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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, 2008

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 (NASDAQ Global Market)**

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, 2008, was approximately $117,729,319, based on the price at which the registrant's common stock was last sold on June 30, 2008 ($7.27).

As of February 28, 2009, the registrant had 24,965,173 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 2009 annual meeting of stockholders, 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, 2008, are incorporated by reference into Part III of this report.

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Cautionary Note Regarding Forward-Looking Statements

This annual report includes forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and 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, other than statements of historical fact, regarding the timing for a decision by AstraZeneca whether to conduct further development of AZD3480 (TC-1734) in Alzheimer's disease or attention deficit/hyperactivity disorder, or ADHD, the progress or scope of the research and development of our product candidates, such as the number of subjects to be enrolled in any clinical trial, the timing for initiation or completion of or availability of results from any clinical trial or the indication for which any of our product candidates may be developed, any future payments that AstraZeneca or GlaxoSmithKline may make to us, our continued sale of Inversine®, our future operations, financial position, revenues, costs or expenses, or our strategies, prospects, plans, expectations or objectives 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 significant control that AstraZeneca has over the development of AZD3480, including as to whether to conduct any further development of AZD3480 in Alzheimer's disease or ADHD; the conduct and results of the ongoing clinical trial of AZD3480 in ADHD in adults and other studies ongoing being conducted by AstraZeneca, including the amount and timing of resources that AstraZeneca devotes, the performance of third parties engaged to execute them and difficulties or delays in data analysis; the risks that successful results in a particular clinical trial of AZD3480 may not be replicated in other clinical trials or that successful results in clinical trials of AZD3480 in a particular condition characterized by one degree of cognitive impairment may not be predictive of successful results in clinical trials of AZD3480 in a condition characterized by more severe cognitive impairment or in cognitive impairment resulting from a different condition; the conduct and results of clinical trials and non-clinical studies and assessments of TC-5214 and our other product candidates, including the performance of third parties engaged to execute such trials, studies and assessments, delays resulting from any changes to the applicable protocols and difficulties or delays in the completion of subject enrollment or data analysis; our ability to establish additional strategic alliances, collaborations and licensing or other arrangements on favorable terms; and the timing and success of submission, acceptance and approval of regulatory filings. These and other risks and uncertainties are described in greater 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.

In addition, any forward-looking statement in this annual report represents 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, 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 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 have multiple clinical-stage product candidates and preclinical programs in areas where we believe there are significant medical need and commercial potential, as well as proprietary drug discovery technologies. We also have a cognition-focused collaboration with AstraZeneca and a strategic alliance with GlaxoSmithKline.

TC-5214

TC-5214 modulates the activity of various NNR subtypes, including multiple forms of the a4ß2 NNR. We are conducting an ongoing Phase 2b clinical trial of TC-5214 as an augmentation treatment in subjects with major depressive disorder who do not respond well to first-line treatment with the marketed drug citalopram hydrobromide. We may also conduct development of TC-5214 in one or more other indications.

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. We previously completed a Phase 2 clinical trial of the racemate mecamylamine hydrochloride as an augmentation treatment in subjects with major depressive disorder who did not respond well to first-line treatment with citalopram. In our evaluation in various preclinical models of depression, TC-5214 more often exhibited antidepressant activity, had equal or superior potency and exhibited a more favorable safety profile as compared to mecamylamine. We have no current plans to conduct further clinical development of racemic mecamylamine and intend instead to develop TC-5214.

AZD3480 (TC-1734), AZD1446 (TC-6683) and AstraZeneca Collaboration

AZD3480 (TC-1734) is a novel small molecule that modulates the activity of the a4ß2 NNR. We have a collaborative research and license agreement with AstraZeneca AB for the development and worldwide commercialization of AZD3480 as a treatment for various conditions characterized by cognitive impairment, including Alzheimer's disease and ADHD. We and AstraZeneca are conducting an ongoing exploratory Phase 2 trial of AZD3480 in adults with ADHD. In 2008, AstraZeneca completed two Phase 2b clinical trials of AZD3480, one in mild to moderate Alzheimer's disease and one in cognitive dysfunction in schizophrenia. We expect AstraZeneca to make a decision whether to conduct further development of AZD3480 in either or both of Alzheimer's disease or ADHD in the second quarter of 2009. In December 2008, we and AstraZeneca announced that AZD3480 is not expected to be advanced into Phase 3 clinical development in cognitive dysfunction in schizophrenia.

We and AstraZeneca are conducting a preclinical research collaboration under the agreement that is designed to discover and develop additional compounds that, like AZD3480, act on the a4ß2 NNR as treatments

for conditions characterized by cognitive impairment. AstraZeneca is responsible for funding the research collaboration, which began in January 2006 and is scheduled to expire in January 2010. AstraZeneca initiated Phase 1 clinical development of the most advanced compound arising from the preclinical research collaboration, AZD1446 (TC-6683), in December 2008.

Except for the exploratory Phase 2 trial of AZD3480 in adults with ADHD, AstraZeneca is responsible for the clinical development and commercialization of AZD3480, AZD1446 and any other compounds that arise from the preclinical research collaboration that it elects to advance. We have the option to co-promote AZD3480, AZD1446 and any other compounds that arise from the preclinical research collaboration that are selected for advancement to specified classes of specialist physicians in the United States.

TC-5619

TC-5619 is a novel small molecule that we plan to develop for cognitive dysfunction in schizophrenia or potentially one or more other conditions characterized by cognitive impairment. TC-5619 modulates the activity of the a7 NNR. We have completed a Phase 1 single rising dose clinical trial and a Phase 1 multiple rising dose clinical trial of TC-5619 in healthy volunteers. 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 previously initiated under our agreement with AstraZeneca and a related election made by AstraZeneca, 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 schizophrenia and various conditions characterized by cognitive impairment on terms specified in the agreement.

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. We are eligible under the agreement to receive 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 collaboration agreement with AstraZeneca.

TC-2216 or enantiomer

TC-2216 is a product candidate for depression and anxiety disorders. TC-2216, which is a racemate, and its enantiomers inhibit the activity of the a4ß2 NNR. We completed a Phase 1 single rising dose clinical trial of TC-2216 in healthy volunteers in the first quarter of 2008. Based on 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 2009. If we elect to continue development in the future, we are likely to elect to develop one of the enantiomers of TC-2216 instead of conducting further clinical development of TC-2216.

Pentad™

Our drug discovery activities utilize sophisticated proprietary computer-based molecular design methodologies and extensive biological and chemical data for a library of diverse compounds developed and collected over more than 20 years. We refer to these technologies collectively as Pentad.

Inversine

We have one product approved by the U.S. Food and Drug Administration, or FDA, for marketing, which is known as Inversine. 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. Mecamylamine hydrochloride is the active ingredient in Inversine. As a result of increased FDA fees and declining prescriptions for Inversine, we expect that we may discontinue sales of Inversine as soon as the second half of 2009.

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 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 describing 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 cognition-focused collaboration with AstraZeneca, as well as a strategic 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. We intend to selectively seek additional alliances and collaborations to assist us in furthering the development of some of our product candidates. In particular, we intend to enter into these alliances and collaborations for target indications for which our potential collaborator has particular expertise or that involve large primary care markets 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 for specialists, particularly in neurology and psychiatry, in the United States and, potentially in some cases, other markets. Under our agreement with AstraZeneca, we have the option to co-promote AZD3480 and any compounds arising out of the research collaboration that are selected for advancement to specified classes of specialist 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 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.

Our Product Development Pipeline

The following table summarizes our pipeline of clinical-stage product candidates.

Product Candidate	Planned Target Indication(s)	Status of Development	Commercial Rights
TC-5214	Major depressive disorder (augmentation treatment) and potentially one or more other indications	Phase 2b trial in major depressive disorder ongoing	Targacept
AZD3480 (TC-1734)	Alzheimer's disease; ADHD	Exploratory Phase 2 trial in ADHD ongoing; Phase 2b trial in mild to moderate Alzheimer's disease complete	AstraZeneca
TC-5619	Cognitive dysfunction in schizophrenia or one or more other conditions characterized by cognitive impairment	Phase 1 complete	subject to option of AstraZeneca*
AZD1446 (TC-6683)	Alzheimer's disease, ADHD or one or more other conditions characterized by cognitive impairment	Phase 1 trial ongoing	AstraZeneca
TC-2216 or enantiomer	Depression and anxiety disorders	Phase 1 single rising dose trial of TC-2216 completed; no further clinical development expected in 2009	Targacept

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

We are conducting our ongoing Phase 2b trial of TC-5214 in India and the United States and anticipate that we will conduct our planned Phase 2 clinical trial of TC-5619 in the United States. We and AstraZeneca are conducting the ongoing exploratory Phase 2 trial of AZD3480 in adults with ADHD at a single site in the United States. AstraZeneca is conducting the Phase 1 trial of AZD1446 in Sweden.

Information regarding our research and development expenses for the fiscal years ended December 31, 2008, 2007 and 2006 is included under "Management's Discussion and Analysis of Financial Condition and Results of Operations" in this annual report.

TC-5214

TC-5214 modulates the activity of various NNR subtypes, including multiple forms of the a4ß2 NNR. We are conducting an ongoing Phase 2b clinical trial of TC-5214 as an augmentation treatment in subjects with major depressive disorder who do not respond well to first-line treatment with the marketed drug citalopram hydrobromide. Citalopram is from the class of drugs known as selective serotonin reuptake inhibitors and is

marketed as Celexa in the United States. We may also conduct development of TC-5214 in one or more other indications. In 2008, we completed a Phase 1 single rising dose clinical trial of TC-5214 in healthy volunteers.

TC-5214 is one of the two enantiomers of mecamylamine hydrochloride. We previously conducted a Phase 2 clinical trial of the racemate mecamylamine hydrochloride as an augmentation treatment to citalopram in subjects with major depressive disorder who did not respond well to first-line treatment with citalopram. In our evaluation in various preclinical models of depression, TC-5214 more often exhibited antidepressant activity, had equal or superior potency and exhibited a more favorable safety profile as compared to mecamylamine. We have no current plans to conduct further clinical development of racemic mecamylamine and intend instead to develop TC-5214.

Ongoing Phase 2b Clinical Trial in Major Depressive Disorder. We are conducting our ongoing Phase 2b clinical trial of TC-5214 in major depressive disorder at approximately three sites in the United States and 24 sites in India. The trial includes an open label phase and a double blind, placebo controlled phase. The term “double blind” means that neither the subjects nor the clinical investigators know during the trial which subjects receive drug and which subjects receive placebo.

