, 2002, between the Company and Wake Forest University Health Sciences (incorporated by reference to Exhibit 10.19 to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.18(a)+	Collaborative Research and License Agreement, dated as of December 27, 2005, by and between the Company and AstraZeneca AB (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2006)
10.18(b)	Amendment No. 1 dated November 10, 2006 to Collaborative Research and License Agreement between the Company and AstraZeneca AB dated December 27, 2005 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2006)
10.19+	Exclusive License Agreement, dated January 22, 2007, by and between the Company and Yale University (incorporated by reference to Exhibit 10.20 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2006)
10.20	Modified AIA Document B141 Standard Form of Agreement Between Owner and Architect, dated January 22, 2007, by and between the Company and O'Brien Atkins Associates, PA (incorporated by reference to Exhibit 10.21 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2006)

Exhibit Number	Description
10.21	Modified AIA Document A111 Standard Form of Agreement Between Owner and Contractor where the basis of payment is Cost of the Work Plus a Fee and modified AIA Document A201 General Conditions of the Contract for Construction, dated January 22, 2007, by and between the Company and Shelco, Inc. (incorporated by reference to Exhibit 10.22 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2006)
10.22+	Product Development and Commercialization Agreement, dated July 27, 2007, by and between the Company, on the one hand, and SmithKline Beecham Corporation, doing business as GlaxoSmithKline, and Glaxo Group Limited, on the other hand (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2007)
10.23	Stock Purchase Agreement, dated July 27, 2007, by and between the Company and Glaxo Group Limited (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2007)
10.24	Master Clinical Services Agreement, dated May 10, 2005, between the Company and Forenap Pharma EURL (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2007)
10.25*	Description of Annual Cash Incentive Program (incorporated by reference to Exhibit 10.23 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2006)
10.26*	Description of Non-Employee Director Compensation Program (incorporated by reference to Exhibit 10.24 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2006)
23.1	Consent of Ernst & Young LLP
24.1	Power of Attorney (included on signature page)
31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1	Certification of the Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

+ Confidential treatment has been granted with respect to certain portions of this Exhibit, which portions have been omitted and filed separately with the SEC as part of an application for confidential treatment.

* Denotes management compensation plan or contract

Our SEC file number for documents filed with the SEC pursuant to the Securities Exchange Act of 1934, as amended, is 000-51173.

EXHIBIT 31.1

CERTIFICATION

I, J. Donald deBethizy, certify that:

1. I have reviewed this Annual Report on Form 10-K of Targacept, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 14, 2008

By: /s/ J. DONALD DEBETHIZY

J. Donald deBethizy

President and Chief Executive Officer

EXHIBIT 31.2

CERTIFICATION

I, Alan A. Musso, certify that:

1. I have reviewed this Annual Report on Form 10-K of Targacept, Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

(a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

(b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

(c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

(d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

(a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

(b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 14, 2008

By: /s/ ALAN A. MUSSO

Alan A. Musso

Vice President, Chief Financial Officer and Treasurer

EXHIBIT 32.1

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Targacept, Inc. (the "Company") for the period ended December 31, 2007 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, J. Donald deBethizy, President and Chief Executive Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 14, 2008

By: /s/ J. DONALD DEBETHIZY

J. Donald deBethizy
President and Chief Executive Officer

EXHIBIT 32.2

CERTIFICATION PURSUANT TO 18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of Targacept, Inc. (the "Company") for the period ended December 31, 2007 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Alan A. Musso, Vice President, Chief Financial Officer and Treasurer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

(1) The Report fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: March 14, 2008

By: /s/ ALAN A. MUSSO

Alan A. Musso
Vice President, Chief Financial Officer and Treasurer

SELECTED FINANCIAL DATA

	Year Ended December 31,				
	2007	2006	2005	2004	2003
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Net operating revenues	$ 11,576	$ 27,538	$ 1,180	$ 3,738	$ 2,458
Operating expenses:					
Research and development	34,620	21,788	24,252	22,771	18,179
General and administrative	8,013	5,696	4,753	5,163	3,600
Transaction charges	—	—	1,635	—	—
Cost of product sales	715	457	481	198	743
Total operating expenses	43,348	27,941	31,121	28,132	22,522
Loss from operations	(31,772)	(403)	(29,941)	(24,394)	(20,064)
Interest and dividend income	3,837	2,584	1,174	505	791
Interest expense	(138)	(84)	(225)	(132)	(122)
Loss on disposal of fixed assets	—	—	—	(4)	—
Net (loss) income	(28,073)	2,097	(28,992)	(24,025)	(19,395)
Deemed dividend-beneficial conversion feature for Series C redeemable convertible preferred stock issued December 2004	—	—	—	(10,312)	—
Preferred stock accretion	—	(3,333)	(11,238)	(8,744)	(8,341)
Net loss attributable to common stockholders	$ (28,073)	$ (1,236)	$ (40,230)	$ (43,081)	$ (27,736)
Basic and diluted net loss per share applicable to common stockholders	(1.42)	$ (0.09)	$ (153.54)	$ (196.53)	$ (254.33)
Shares used to compute basic and diluted net loss per share	19,720,732	13,595,523	262,013	219,213	109,053