In the first phase of the trial, subjects diagnosed with major depressive disorder receive citalopram for eight weeks to determine the extent of therapeutic response. Subjects who do not respond well based on predefined criteria on the Montgomery-Asburg Depression Rating Scale, or MADRS, and the Clinical Global Impression subscale for severity of illness, or CGI-SI, are randomized into the double blind, placebo controlled second phase of the trial. MADRS is a scale on which the clinician evaluates the subject’s depressed mood and other symptoms of depression and anxiety and CGI-S is a scale on which the clinician assesses how ill a subject is based on his or her total clinical experience. Subjects in the second phase receive either TC-5214 or placebo, together with continued citalopram therapy, for an additional eight weeks.

As of February 28, 2009, we have enrolled 586 subjects into the first phase of the ongoing Phase 2b trial of TC-5214 and the trial is fully enrolled. We project that over 220 subjects will be randomized into the second phase of the trial. The primary endpoint of the trial is group mean change from baseline in the second phase of the trial as measured by HAM-D. The trial also includes a number of secondary endpoints. We expect top-line results from the trial to be available in mid 2009.

Major depressive disorder is characterized by a combination of symptoms that interfere with a person’s ability to work, sleep, study, eat and enjoy once-pleasurable activities. It is disabling and can prevent a person from functioning normally. The market research firm Business Insights estimated that, in 2007, there were approximately 44 million people with major depressive disorder in the world’s seven major pharmaceutical markets—the United States, France, Germany, Italy, Spain, the United Kingdom and Japan. The Sequenced Treatment Alternatives to Relieve Depression, or STAR*D, study undertaken by the National Institute of Mental Health between 2001 and 2006 showed the inadequacy of currently available therapies for major depressive disorder. In the first phase of the STAR*D study, approximately 2,800 persons with major depressive disorder were given citalopram hydrobromide for 12 to 14 weeks. Only about one-third of the participants became symptom free, which is referred to as achieving “remission,” and about 10-15 percent more responded, but did not reach remission.

Completed Phase 2 Clinical Trial of Racemic Mecamylamine Hydrochloride. In 2006, we completed a Phase 2 clinical trial of the racemate mecamylamine hydrochloride as an augmentation treatment to citalopram hydrobromide in subjects with major depressive disorder who did not respond well to first-line treatment with citalopram. We refer to this treatment combination as TRIDMAC™. We conducted the trial at one site in the United States and eight sites in India. Like the ongoing Phase 2b clinical trial of TC-5214 described above, the completed Phase 2 clinical trial of TRIDMAC had two phases, an open label phase in which subjects received citalopram for six weeks and a double blind, placebo controlled phase in which subjects 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 at the end of

the open label phase 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. Subjects 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.

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. The p-value required to achieve statistical significance in a clinical trial depends on the particular design and objective of the trial.

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 in favor of TRIDMAC, but not statistical significance, on a per protocol basis, with a p-value of 0.059. The result on the achievement of remission endpoint favored the TRIDMAC dose group over the placebo dose 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 dose group over the placebo dose 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.

AZD3480 (TC-1734)

AZD3480 (TC-1734) is a novel small molecule in development in collaboration with AstraZeneca. AZD3480 modulates the activity of the a4ß2 NNR. We and AstraZeneca are evaluating AZD3480 in an ongoing exploratory Phase 2 trial in adults with ADHD. In 2008, AstraZeneca completed two Phase 2b clinical trials of AZD3480, one in mild to moderate Alzheimer's disease and one in cognitive dysfunction in schizophrenia. Pending completion of the trial in adults with ADHD and other ongoing evaluations, we expect AstraZeneca to make a decision whether to conduct further development of AZD3480 in either or both of Alzheimer's disease or ADHD in the second quarter of 2009. In December 2008, we and AstraZeneca announced that AZD3480 is not expected to be advanced into Phase 3 clinical development in cognitive dysfunction in schizophrenia.

Prior to 2008, we evaluated AZD3480 in two Phase 2 clinical trials in age associated memory impairment, or AAMI, a common condition characterized by gradual memory loss or other cognitive impairment that generally occurs with normal aging, and a third Phase 2 clinical trial in mild cognitive impairment, or MCI, as well as four Phase 1 clinical trials.

Ongoing Exploratory Phase 2 Trial in Adults with ADHD

We and AstraZeneca are collaborating on the execution of an exploratory Phase 2 trial of AZD3480 in adults with ADHD. The trial is being conducted at a single site in Vermont. The trial is designed to evaluate 24 subjects and enrollment was completed in February 2009. We expect the trial to be completed in the second quarter of 2009.

The trial utilizes a double blind, placebo controlled, crossover design. The primary objective of the trial is to assess the effects of 5mg and 50mg daily doses of AZD3480 as measured by the Conners Adult ADHD Rating Scale—Investigator Rating in adults with ADHD. The crossover design means that each subject receives, in random order and for prescribed periods, each dose strength of AZD3480 and placebo, with the three dosing periods separated by periods without any dosing. This enables each subject to serve as his or her own control. We are responsible for managing and funding the trial, and AstraZeneca is responsible for providing clinical trial materials and communicating with regulatory authorities.

ADHD is a condition that develops during childhood and, if not adequately treated, can have long-term adverse effects into adolescence and adulthood. The principal characteristics of ADHD are inattention, hyperactivity and impulsivity. For an adult to be diagnosed with ADHD, the ADHD symptoms must have begun during childhood and continued throughout adulthood. The market research firm Business Insights estimated that, in 2008, there were approximately 25 million adults with ADHD in the world's seven major pharmaceutical markets.

Completed Phase 2b Clinical Trial in Mild to Moderate Alzheimer's Disease

In 2008, AstraZeneca completed two Phase 2b double blind, placebo controlled, dose finding clinical trials of AZD3480, one in mild to moderate Alzheimer's disease and one in cognitive dysfunction in schizophrenia. The trial in mild to moderate Alzheimer's disease, known as the "Sirocco" trial, was conducted at 84 sites in Western Europe, Eastern Europe and Canada. In the Sirocco trial, 567 subjects who were between 60 and 85 years old and diagnosed with probable Alzheimer's disease classified as mild or moderate in severity were randomly assigned to one of three dose groups of AZD3480, to the active comparator donepezil, or to placebo and dosed over a 12-week period. The dose groups of AZD3480 ranged from a dose lower than we previously evaluated in our Phase 2 clinical trials of AZD3480 to up to 100mg. The primary outcome measure of the trial was change from baseline after 12 weeks on the Alzheimer's Disease Assessment Scale-cognitive subscale, or ADAS-Cog. Some of the secondary outcome measures of the trial included the Alzheimer's Disease Cooperative Study—Clinical Global Impression of Change, or ADCS-CGIC, which is a 7-point clinician assessment of change in behavior and the ability to function, the Mini Mental State Examination, or MMSE, which is a quantitative, 30-point cognition scale, and a computer-based test battery developed by CDR Ltd. to test cognitive function.

The results of the Sirocco trial were inconclusive. Neither the active comparator donepezil nor AZD3480 met the trial's criteria for statistical significance on the primary outcome measure, ADAS-Cog. On the secondary outcome measures, subjects dosed with AZD3480 showed an improvement on ADCS-CGIC and the MMSE at two of the three doses tested as compared to subjects dosed with placebo. Of the three AZD3480 doses evaluated, subjects in the middle dose group showed the most improvement on both measures as compared to subjects dosed with placebo, with a 0.5 point advantage on ADCS-CGIC and a 0.9 point advantage on the MMSE. Subjects dosed with donepezil also showed an improvement as compared to subjects dosed with placebo on ADCS-CGIC, with a 0.2 point advantage, and the MMSE, with a 1.0 point advantage. No improvement was shown in any domain of the CDR test battery in the pooled dataset of all subjects in the donepezil dose group or any of the AZD3480 dose groups as compared to the placebo dose group. AZD3480 exhibited an overall safety and tolerability profile comparable to placebo in the trial.

Alzheimer's disease, the most common form of dementia, is a debilitating brain disorder for which there is no cure. The market research firm Business Insights estimated that, in 2007, there were approximately

6.6 million people with Alzheimer's disease in the world's seven major pharmaceutical markets. The disease progresses in stages from mild to moderate to severe and gradually destroys a person's memory and ability to learn, reason, make judgments, communicate and carry out daily activities. Mild Alzheimer's disease is characterized by mild forgetfulness and difficulty acquiring basic information and communicating. Patients generally exhibit the symptoms of mild Alzheimer's disease for two to four years before progressing to the moderate stage. Moderate Alzheimer's disease is characterized by forgetfulness, failure to recognize friends and family, disorientation regarding time and place and personality changes. Patients generally exhibit the symptoms of moderate Alzheimer's disease for up to ten years before progressing to the severe stage. Severe Alzheimer's disease is characterized by difficulty performing simple tasks and activities associated with daily living. Patients with severe Alzheimer's disease require continuous care and generally do not survive for more than three years.

Completed Phase 2b Clinical Trial in Cognitive Dysfunction in Schizophrenia

AstraZeneca's Phase 2b clinical trial of AZD3480 in cognitive dysfunction in schizophrenia completed in 2008, known as the "HALO" trial, was conducted at approximately 70 enrolling sites in the United States and Canada. In the trial, 445 subjects diagnosed with schizophrenia who were between 18 and 55 years old, active smokers, taking a marketed drug from the class known as atypical anti-psychotics and clinically stable were randomly assigned to one of three dose groups of AZD3480 or to placebo and dosed, together with continued treatment with the applicable atypical anti-psychotic, over a 12-week period. The primary endpoints of the trial were change from baseline after 12 weeks on scores for attention/vigilance, working memory, verbal learning, speed of processing and reasoning and problem solving as measured by a computerized test battery known as IntegNeuro. As used in this annual report, the terms "endpoint" and "outcome measure" have the same meaning. AZD3480 did not meet the HALO trial's criteria for statistical significance on any of the primary endpoints. In December 2008, we and AstraZeneca announced that AZD3480 is not expected to be advanced into Phase 3 clinical development in cognitive dysfunction in schizophrenia.

Phase 2 Clinical Trial in AAMI Completed in 2006

In 2006, we completed a double blind, placebo controlled Phase 2 clinical trial of AZD3480 in AAMI 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, 50mg of AZD3480 and placebo. The trial assessed the effects of AZD3480 on various aspects of cognitive function 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 five factors—power of attention, continuity of attention, working or short-term memory, episodic or long-term memory and speed of memory.

There were three co-primary efficacy endpoints for the 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.

On both a per protocol basis and an intent to treat basis, subjects in the 50mg AZD3480 dose group showed improvement as compared to subjects in the placebo dose group on all three co-primary efficacy endpoints and

subjects in the 25mg AZD3480 dose group showed improvement as compared to subjects in the placebo dose group on the power of attention endpoint. These results were statistically significant, with p-values less than 0.05. The per protocol dataset included 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 dataset included all subjects who received at least one dose of trial medication (AZD3480 or placebo) and completed at least one cognitive function assessment.

Previous Clinical Trials

Prior to the Phase 2 clinical trial of AZD3480 in AAMI described above, we completed two double blind, placebo controlled, crossover design Phase 2 clinical trials of AZD3480. 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. In the AAMI trial, we evaluated four doses of AZD3480, 50mg, 100mg, 125mg and 150mg. In the MCI trial, we evaluated two doses of AZD3480, 50mg and 100mg. Each trial assessed the effects of AZD3480 on various aspects of 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.

The results of the AAMI trial were most favorable in the 50mg AZD3480 dose group. In that dose group, we achieved statistically significant results in favor of AZD3480 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 and the number of subjects in that dose group for that test factor that were dosed with placebo.

The favorable results in the 50mg dose group were less pronounced in the other dose groups. However, in each of the other dose groups, we achieved a statistically significant result in favor of AZD3480 on at least one of the CDR test factors at at least one of the time points evaluated.

In the 100mg dose group of the MCI trial, we achieved a statistically significant result in favor of AZD3480 on the episodic memory factor. The results in the 50mg AZD3480 dose group did not favor AZD3480.

Prior to our Phase 2 clinical trials of AZD3480, we completed four Phase 1 clinical trials in 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. Pharmacokinetics refers to a compound's absorption, distribution and metabolism in, and excretion from, the body.

TC-5619

TC-5619 is a novel small molecule that we plan to develop for cognitive dysfunction in schizophrenia or potentially one or more other conditions characterized by cognitive impairment. We have completed a Phase 1 single rising dose clinical trial and a Phase 1 multiple rising dose clinical trial of TC-5619. TC-5619 was

generally well tolerated in both Phase 1 trials at doses at least 100 times greater than the doses that we expect to evaluate in future trials.

TC-5619 modulates the activity of the a7 NNR. In a 2004 survey of 46 cognitive neuroscientists and neuropharmacologists conducted in connection with a National Institute of Mental Health initiative known as Measurement and Treatment Research to Improve Cognition in Schizophrenia, or MATRICS, a7 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 made an election in November 2007 pursuant to which we would 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 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, first commercial sale and first detail milestones for three indications, 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 TC-5619.

Schizophrenia is a chronic, severe and disabling form of psychosis. In addition to symptoms such as delusions, hallucinations, the inability to disregard familiar stimuli, sometimes referred to as sensory gating, disorganized speech, grossly disorganized or catatonic behavior and prolonged loss of emotion, feeling, volition or drive, schizophrenia is often marked by impairment in cognitive functions, such as attention, vigilance, memory, and reasoning. The market research firm Business Insights estimated that, in 2007, there were approximately 7.9 million people with schizophrenia in the world’s seven major pharmaceutical markets. It has been estimated that up to 75% of persons with schizophrenia are cognitively impaired. There is currently no drug approved specifically for cognitive dysfunction in schizophrenia.

AZD1446 (TC-6683)

AZD1446 (TC-6683) is a novel small molecule that we discovered and advanced as part of the preclinical research collaboration that we are conducting with AstraZeneca. AZD1446 modulates the activity of the a4ß2 NNR and is in development for Alzheimer’s disease, ADHD or one or more other conditions characterized by cognitive impairment. AstraZeneca initiated Phase 1 clinical development of AZD1446 in December 2008.

TC-2216 or enantiomer

Depression and anxiety disorders often occur together, and anti-depressants are often also used to treat anxiety disorders. TC-2216 is a product candidate for depression and anxiety disorders. TC-2216, which is a racemate, and its enantiomers inhibit the activity of the a4ß2 NNR. We completed a Phase 1 single rising dose clinical trial of TC-2216 in healthy volunteers in the first quarter of 2008. Based on 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 2009. If we continue development in the future, we are likely to elect to develop one of the enantiomers of TC-2216 instead of conducting further clinical development of TC-2216.

TC-6499

TC-6499 is a novel small molecule that modulates the activity of the a4ß2 NNR. We have completed three Phase 1 clinical trials of TC-6499 in healthy volunteers. In March 2009, we announced that the results from a Phase 1 multiple rising dose trial did not project a therapeutic margin sufficient to support further development of TC-6499 as a treatment for neuropathic pain. We have no current plans to conduct additional clinical development of TC-6499.

Our Preclinical Research Programs

In addition to our clinical-stage product candidates, we focus preclinical research efforts in areas in which we believe NNRs can be exploited for medical benefit and 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 a4ß2 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 the therapeutic focus areas of our agreement with GlaxoSmithKline. In addition, we have a program focused on the role of NNRs in inflammation. In 2008, we achieved milestone events under our alliance with GlaxoSmithKline based on progress in our smoking cessation and preclinical pain programs. The financial resources that we apply to and the progress that we may make in any particular preclinical program may vary from period to period and year to year.

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 a6, a4, ß2 and ß4 NNR subunits may be involved. These studies have shown that selectively modulating NNRs that include a6, a4, ß2 or ß4 subunits reduced the rewarding effects of nicotine administration in mice or the withdrawal effects of stopping nicotine administration in mice. Other studies have shown that mice deficient in the ß2 NNR subunit failed to self-administer nicotine and had reduced activity in the brain regions associated with reward and pleasure.

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, an association has been shown between certain NNR subunits and brain activity associated with reward and pleasure. Accordingly, we believe that compounds that modulate NNRs may have the potential to decrease the rewarding effects of drugs of abuse such as alcohol or cocaine.

Obesity

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 often 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 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 a6, a4 and ß2 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 a 7 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 and chemical data for 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 and prioritization 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 believed to have a greater likelihood of clinical success.

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 $718,000 for the year ended December 31, 2008, $518,000 for the year ended December 31, 2007, and $585,000 for the year ended December 31, 2006. As a result of increased FDA fees and declining prescriptions for Inversine, we expect that we may discontinue sales of Inversine as soon as the second half of 2009.

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 as a treatment for specified conditions characterized by cognitive impairment, including Alzheimer's disease, cognitive dysfunction in schizophrenia, ADHD, AAMI, MCI and any other indication that is deemed a cognitive disorder under the agreement, as well as schizophrenia. The agreement became effective in January 2006.

Under the agreement, we and AstraZeneca are conducting an ongoing exploratory Phase 2 trial of AZD3480 in adults with ADHD. In 2008, AstraZeneca completed two Phase 2b clinical trials of AZD3480, one in mild to moderate Alzheimer's disease and one in cognitive dysfunction in schizophrenia. We expect AstraZeneca to make a decision whether to conduct further development of AZD3480 in either or both of Alzheimer's disease or ADHD in the second quarter of 2009. In December 2008, we and AstraZeneca announced that AZD3480 is not expected to be advanced into Phase 3 clinical development in cognitive dysfunction in schizophrenia. We and AstraZeneca are also conducting a preclinical research collaboration under the agreement. AstraZeneca initiated Phase 1 clinical development of the most advanced compound arising from the preclinical research collaboration, AZD1446, in December 2008.

As a result of a process that we previously initiated under the agreement and a related election made by AstraZeneca, 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 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. We are eligible to receive other payments of up to $197 million, if AstraZeneca decides to conduct further development of AZD3480 in both Alzheimer's disease and ADHD and if development, regulatory, first commercial sale and first detail milestones for AZD3480 are achieved for both indications, and stepped double-digit royalties on any future AZD3480 product sales. If AZD3480 is developed under the agreement for an indication in addition to Alzheimer's disease and ADHD, we would also be eligible to receive payments of up to $52 million, contingent upon the achievement of development, regulatory, first commercial sale and first detail milestones for AZD3480 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.

With respect to AZD1446, AstraZeneca has paid us $2.2 million upon the achievement of development and regulatory milestones. We are also eligible to receive other payments of up to $108 million, contingent upon the achievement of development, regulatory, first commercial sale and first detail milestones for AZD1446 for two indications, and stepped royalties on any future AZD1446 product sales.

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 for three indications, 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 12 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 expire between 2016 and 2026. The foreign patent rights that have issued and correspond to our issued U.S. patent rights expire between 2017 and 2019. We also have pending U.S. and foreign patent applications that, if issued, would expire between 2017 and 2028. The U.S. patent rights to the chemical genus that includes TC-5619 expire in 2019. The foreign patent rights corresponding to our issued U.S. patent rights expire in 2024. 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. In addition, we have pending U.S. and foreign patent applications with respect to AZD1446 that, if issued, would expire in 2027. 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, act on the a4ß2 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 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. Under the agreement, for each compound discovered and developed as part of the research collaboration, we are eligible to receive additional payments of up to $75 million, contingent upon the achievement of development, regulatory, first commercial sale and first detail milestones for a single indication, additional contingent payments based on the achievement of milestones for additional indications and stepped royalties on any future product sales. The planned term of the research collaboration is four years and is scheduled to expire in January 2010. The term of the research collaboration can be extended by mutual agreement.

Development and Commercialization Costs. AstraZeneca is responsible for the clinical development and commercialization of AZD3480, AZD1446 and any other compounds that arise from the research collaboration that it elects to advance and for substantially all current and future development costs, except for the ongoing exploratory Phase 2 trial of AZD3480 in adults with ADHD. We have the option to co-promote AZD3480, AZD1446 and any other compounds that arise from 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 an agreed development plan for TC-5619 that includes a planned Phase 2 clinical proof of concept trial, AstraZeneca elects to license rights to TC-5619, AstraZeneca would assume responsibility for and fund all future development and commercialization of TC-5619.

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

With respect to any compound that meets pre-defined criteria for any NNR other than the a4ß2 NNR, at the time the compound has completed the preclinical testing necessary to initiate clinical development, we are entitled to offer to AstraZeneca the right to develop and commercialize it 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 meets pre-defined criteria for any NNR other than the a4ß2 NNR, we are generally not permitted to develop or commercialize the compound for any indication for which AstraZeneca has development and commercialization rights under the agreement.

If we offer a compound to AstraZeneca, AstraZeneca could license the compound from us, together with metabolites of the compound and derivatives and other compounds related to the compound that meet specified criteria, 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, first commercial sale and first detail 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 meet pre-defined criteria for any NNR for any indication for which AstraZeneca has development and commercialization rights under the agreement except through this process.

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

If AstraZeneca commences clinical development outside of the collaboration of a compound that acts on any NNR other than the a7 NNR and meets other pre-defined criteria, the restriction on our right to develop and commercialize compounds that meet pre-defined criteria for any NNR, other than the a 4ß2 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. 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 contingent milestone payments from GlaxoSmithKline as we advance product candidates in each therapeutic focus area through preclinical and Phase 1 clinical development. Our research and development activities in the alliance are 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.