	As of December 31,				
	2007	2006	2005	2004	2003
			(in thousands)		
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 87,040	$ 54,190	$ 24,851	$ 53,075	$ 42,977
Working capital	77,217	69,903	20,531	50,079	40,526
Total assets	98,965	81,368	28,001	58,204	47,390
Long-term debt, net of current portion	1,686	816	1,409	3,443	1,462
Redeemable convertible preferred stock	—	—	183,628	171,778	130,134
Accumulated deficit	(164,235)	(136,162)	(174,983)	(134,754)	(91,672)
Total stockholders' equity (deficit)	51,584	64,999	(162,481)	(122,966)	(90,796)

J. Donald deBethizy, Ph.D.
President and Chief Executive Officer

Merouane Bencherif, M.D., Ph.D.
Vice President, Preclinical Research

Jeffrey P. Brennan
Vice President, Business and Commercial Development

William S. Caldwell, Ph.D.
Vice President, Drug Discovery and Development

Geoffrey C. Dunbar, M.D.
Vice President, Clinical Development and Regulatory Affairs

Alan A. Musso, C.P.A., C.M.A.
Vice President, Chief Financial Officer and Treasurer

Peter A. Zorn, Esq.
Vice President, Legal Affairs, General Counsel and Secretary

Karen A. Hicks
Senior Director of Human Resources

Mauri K. Hodges, C.P.A., C.C.P.
Senior Director of Finance and Controller

Targacept Senior Management Team

American Stock Transfer & Trust Company
59 Maiden Lane
New York, NY 10038
800.937.5449
www.amstock.com

Ernst & Young LLP
202 Centreport Drive, Suite 200
Greensboro, NC 27409

Mark Skaletsky, Chairman of the Board
Chairman and Chief Executive Officer, Trine Pharmaceuticals

M. James Barrett, Ph.D.
General Partner, New Enterprise Associates

Charles A. Blixt, Esq.
General Counsel, Reynolds American (Retired)

Julia R. Brown
Advisor to the CEO, Amylin Pharmaceuticals

G. Steven Burrill
Chief Executive Officer, Burrill & Company, LLC

J. Donald deBethizy, Ph.D.
President and Chief Executive Officer, Targacept

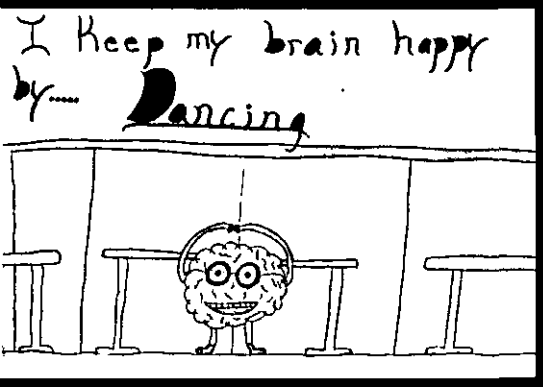
Alan W. Dunton, M.D.
Chief Executive Officer, Panacos Pharmaceuticals

Errol B. De Souza, Ph.D.
President and Chief Executive Officer, Archemix Corporation

John P. Richard
Managing Director, Georgia Venture Partners

Ralph Snyderman, M.D.
Chancellor Emeritus, Duke University
James B. Duke Professor of Medicine,
Duke University School of Medicine

Statements in this 2007 Annual Report that are not purely historical in nature, including, without limitation, statements regarding the progress, timing or scope of the research and development of our product candidates or related regulatory filings or clinical trials, any future payments that AstraZeneca or GlaxoSmithKline may make to us, or our plans, expectations, future operations, financial position, revenues, costs or expenses, constitute forward-looking statements made under The Private Securities Litigation Reform Act of 1995. For important information regarding forward-looking statements, please read the Cautionary Note Regarding Forward-Looking Statements included in our Annual Report on Form 10-K for the year ended December 31, 2007, which applies also to any forward-looking statement included elsewhere in this 2007 Annual Report. In particular, please be aware that actual results may differ materially from those expressed or implied by forward-looking statements as a result of various important factors, including our critical accounting policies and the risks and uncertainties described under the heading "Cautionary Note Regarding Forward-Looking Statements" or "Risk Factors" in our most recent Annual Report on Form 10-K, in our subsequent Quarterly Reports on Form 10-Q or in other filings that we make with the Securities and Exchange Commission. As a result of the risks and uncertainties, the results or events indicated by the forward-looking statements may not occur. We caution you not to place undue reliance on any forward-looking statement.



Targacept plays a strong role in many community outreach activities focusing on biotechnology, economic and workforce development, and education. In Winston-Salem, the first annual children's Brain Art Contest was one event of many celebrating Brain Awareness Week, an international effort to advance public awareness about the progress and benefits of brain research.

TARGACEPT

Targacept, Inc.
200 East First Street, Suite 300
Winston-Salem, NC 27101-4165
336.480.2100
336.480.2107 facsimile

Targacept is traded on the NASDAQ Global Market under the symbol TRGT.

WWW.TARGACEPT.COM

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