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. As of February 28, 2009, we had received an additional $7.5 million based on achievement of discovery and development milestones under the 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. The amounts that we are eligible to receive include up to $16 million in each of the five therapeutic areas, contingent upon the achievement of specified milestones prior to Phase 2 clinical proof of concept.

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 15 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 activity derived from binding to NNRs. 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 jurisdictions internationally that we consider key pharmaceutical markets. We also rely upon trade secrets and contracts to protect our proprietary information.

As of February 28, 2009, our patent estate included 70 patents issued in the United States, 46 patent applications pending in the United States and over 300 counterpart patents and 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
TC-5214	Pharmaceutical composition of S-mecamylamine	January 2020
	Methods of use of S-mecamylamine for neuropsychiatric disorders, including depression	February 2020
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
	Composition of matter for the preferred salt (p-hydroxybenzoate) of AZD3480	August 2026
TC-5619	Composition of matter for a family of compounds that includes TC-5619	August 2019
	Composition of matter for a racemic mixture that includes TC-5619	March 2019
TC-2216	Composition of matter for TC-2216 as well as a family of compounds that includes TC-2216	June 2023

In addition to these patents, 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 jurisdictions internationally that we consider key pharmaceutical 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 date 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 under patents and patent applications owned by USFRF to develop and

commercialize TC-5214, mecamylamine hydrochloride and other specified compounds. The licensed patents and patent applications include issued patents covering the pharmaceutical composition of TC-5214 and methods of use of each of TC-5214, the other enantiomer of mecamylamine hydrochloride and mecamylamine hydrochloride for the treatment of various disorders, including depression. Under the agreement, we are obligated to pay to USFRF:

- an annual license fee until we or a sublicensee file an NDA or foreign equivalent for use of a product subject to the license to treat a neuropsychiatric disease or disorder;
- an annual fee to maintain our right of first refusal to acquire rights under 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 that we receive 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 one or more products subject to the license. In particular, we are required to spend a specified minimum amount on research and development of products subject to the license each year until we or a sublicensee file an NDA or foreign equivalent for use of a product subject to the license to treat a neuropsychiatric disease or disorder. 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 and specified initial dispute resolution procedures are unsuccessful, we can submit the matter to binding arbitration. In addition, if we or a sublicensee do not file an NDA or foreign equivalent for use of a product subject to the license to treat a neuropsychiatric disease or disorder on or before December 31, 2012, USFRF can make our license nonexclusive.

We may terminate the agreement at any time. USFRF 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 that includes a valid claim.

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, including major depressive disorder. Under the agreement, we are obligated 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 $1.5 million for each product subject to the license for which specified regulatory and first commercial sale milestones are achieved;
- royalties on 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 owned or licensed by us or with an

agreement by us to collaborate to discover, research, develop or commercialize compounds or products for therapeutic use in humans.

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 subject to the license. If not earlier terminated, the agreement will expire upon expiration of the last to expire of the licensed patent rights that includes a valid claim.

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. 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, by 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 for target indications for which our potential collaborator has particular expertise or that involve large primary care markets 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.

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 $170,000 in 2008, $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 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, acts on several NNR subtypes as well as other molecular targets in the body. Chantix is approved 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 Roche, with a compound in Phase 2 for Alzheimer's disease and cognitive impairment associated with schizophrenia (which we refer to as cognitive dysfunction in schizophrenia), and Abbott Laboratories, with one compound in Phase 2 for Alzheimer's disease and ADHD, a second compound in Phase 2 for ADHD and two other compounds in Phase 1 for cognitive disorders or schizophrenia. Other companies that we believe have active NNR-based programs include AstraZeneca, Eli Lilly, Sanofi-Aventis, Wyeth, Bristol Myers Squibb, GlaxoSmithKline, Johnson & Johnson, Novartis, NeuroSearch A/S, Solvay, Servier, CoMentis, EnVivo Pharmaceuticals, Xytis and Galantos Pharma. 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. We believe that the primary competitive products for use in indications that we are currently targeting with our most advanced product candidates include:

- for major depressive disorder, 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 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; and
- for ADHD, stimulants such as Adderall XR and Vyanase from Shire, Concerta from Johnson & Johnson and Ritalin LA from Novartis, and Strattera, a non-stimulant acting as a norepinephrine reuptake inhibitor, from Eli Lilly.

There is currently no approved product for cognitive dysfunction in schizophrenia.

Many of these products have well-known brand names, are distributed by large pharmaceutical companies with substantial resources, have achieved widespread acceptance among physicians and patients and are or may become available in lower priced generic form. Furthermore, pharmaceutical, biopharmaceutical 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 and favorable side effect profiles of our products. 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 into products and to exploit these products 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 favoring the use of lower priced generic products over branded products.

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, the Food and Drug Administration Amendments Act of 2007, or FDAAA, gives the FDA 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. Failure to comply with any requirements under FDAAA may result in significant penalties. FDAAA also authorizes significant civil money penalties for the dissemination of false or misleading direct-to-consumer advertisements, allows the FDA to require companies to submit direct-to-consumer television drug advertisements for FDA review prior to public dissemination and 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 Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, imposes requirements for the distribution and pricing of prescription drugs for Medicare beneficiaries, and expands the prescription drug benefit under Medicare Part D. 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, although 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 long-term effect the MMA will have on the prices paid for currently approved drugs and the pricing options for newly approved drugs. 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 28, 2009, we had 113 full-time employees, 43 of whom are Ph.D.s, M.D.s or both, and one part-time employee. 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 and 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 properties 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, 2008, we had an accumulated deficit of $189.9 million. We had net loss of $25.7 million for the year ended December 31, 2008, net loss of $28.1 million for the year ended December 31, 2007 and net income of $2.1 million for the year ended

December 31, 2006. 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 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 product candidates arising from 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 2008 and 2007 from our collaboration with AstraZeneca and our alliance with GlaxoSmithKline. We expect that a substantial portion of our revenue in the next few years will depend on the following:

- whether AstraZeneca determines to continue development of AZD3480 in either or both of Alzheimer's disease and ADHD following completion of the ongoing exploratory Phase 2 trial in adults with ADHD and, if AstraZeneca determines to continue development, the successful achievement of milestone events in such development under our agreement;
- the successful achievement of research and development-related milestone events under our agreement with GlaxoSmithKline;
- whether, following our completion of a planned Phase 2 clinical trial of TC-5619, AstraZeneca exercises its right to license TC-5619;
- for 2009, our conduct of research in our preclinical research collaboration with AstraZeneca; and
- whether we establish additional strategic alliances, collaborations and licensing or other arrangements on terms favorable to us.

As of February 28, 2009, we had one source of product revenue, Inversine. We acquired the rights to Inversine in August 2002. Sales of Inversine generated net revenue of only $718,000 for the year ended December 31, 2008, $518,000 for the year ended December 31, 2007 and $585,000 for the year ended December 31, 2006. 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 have historically been 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. As a result of increased FDA fees and declining prescriptions for Inversine, we expect that we may discontinue sales of Inversine as soon as the second half of 2009. Even if we do not elect to discontinue sales of Inversine, 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 revenue from sales of 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 capital and our failure to obtain additional capital when needed could force us to delay, reduce or eliminate our product development programs or future commercialization efforts.

In the foreseeable future, we will require substantial additional capital in order to continue to conduct the research and development and clinical and regulatory activities necessary to bring our product candidates to market or, where applicable for a particular product candidate, to the stage of development when a current or potential future collaborator of ours may assume responsibility under the terms of the applicable agreement for

funding further development and subsequent commercialization and to establish marketing and sales capabilities. Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the results of the ongoing exploratory Phase 2 trial of AZD3480 in adults with ADHD and the decision by AstraZeneca whether to conduct additional development of AZD3480 in either or both of Alzheimer's disease and ADHD;
- 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 extent to which we retain development and commercialization rights or responsibilities for our product candidates that are not subject to our collaboration with AstraZeneca or our alliance with GlaxoSmithKline and incur associated development and manufacturing costs and costs to establish sales and marketing functions;
- our ability to establish strategic alliances, collaborations and licensing or other arrangements on terms favorable to us;
- the costs, timing and outcomes of regulatory reviews or other regulatory actions;
- 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 manufacturing-related services for our product candidates in clinical and late preclinical development;
- the rate of technological advancements for the indications that we target;
- 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 plans provide 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 2011. 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. It is likely that our ability to raise funds in the foreseeable future will be adversely impacted by recent deterioration in the U.S. and global financial markets, and 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, delay or downsize clinical trials or manufacturing or other development activities 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.

The planned four-year term of our preclinical research collaboration with AstraZeneca, from which we derive research fee revenue, expires in January 2010.

We and AstraZeneca are conducting a preclinical research collaboration under our agreement that is designed to discover and develop additional compounds that, like AZD3480, act on the a4ß2 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 planned four-year research term, which began in January 2006 and is scheduled to expire in January 2010.

We have received an aggregate of $20.5 million in research fees from AstraZeneca as of December 31, 2008, and research fee revenue generated from the preclinical research collaboration represented 44% of our net operating revenues for the year ended December 31, 2008, 60% of our net operating revenues for the year ended December 31, 2007 and 17% of our net operating revenues for the year ended December 31, 2006. Expiration of the research term of the preclinical research collaboration could have a negative impact on our future net operating revenues.

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.

We are conducting a Phase 2b trial of TC-5214 as an augmentation treatment for major depressive disorder and we and AstraZeneca are conducting an exploratory Phase 2 trial of AZD3480 in adults with ADHD. In 2008, AstraZeneca completed two Phase 2b clinical trials of AZD3480, one in mild to moderate Alzheimer’s disease and one in cognitive dysfunction in schizophrenia. We have completed multiple Phase 1 clinical trials of TC-5619. Our ability to generate product or royalty revenue over the next few years will depend heavily on the successful development and commercialization of TC-5214, AZD3480 and TC-5619. Except for AZD1446, which is currently in Phase 1 clinical development, 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 condition;
- 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.

Favorable results in clinical trials of AZD3480 in a condition characterized by one degree of cognitive impairment may not be predictive of favorable results in clinical trials of AZD3480 in a condition characterized by more severe cognitive impairment or in cognitive impairment resulting from a different condition.

Clinical trials of AZD3480 that have been completed in different indications have generated a range of efficacy results. In Phase 2 trials of AZD3480 that we previously conducted in age associated memory impairment, or AAMI, and mild cognitive impairment, or MCI, AZD3480 demonstrated positive effects on some measures of cognition. In a larger Phase 2 trial of AZD3480 that we subsequently conducted in AAMI, we achieved statistically significant results in favor of AZD3480 on the trial's three co-primary efficacy endpoints. In a Phase 2b trial of AZD3480 in mild to moderate Alzheimer's disease completed by AstraZeneca in 2008, known as the Sirocco trial, the results were inconclusive. Neither the active comparator used in the trial, donepezil, nor AZD3480 met the criteria for statistical significance on the primary outcome measure in the Sirocco trial. In a separate Phase 2b trial in cognitive dysfunction in schizophrenia of AZD3480 also completed by AstraZeneca in 2008, known as the HALO trial, AZD3480 did not meet the trial's criteria for statistical significance on the primary outcome measures.

We and AstraZeneca are conducting an ongoing exploratory Phase 2 trial of AZD3480 in adults with ADHD. Neither we nor AstraZeneca has previously conducted any clinical trial of AZD3480 in adults with ADHD. Those findings from any of the completed Phase 2 trials of AZD3480 in AAMI, MCI or mild to moderate Alzheimer's disease that were favorable were not predictive of the effects of AZD3480 in persons with schizophrenia in the HALO trial and may not be predictive of the effects of AZD3480 in adults with ADHD. Moreover, even if the outcome of the exploratory Phase 2 trial of AZD3480 in adults with ADHD is favorable, the results may not be predictive of the results of any future clinical trials of AZD3480 in ADHD, Alzheimer's disease or any other indication.

If AstraZeneca determines to conduct additional clinical development of AZD3480 in Alzheimer's disease or ADHD but future trials are not successful, we and AstraZeneca will not in the future obtain the regulatory approvals required to market AZD3480 for Alzheimer's disease or ADHD even with favorable results in completed or any future trials of AZD3480 in any other indication.

If AstraZeneca determines to conduct additional clinical development in Alzheimer's disease but future trials do not establish the safety and efficacy of AZD3480 as a treatment for Alzheimer's disease, we and AstraZeneca will not in the future obtain the regulatory approvals required to market AZD3480 for Alzheimer's disease even with favorable results in completed or any future trials of AZD3480 in any other indication. Likewise, if AstraZeneca determines to conduct additional clinical development in ADHD but future trials do not establish the safety and efficacy of AZD3480 as a treatment for ADHD, we and AstraZeneca will not in the future obtain the regulatory approvals required to market AZD3480 for ADHD even with favorable results in completed or any future trials of AZD3480 in any other indication.

AZD3480 is metabolized at a different rate by extensive metabolizers through its primary metabolic pathway than it is by intermediate or poor metabolizers. 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.

The results of AstraZeneca's Sirocco trial were inconclusive and therefore did not establish definitively a dose range in which AZD3480 has positive medical effects in persons with Alzheimer's disease. Also, the ongoing exploratory Phase 2 trial in adults with ADHD is the first time AZD3480 has been studied in persons with ADHD and any dose range in which AZD3480 may have positive medical effects in persons with ADHD has not been established. In both the Sirocco and HALO trials, AstraZeneca limited the highest dose evaluated in some of the trial subjects based on their individual metabolisms being slow. If AstraZeneca determines to conduct further clinical development of AZD3480 in Alzheimer's disease or ADHD and similarly limits the highest dose evaluated in future trials based on individual slow metabolisms, and if the doses at which AZD3480 are evaluated in the future trials are not within the dose range that would have positive medical effects in persons with Alzheimer's disease or ADHD, the future trials will not be successful. Moreover, it is possible that, even if any future trials establish a dose range in which positive medical effects are achieved in persons with Alzheimer's disease or ADHD and we or AstraZeneca receive in the future the regulatory approvals required to market and sell AZD3480, the FDA or other applicable regulatory authorities could limit the patient population for which AZD3480 is approved to those who are extensive or intermediate metabolizers through the primary metabolic pathway of AZD3480 if the effective dose range is not sufficiently low to be determined safe in poor or slow metabolizers. If the FDA or other applicable regulatory authorities limit the patient population for which AZD3480 is approved in this manner, the commercial potential of AZD3480 could be materially and adversely affected.

If favorable results of our completed clinical trial of mecamylamine hydrochloride as an augmentation treatment for major depressive disorder are not predictive of the results of our ongoing and potential future clinical trials of TC-5214 as an augmentation treatment for major depressive disorder, 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 treatment to citalopram hydrobromide. In our completed Phase 2 clinical trial of TRIDMAC in major depressive disorder, we achieved 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, or HAM-D, 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 developing TC-5214 in lieu of further development of mecamylamine hydrochloride and are conducting an ongoing Phase 2b clinical trial of TC-5214 as an augmentation treatment to citalopram hydrobromide for major depressive disorder. 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 in our completed trial of TRIDMAC may not be predictive of the results in our ongoing trial of TC-5214 or in any future clinical trial of TC-5214 that we may conduct.

In addition, although we consider the trial designs of our completed trial of TRIDMAC and our ongoing trial of TC-5214 in major depressive disorder to be similar, they are not identical. For example, subjects in our

completed Phase 2 clinical trial of TRIDMAC received citalopram for six weeks in the first phase of the trial and subjects in our ongoing Phase 2b clinical trial of TC-5214 receive citalopram for eight weeks in the first phase of the trial. Also, in our completed Phase 2 clinical trial of TRIDMAC, we used HAM-D to determine the extent of therapeutic response in the first phase of the trial. In our ongoing trial of TC-5214, we use the Montgomery-Asburg Depression Rating Scale to determine the extent of therapeutic response in the first phase of the trial. It is possible that either of these differences, or any other difference between the two trial designs, could impact the likelihood that the favorable results in our completed trial of TRIDMAC will be predictive of similar results in our ongoing trial of TC-5214.

Even if the outcome of our Phase 2b clinical trial of TC-5214 as an augmentation treatment for major depressive disorder is favorable, our initiation of Phase 3 development may be delayed, which could have an adverse effect on the overall development timeline for TC-5214, our receipt of revenue from potential product sales of TC-5214 or our ability to secure a collaboration or alliance with respect to TC-5214.

In light of the unsuccessful results of AstraZeneca's HALO trial in persons with schizophrenia completed in 2008, the uncertainty of whether AstraZeneca will determine to continue development of AZD3480 in either or both of Alzheimer's disease and ADHD and the unfavorable conditions in the global credit and financial markets and unfavorable financing environment that currently exist, we designed our operating plan for 2009 to extend the period that our current resources are expected to enable us to meet our operating requirements. In particular, we plan to defer incurring expenses related to the production of clinical trial material for potential Phase 3 clinical trials for TC-5214 until completion of the ongoing Phase 2b clinical trial of TC-5214 as an augmentation treatment for major depressive disorder and contingent on a favorable outcome in that Phase 2b trial. As a result, if the outcome of the ongoing trial of TC-5214 is favorable and we advance TC-5214 into Phase 3 clinical development, initiation of Phase 3 clinical development may be delayed to enable the production of clinical trial material. A delay in the initiation of Phase 3 development could extend our overall development timeline or increase our development costs for TC-5214, delay our receipt of revenue from potential product sales or have an adverse effect on our ability to establish a strategic alliance, collaboration or licensing or other arrangement with respect to TC-5214 on terms favorable to us.

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 and regulatory authorities in the United States and by similar agencies in other countries. We or a collaborator of ours must receive regulatory approval of each product candidate before we or the collaborator 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 and our collaborators may never receive the required regulatory approvals. In addition, the FDA, the U.S. Congress or foreign governmental or regulatory authorities may from time to time change approval policies or adopt new laws or regulations that could prevent or delay our receipt of required approvals. Even if we or a collaborator of ours receives 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 pivotal clinical trials. However, additional clinical trials may be required by the FDA or foreign regulatory authorities following completion of pivotal clinical trials 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 a collaborator of ours interprets 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.

If we or a collaborator of ours obtains the requisite regulatory approval for a particular product candidate, the approval may not extend to all indications for which approval was sought, which could limit the use of the product and adversely impact our 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 or a collaborator of ours 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 clinical trials of any of our product candidates could occur at any stage of testing. If we or a collaborator of ours experiences failures in our ongoing or future clinical trials, or if we or a collaborator of ours is not able to design clinical trials to establish the safety and efficacy of our product candidates and otherwise achieve the objectives of the trials, our product candidates may never be approved for sale or become commercially available.

We and our collaborators 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 or a collaborator of ours 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 or a collaborator of ours, 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 or a collaborator of ours does not prove in clinical trials that our product candidates are safe and effective, marketing approvals from the FDA and other applicable regulatory authorities will not be obtained. In particular, one or more of our product candidates may not exhibit the expected medical benefits in humans, may cause harmful side effects or may have other unexpected characteristics that preclude regulatory approval for any or all indications of use or limit commercial use if approved. For example, in the last two years, we ceased development of TC-2696, which we had been developing as a treatment for acute post-operative pain, following an unsuccessful Phase 2 clinical trial in third molar extraction patients and we and AstraZeneca announced that, following an unsuccessful Phase 2b trial, AZD3480 is not expected to progress into Phase 3 clinical trials for cognitive dysfunction in schizophrenia.

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 preclinical studies or early 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. For example, our previous Phase 2 clinical trials of AZD3480 in AAMI that we completed in March 2006 used three factors from the CDR test battery as co-primary efficacy endpoints and achieved statistically significant results in favor of AZD3480 on all of them. However, the CDR test battery was used as a secondary outcome measure in AstraZeneca's Sirocco trial of AZD3480 in mild to moderate Alzheimer's disease and the favorable findings from the AAMI trial on the CDR test battery were not replicated in the Alzheimer's disease trial.

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. Any of the following events, among others, 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, ethics committees 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 subjects 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 or foreign regulatory authorities could require us or any of our current or potential future collaborators to conduct clinical trials with a larger number of subjects than projected for any of our product candidates. We or a collaborator of ours 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.

We do not know whether any clinical trial of our product candidates 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.

Regulatory authorities may require more data for any of our product candidates than we currently anticipate, which could cause us to incur additional costs, extend our development timelines or delay our receipt of any revenue from potential product sales.

The FDA or other applicable regulatory authorities may require more preclinical or clinical data for any of our product candidates or more time to evaluate that data than we currently anticipate because drugs that act on NNRs are not a well established class of drugs or because of experiences with drugs that act on NNRs that are developed or marketed by third parties. In particular, in February 2008, the FDA issued a public health advisory with regard to Pfizer's aid for smoking cessation product, Chantix, which acts on several NNR subtypes as well as other molecular targets in the body. 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. In May 2008, the FDA updated its advisory and noted that Pfizer had updated the warnings and precautions section of the Chantix prescribing information, or labeling. All of our product candidates currently in development affect the activity of one or more NNR subtypes. If the FDA or any foreign regulatory authority determines that any adverse medical experiences associated with Chantix have relevance to one or more of our product candidates, it may require us or a collaborator of ours to generate more clinical data than we currently anticipate to establish the safety of the affected product candidate, which could increase the cost of the development program for the affected product candidate, extend the development timeline for the affected product candidate or delay our receipt of revenue from potential product sales of the affected product candidate.

Our product candidates will remain subject to ongoing regulatory review even if they receive marketing approval. If we or a collaborator of ours fails 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 or a collaborator of ours receives 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 medical experiences that limit or prevent its widespread use or commercial potential, force us or a collaborator of ours to withdraw it from the market or impede or delay the ability of us or a collaborator of ours to obtain regulatory approvals in additional countries. If any of our product candidates causes adverse medical experiences or becomes associated with any third party product that is associated with adverse medical experiences such as those described above for Chantix, the overall commercial success of the affected product candidate may be negatively impacted.

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 requirements of the FDA and other applicable U.S. or foreign governmental or 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 multiple 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. For example, through 2007, we spent managerial and financial resources on clinical trials for TC-2696, a product candidate that we had been developing for acute

post-operative pain. We ceased development of TC-2696 following an unsuccessful 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 contingent milestone payments from GlaxoSmithKline as we advance product candidates in each therapeutic focus area through preclinical and Phase 1 clinical development. If we do not achieve 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

If AstraZeneca determines either not to conduct any further development of AZD3480 or to conduct further development of AZD3480 that does not entitle us to receive a milestone payment under the terms of our agreement, our business, financial condition and results of operations could be adversely affected.

The results of AstraZeneca's Sirocco trial of AZD3480 in mild to moderate Alzheimer's disease were inconclusive. Neither the active comparator used in the trial, donepezil, nor AZD3480 met the criteria for statistical significance on the primary outcome measure. Under the terms of our collaboration agreement, AstraZeneca has control over the decision whether to conduct any further development in Alzheimer's disease, as well as ADHD or any other indication for which AstraZeneca has development and commercialization rights under the agreement. There is no assurance that AstraZeneca will determine to conduct any further development of AZD3480 in Alzheimer's disease, ADHD or any other indication.

If the outcome of the ongoing exploratory Phase 2 trial of AZD3480 that we and AstraZeneca are conducting in adults with ADHD is unfavorable, AstraZeneca may be more likely to determine not to conduct any further development of AZD3480, even in Alzheimer's disease. In addition, in December 2008, AstraZeneca initiated Phase 1 clinical development of AZD1446, the most advanced compound arising from our preclinical research collaboration and a product candidate that, like AZD3480, acts on the a4ß2 NNR. The advancement of AZD1446 has narrowed the projected potential time to market differential between AZD3480 and AZD1446. In addition, the remaining patent life for AZD1446 is longer than for AZD3480 and the financial terms for AstraZeneca under our agreement are more favorable for AZD1446 than for AZD3480. Any of these or other factors may make AstraZeneca more likely to determine not to conduct any further development of AZD3480. If AstraZeneca determines not to conduct further development of AZD3480, we would not receive any future milestone or other payments with respect to AZD3480 from AstraZeneca, which could adversely affect our business, financial condition and results of operations. Even if AstraZeneca determines to conduct further development of AZD3480, its near-term development activities may not entitle us to receive a milestone payment under the terms of our agreement.

The successful development and commercialization of AZD3480 depends substantially on our collaboration with AstraZeneca. If AstraZeneca determines not to conduct further development of AZD3480, is unable to conduct further development of or commercialize AZD3480, experiences significant delays in doing so or terminates our agreement, our business will be materially harmed.

We entered into our collaboration agreement with AstraZeneca in December 2005. 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 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 and has exercised its right with respect to the prosecution of some of our patents with respect to AZD3480.

AstraZeneca is generally responsible for conducting and funding substantially all development of AZD3480, except for the ongoing exploratory Phase 2 trial in adults with ADHD, and has significant control over the conduct and timing of development efforts with respect to AZD3480. We have little control over the amount and timing of resources that AstraZeneca devotes to the development of AZD3480. If AstraZeneca determines to conduct further development of AZD3480 but fails to devote sufficient financial and other resources to such development, the development and potential commercialization of AZD3480 would be delayed. This would result in a delay in milestone payments and, if regulatory approval to market and sell AZD3480 is obtained, royalties that we could receive on product sales.

In addition, if AstraZeneca determines not to conduct further development of AZD3480 and the determination does not result in a failure to meet its diligence obligations under the agreement, we would not be

permitted to conduct development of AZD3480 independently or with another collaborator, even if the results of the ongoing exploratory Phase 2 trial of AZD3480 in adults with ADHD are favorable. If neither we nor AstraZeneca conducts further development of AZD3480, we will not benefit from any commercial potential of AZD3480 in Alzheimer's disease, ADHD or any other indication.

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. If AstraZeneca terminates our agreement at any time, for any reason, it would negatively impact our development of AZD3480 and materially harm our business and could accelerate our need for additional capital. In particular, we would have to fund any clinical development and commercialization of AZD3480 on our own, seek another collaborator or licensee for clinical development and commercialization or abandon the development and commercialization of AZD3480.

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.

If AstraZeneca elects to license TC-5619 following our completion of the agreed development plan, 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. If AstraZeneca were to fail to devote sufficient financial and other resources to the development of TC-5619, whether in favor of an internal 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 product 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. If GlaxoSmithKline were to fail to devote sufficient financial and other resources to the development of our licensed product candidates, whether in favor of internal product candidates or for any other reason, the development and potential commercialization of our licensed product candidates would be delayed. This would result in a delay in milestone payments and, if regulatory approval to market and sell a licensed product candidate is obtained, royalties that we could receive on product sales. Our ability to generate further revenue from the alliance would depend on GlaxoSmithKline's efforts and 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 our 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 for target indications for which our potential collaborator has particular expertise or that represent

large primary care markets that must be served by large sales and marketing organizations. 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 many risks to us, including:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these alliances and collaborations or to the development of our licensed product candidates;
- collaborators may interpret clinical trial or non-clinical study results differently than we do, 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;
- collaborators 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 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 or commercialization of products 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.

Our ability to establish additional alliances and collaborations may be limited by the terms of our agreements with AstraZeneca and GlaxoSmithKline. 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 to assist us in furthering development and potential commercialization of some of our product candidates. We intend to do so especially for target indications for which our potential collaborator has particular

expertise or that involve large primary care markets 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 meets pre-defined criteria for any NNR other than the a4ß2 NNR that we may in the future seek to exploit for any condition characterized by cognitive impairment for which AstraZeneca has development and commercialization rights under our agreement. 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 meets pre-defined criteria for any NNR other than the a4ß2 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, for so long as we are required to conduct research activities in a particular therapeutic focus area of the alliance, or for so long as there are any product candidates in development or being commercialized in the alliance in that therapeutic focus area, we will work in the therapeutic focus area exclusively with GlaxoSmithKline with respect to product candidates with activity in the therapeutic focus area derived from binding to NNRs. 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 single third-party contract manufacturers for each of 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 receipt of regulatory

approvals 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 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 current good manufacturing practices, or cGMP, mandated by the FDA or foreign regulatory authorities and required for approval of our product candidates or fail to document its adherence to cGMP, 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.

In particular, we rely on an agreement with Poli Industria Chimica and Interchem Corporation for pharmaceutical development and supply of the active ingredient form of TC-5214. The agreement was assigned to us in 2002 by Layton Bioscience, Inc. As permitted by applicable regulation, Poli Industria Chimica has filed a drug master file with the FDA that describes aspects of the process that it uses to manufacture the active ingredient form of TC-5214. Poli Industria Chimica has authorized us to reference the drug master file, but we do not have access to its contents. If our agreement were to terminate for any reason or if Poli Industria Chimica were to breach or fail to perform as agreed under our agreement, we would have to engage another contract manufacturer to manufacture TC-5214, which could delay or prevent the initiation or completion of clinical trials of TC-5214, the submission of applications for regulatory approvals of TC-5214, the receipt of regulatory approvals for TC-5214 or the commercialization of
TC-5214 or result in higher costs or lost product revenue as described above. In addition, the extent to which we or a replacement contract manufacturer would have rights under the agreement to continue to reference the drug master file or otherwise to use the know how or data generated by Poli Industria Chimica in manufacturing the active ingredient form of TC-5214 is uncertain, which could increase these risks.

We expect to rely initially on a single contract manufacturer for any product candidate that we successfully bring to market. Changing any manufacturer that we 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 or foreign regulatory authorities 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 any 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 U.S. Drug Enforcement Agency and corresponding state and foreign agencies to ensure strict compliance with cGMP, 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 and foreign regulatory authorities require 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. These risks may be heightened for clinical trials that we conduct outside of North America and Western Europe. In particular, most of the clinical trial sites for our ongoing Phase2b clinical trial of TC-5214 are located in India. Language barriers and the limited experience of some clinical investigators in India in conducting clinical trials in accordance with standards set forth by the FDA and applicable regulatory authorities in India may increase the risk of non-compliance. The failure of third parties to carry out their obligations could impair the credibility or reliability of the data generated in clinical trials of our product candidates, require a trial to be repeated and increase the overall cost of a development program, delay or prevent the development, approval and commercialization of our product candidates or result in enforcement action against us.

If current market conditions adversely affect the ability of third parties to carry out their obligations to us or our collaborators, the development of our product candidates may be delayed.

Current unfavorable conditions in the global credit and financial markets may adversely affect the ability of third parties with which we or a collaborator of ours contract for services related to clinical trials or manufacturing of any of our product candidates to carry out their obligations. The unfavorable market conditions may cause any of these third parties to be unable to obtain financing for its operations or not to sufficiently staff or otherwise resource its obligations to us or a collaborator of ours. A significant interruption in the performance of these third parties may result in delays in the conduct or completion of clinical trials for our product candidates. A delay in the conduct or completion of clinical trials for any of our product candidates may extend the overall development timeline or increase the development costs for the product candidate, delay our receipt of revenue from potential sales of the product candidate or have an adverse effect on our ability to establish a strategic alliance, collaboration or licensing or other arrangement with respect to the product candidate on terms favorable to us.

Risks Related to Our Intellectual Property

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

Our continued success depends significantly on our ability, 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 either in 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 may not be able to market any product that is covered by the licensed patents.

If we or a collaborator do not file for regulatory approval of TC-5214 by December 31, 2012 and USFRF does not extend the date or waive the requirement, USFRF can make our license to patent rights covering TC-5214 nonexclusive.

We license patent rights covering the pharmaceutical composition and methods of use of TC-5214 from the University of South Florida Research Foundation, or USFRF. The terms of our agreement with USFRF provide that, if we or a collaborator do not file an NDA or foreign equivalent for use of a product subject to the license to treat a neuropsychiatric disease or disorder on or before December 31, 2012, USFRF has the right to make our license nonexclusive. If we are unable to meet that date and USFRF is unwilling to either extend the date or waive the requirement and makes our license nonexclusive, we will not be able to enforce the licensed patent rights against USFRF or any third party that secures a license to the same patent rights from USFRF. In that event, USFRF or any third party licensee of USFRF could potentially exploit TC-5214 commercially and compete with us, unless other patent rights that we own or license would be infringed.

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 of 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 foreign regulatory authorities. Even if we have patent protection for the indication for which the product is prescribed, 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 for, but do not have patent rights covering the composition of, 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, physicians could potentially prescribe mecamylamine as a treatment for major depressive disorder. 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 sales 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. 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. 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 any of our product candidates that is successfully developed will also depend in part on the extent to which coverage and adequate payment 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 pharmaceutical companies provide predetermined discounts from list prices and frequently challenge 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 product candidates 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 product candidates that is 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 for Alzheimer’s disease, AZD3480 or AZD1446 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.

The American Recovery and Reinvestment Act of 2009, which became effective in February 2009, provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research is to be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes for Health, and periodic reports on the status of the research and related expenditures are to be made to the U.S. Congress. Although the results of the comparative effectiveness studies are not intended to mandate any policies for public or private payors, it is unclear what if any effect the research will have on the sales of any product candidate that we successfully develop if the product candidate or the condition that it is intended to treat is the subject of the research. Decreases in third-party reimbursement for any of our product candidates that is successfully developed or a decision by a third-party payor to not cover any of our product candidates that is successfully developed could reduce prescriptions by physicians of the product candidate and have an adverse effect on our potential revenue from sales of the product candidate.

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, biopharmaceutical, 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 tolerable, more convenient, less costly or otherwise more competitive 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, acts on several NNR subtypes as well as other molecular targets in the body. Chantix is approved 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 Roche, with a compound in Phase 2 for Alzheimer’s disease and cognitive impairment associated with schizophrenia (which we refer to as cognitive dysfunction in schizophrenia), and Abbott Laboratories, with one compound in Phase 2 for Alzheimer’s disease and ADHD, a second compound in Phase 2 for ADHD and two other compounds in Phase 1 for cognitive disorders or schizophrenia. Other companies that we believe have active NNR-based programs include AstraZeneca, Eli Lilly, Sanofi-Aventis, Wyeth, Bristol

Myers Squibb, GlaxoSmithKline, Johnson & Johnson, Novartis, NeuroSearch A/S, Solvay, Servier, CoMentis, EnVivo Pharmaceuticals, Xytis and Galantos Pharma. 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. We believe that the primary competitive products for use in indications that we are currently targeting with our most advanced product candidates include:

- for major depressive disorder, 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 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; and
- for ADHD, stimulants such as Adderall XR and Vyanase from Shire, Concerta from Johnson & Johnson and Ritalin LA from Novartis, and Strattera, a non-stimulant acting as a norepinephrine reuptake inhibitor, from Eli Lilly.

There is currently no approved product for cognitive dysfunction in schizophrenia.

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 in amounts that we believe to be appropriate for our current operations. 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 expect that we will 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 in our efforts to comply with these laws and regulations, but our efforts may not ensure compliance in all cases. 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 any promotional activities that we undertake 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 and under specified conditions disseminate articles published in peer-reviewed journals that discuss off-label uses of approved products to physicians. To the extent allowed, we may in the future disseminate peer-reviewed articles on our products to physicians. We do not currently promote Inversine. However, if we undertake any promotional activities in the future for Inversine or any other product candidate for which we receive regulatory approval in the future 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 also rely on consultants and advisors from time to time 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. Any continued growth could place a significant strain on our managerial, operational and financial resources. To manage our growth, we must continue to implement and improve our managerial, operational and financial systems and controls and reporting processes and procedures. We may not be able to manage our growth effectively. Moreover, if our existing systems and internal controls over financial reporting are not implemented properly or are not adequate, we could be exposed to an increased risk of incurring financial or accounting irregularities or fraud, which would cause our stock price to suffer.

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 experienced extreme price and volume fluctuations. The market prices of securities of pharmaceutical, biopharmaceutical 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 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 payments from AstraZeneca, GlaxoSmithKline or 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 extent to which we retain development and commercialization rights or responsibilities for our product candidates that are not subject to our collaboration with AstraZeneca or our alliance with GlaxoSmithKline and incur associated development and manufacturing costs and costs to establish sales and marketing functions;
- our ability to establish strategic alliances, collaborations and licensing or other arrangements on terms favorable to us;
- our inability, or the inability of AstraZeneca, GlaxoSmithKline or any potential future collaborator, 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 cost, timing and outcomes of regulatory approvals or other regulatory actions;
- the number and characteristics of product candidates that we pursue;

- general and industry-specific economic conditions that may affect the research and development expenditures of AstraZeneca, GlaxoSmithKline or any of our potential future collaborators;
- the expiration or termination of agreements with AstraZeneca, GlaxoSmithKline or any potential future collaborator, or the execution of new agreements; and
- general conditions in the pharmaceutical, biopharmaceutical or biotechnology industries or in the U.S. or global credit or financial markets.

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 as compensation to our employees, directors or consultants, 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 our principal stockholders beneficially own or control approximately 35% of the outstanding shares of our common stock, based on the shares outstanding as of February 28, 2009. Accordingly, our executive officers, directors and their affiliates and our 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 66 2/3 % of the outstanding shares of our capital stock entitled to vote in order for the stockholders 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, 2008.

PART II

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

Market Information

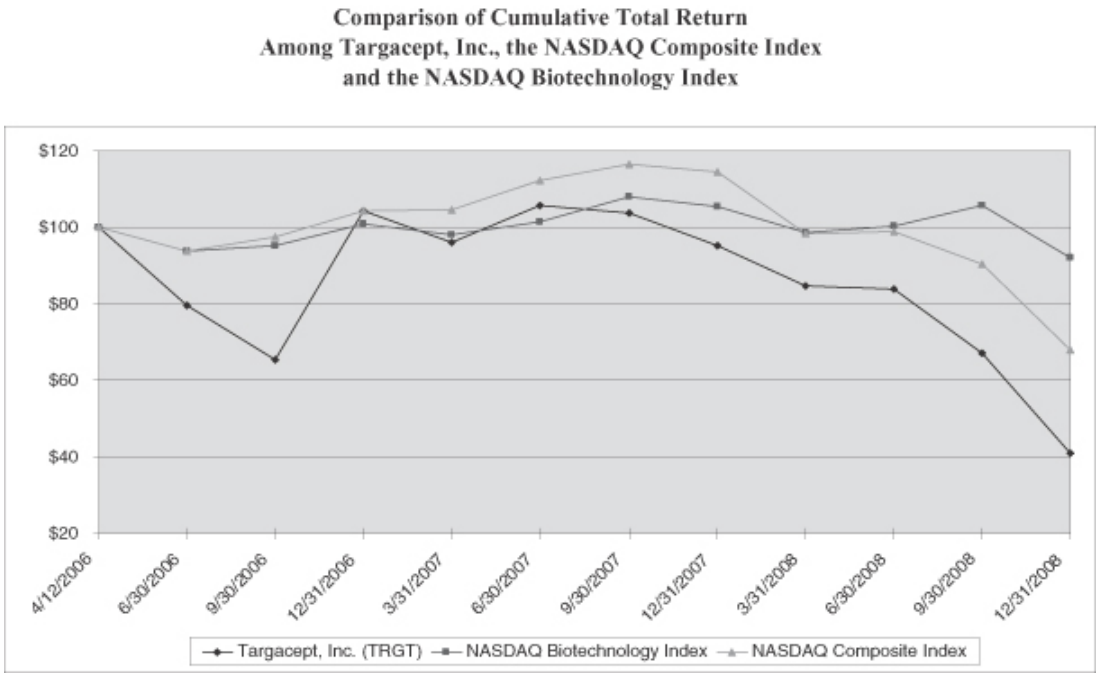
Our common stock trades on the NASDAQ Global Market under the symbol "TRGT." The following table sets forth, for the periods indicated, the high and low sales prices for our common stock:

	Common Stock	
	High	*Low*
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
2008:		
First Quarter	$ 8.61	$ 6.81
Second Quarter	$ 8.50	$ 6.90
Third Quarter	$ 10.11	$ 3.85
Fourth Quarter	$ 6.19	$ 1.40

Comparative Stock Performance Graph

The following graph and related information shall not be deemed "soliciting material" or to be "filed" with the SEC or subject to the liabilities of Section 18 of the Exchange Act, nor shall such information be incorporated by reference into any future filing under the Securities Act or the Exchange Act, except to the extent that we specifically incorporate it by reference into such a filing.

The following graph compares the cumulative total stockholder return for our common stock with the cumulative total stockholder 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 and the reinvestment of any dividends. We have not paid any dividends on our common stock and do not include dividends in the representation of our performance. The performance shown for any prior period does not predict the performance to be expected for any future period.



	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	3/31/08	6/30/08	9/30/08	12/31/08
TARGACEPT, INC.	100	80	65	105	96	106	104	95	85	84	67	41
NASDAQ COMPOSITE INDEX	100	94	98	104	105	112	117	115	98	99	90	68
NASDAQ BIOTECHNOLOGY INDEX	100	94	95	101	98	101	108	106	99	100	106	92

Stockholders

As of February 28, 2009, there were approximately 131 holders of record of our common stock. Because many of our shares are held by brokers or other institutions on behalf of beneficial owners, we are unable to estimate the total number of beneficial owners represented by the holders of record.

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; Use of Proceeds from Registered Securities; Issuer Purchases of Equity Securities

None.

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, 2008, 2007 and 2006 and the balance sheet data as of December 31, 2008 and 2007 from our audited financial statements included in this annual report. We derived the statements of operations data for the years ended December 31, 2005 and 2004 and the balance sheet data as of December 31, 2006, 2005 and 2004 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,				
	2008	2007	2006	2005	2004
	(in thousands, except per share data)				
Statement of Operations Data:					
Net operating revenues	$ 20,085	$ 11,576	$ 27,537	$ 1,180	$ 3,738
Operating expenses:					
Research and development	40,981	34,620	21,788	24,252	22,771
General and administrative	6,499	8,013	5,696	4,753	5,163
Transaction charges	—	—	—	1,635	—
Cost of product sales	749	715	457	481	198
Total operating expenses	48,229	43,348	27,941	31,121	28,132
Loss from operations	(28,144)	(31,772)	(404)	(29,941)	(24,394)
Interest and dividend income	2,734	3,837	2,584	1,174	505
Interest expense	(251)	(138)	(83)	(225)	(132)
Loss on disposal of fixed assets	—	—	—	—	(4)
Net (loss) income	(25,661)	(28,073)	2,097	(28,992)	(24,025)
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)
Net loss attributable to common stockholders	$ (25,661)	$ (28,073)	$ (1,236)	$ (40,230)	$ (43,081)
Basic and diluted net loss attributable to common stockholders per share	(1.04)	(1.42)	$ (0.09)	$ (153.54)	$ (196.53)
Shares used to compute basic and diluted net loss per share	24,664	19,721	13,596	262	219

	As of December 31,				
	2008	2007	2006	2005	2004
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and short-term investments	$ 88,363	$ 87,040	$ 54,190	$ 24,851	$ 53,075
Working capital	78,174	77,217	69,903	20,531	50,079
Total assets	98,551	98,965	81,368	28,001	58,204
Long-term debt, net of current portion	3,408	1,686	816	1,409	3,443
Redeemable convertible preferred stock	—	—	—	183,628	171,778
Accumulated deficit	(189,896)	(164,235)	(136,162)	(174,983)	(134,754)
Total stockholders' equity (deficit)	57,373	51,584	64,999	(162,481)	(122,966)

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 any forward-looking statement due to various 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 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. Our most advanced product candidates are TC-5214, AZD3480 (TC-1734), TC-5619 and AZD1446 and are discussed under the caption "Business" in Item 1 of Part I of this annual report.

We have a cognition-focused collaboration with AstraZeneca. Under our collaboration agreement, we and AstraZeneca are conducting a preclinical research collaboration that is designed to discover and develop compounds that act on the a4ß2 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 addition, AstraZeneca is responsible under the terms of the agreement for substantially all current and future development costs for AZD3480, except for costs to conduct the ongoing exploratory Phase 2 clinical trial of AZD3480 in adults with ADHD.

In addition to our collaboration with AstraZeneca, we have a strategic 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.

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. 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 achievement of a milestone event related to AZD3480 under our agreement with AstraZeneca. Except for these periods, we have never been profitable. As of December 31, 2008, we had an accumulated deficit of $189.9 million. We expect to incur substantial losses for the foreseeable future 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 product candidates arising from 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, 2008, we had received $34.2 million in aggregate upfront fees and milestone payments under our collaboration agreement with AstraZeneca and had recognized an additional $21.3 million in collaboration research and development revenue for research services that we provided in the preclinical research collaboration that we are conducting with AstraZeneca under the agreement. We are eligible to receive other payments of up to $197.0 million, if AstraZeneca decides to conduct further development of AZD3480 in both Alzheimer's disease and ADHD and development, regulatory, first commercial sale and first detail milestones for AZD3480 are achieved for both indications, and stepped double-digit royalties on any future product sales. If AZD3480 is developed under the agreement for an indication in addition to Alzheimer's disease and ADHD, we would also be eligible to receive additional milestone payments upon the achievement of development, regulatory, first commercial sale and first detail milestones for AZD3480 for each such indication. 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.

In addition, we are eligible to receive payments of up to $108.0 million, contingent upon the achievement of development, regulatory, first commercial sale and first detail milestones for AZD1446 for two indications, and stepped royalties on any future AZD1446 product sales. Also, 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, first commercial sale and first detail milestones for three indications, as well as stepped double-digit royalties on any future product sales.

As of December 31, 2008, we had received $42.5 million in aggregate payments under our alliance agreement with GlaxoSmithKline. 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, a $6.0 million payment upon our initiation of a Phase 1 clinical trial of TC-6499 and $1.5 million in payments upon achievement of milestone events related to progress in our smoking cessation program and in our preclinical pain program. 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. In addition, 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. 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 $718,000 for the year ended December 31, 2008, $518,000 for the year ended

December 31, 2007 and $585,000 for the year ended December 31, 2006. We instituted a price increase of 19% for Inversine at the beginning of 2009 and a price increase of 62% for Inversine at the beginning of 2008 to help offset the impact of increased cost of product sales resulting primarily from FDA product and establishment fees. We experienced decreased sales volume during 2008. As a result of increased FDA fees and declining prescriptions for Inversine, we expect that we may discontinue sales of Inversine as soon as the second half of 2009.

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, 2008, 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 successful achievement of milestone events under our agreements with AstraZeneca and 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 85%, 80% and 78% of our total operating expenses for the years ended December 31, 2008, 2007 and 2006, respectively. Research and development expenses include costs associated with:

- the employment of personnel involved in our drug discovery, research and development activities;
- research and development facilities and equipment;
- clinical trials, including fees paid to contract research organizations to monitor and oversee some of our trials;
- costs to conduct research activities under the a4ß2 research collaboration with AstraZeneca;
- the screening, identification and optimization of product candidates;
- formulation and chemical development;
- production of clinical trial materials, including fees paid to contract manufacturers;
- preclinical animal studies, including the costs to engage third-party research organizations;
- quality assurance activities;
- compliance with FDA regulatory requirements;
- consulting, license and sponsored research fees paid to third parties;
- the development and enhancement of our drug discovery technologies that we refer to as Pentad;
- depreciation of capital assets used to develop our products; and
- stock options or other stock-based awards granted to personnel in research and development functions.

We utilize our research and development personnel and infrastructure resources across several programs. We currently have clinical, preclinical and early research programs, 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 cannot state precisely our total costs incurred 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 a collaborator of ours 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 for a particular product candidate may vary significantly 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 therapeutic areas being investigated;
- the duration of the trials and subject follow-up;
- the costs of producing supplies of the product candidate 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. Where a third party has responsibility for or authority over the preclinical or clinical development of a particular 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 whether AstraZeneca or GlaxoSmithKline will exercise any options to license particular product candidates that become exercisable under the terms of our respective agreements, 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 numerous 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, legal and human resource functions. Other general and administrative expenses include expenses associated with stock options and other stock-based awards granted to personnel in those functions, depreciation and other 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 revenue derived under our agreement with AstraZeneca. We incurred net operating losses for 2008, 2007 and each other year since inception and consequently have not paid federal, state or foreign income taxes in any period. As of December 31, 2008, we had net operating loss carryforwards for federal income tax purposes of $113.6 million and for state income tax purposes of $113.5 million. We also had $6.1 million in research and development federal income tax credits as of December 31, 2008. 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 November 2002 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.

Fair Value

We had $0 and $23.0 million invested in student loan auction rate securities, or ARS, as of December 31, 2008 and December 31, 2007, respectively. Student loan ARS are variable rate debt instruments that have a contractual maturity of approximately 20 to 40 years and are intended to provide liquidity via an auction process that resets the applicable interest rate at predetermined calendar intervals, enabling investors to either roll over their holdings or gain immediate liquidity by selling them at par value. Auctions for the student loan ARS that we owned were scheduled at 28-day intervals.

Prior to the first quarter of 2008, our history with the student loan ARS market had been that these investments could be redeemed at any of the regularly scheduled 28-day auctions and we believed that the risk that these investments could not be redeemed within a year was minimal. Accordingly, we had historically viewed student loan ARS as available for use in current operations and classified them as short-term investments, even though their stated maturity dates may have been more than one year beyond the balance sheet date. We recorded our student loan ARS at par based on observable quoted prices from an active market at the balance sheet date.

As of March 31, 2008, we continued to own $16.8 million of student loan ARS. The uncertainties experienced in the credit markets in 2008 affected the student loan ARS market, and, beginning in February 2008, auctions for our student loan ARS failed to settle on their respective settlement dates.

Based on the uncertainty of the short-term liquidity of the student loan ARS that existed as of March 31, 2008, we did not classify our investments in student loan ARS as of that date as short-term investments. We estimated the fair values of our student loan ARS using discounted cash flow models. These models considered, among other things, the expected timing for successful auctions or refinancings in the future, the composition and quality of the underlying collateral and the creditworthiness of the issuer. Based on these models, we estimated the fair value of our student loan ARS owned as of March 31, 2008 to be $16.5 million, which reflected a fair value adjustment of $297,000 that was considered a temporary adjustment, and recorded a corresponding unrealized loss in an amount equal to the fair value adjustment in accumulated other comprehensive income, a component of stockholders' equity.

In June 2008, $1.4 million of $16.8 million total par value of our student loan ARS was redeemed by the issuers of the underlying securities. Based on the June 2008 redemption and expected future redemptions, we determined the carrying value of our student loan ARS as of June 30, 2008 based on observable quoted prices in an active market, reversed the fair value adjustment that had decreased the carrying value of our student loan ARS by $297,000 as of March 31, 2008 and recorded our remaining student loan ARS as of June 30, 2008 as short-term investments at their par value of $15.4 million. The full par value of our remaining student loan ARS was subsequently redeemed by the issuers of the underlying securities in July 2008. Since July 2008, we have not invested in any student loan ARS.

Our short-term investments in certificates of deposit of $37.0 million at December 31, 2008 are recorded at quoted prices of an active market.

Our intangible assets consist of rights assigned to us from Layton Bioscience, Inc., including licensed patent rights and rights related to the Inversine trademark and product technology. We recognized a net loss on sales of Inversine for each of 2008 and 2007 and do not expect to recognize net income from sales of Inversine for future periods. The history of losses on sales of Inversine and the forecast for future periods indicate the carrying value of the intangible asset may not be recoverable. We valued the Inversine trademark and product technology intangible asset originally at $346,000. During the fourth quarter of 2008, as part of our processes for preparation of our financial statements, we performed an impairment analysis of the Inversine trademark and product technology intangible asset using a discounted cash flow model that is based on estimated future net product sales and cost of product sales and considers assumptions such as, among other things, estimated future product sales volumes and estimated future sales price increases. Based on our impairment analysis, we determined that the Inversine trademark and product technology intangible asset had no fair value. As a result, we recorded an impairment charge for the full amount of the unamortized balance of the Inversine trademark and product technology intangible asset as of the valuation date, or $220,000, to research and development expenses in the fourth quarter of 2008. The impairment charge has no effect on our prospective amortization of the licensed patent rights intangible asset to research and development expenses on a straight-line basis over the remaining useful life of the patents.

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. 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 and the recording of revenues and expenses 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, 2008 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, which are referred to together as SEC Topic 13, *Revenue Recognition*, or Topic 13. 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 milestone events; 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 among the separate units. If a collaboration or alliance agreement involves separate units of accounting, we determine the revenue recognition applicable to each unit. If a collaboration or alliance agreement involves a single unit of accounting, we determine the revenue recognition applicable to the entire arrangement.

We defer recognition of non-refundable upfront fees and recognize them into revenue 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 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 period over which we recognize the revenue 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, 2008, 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 milestone events 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 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 research and development 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 a4ß2 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 license grants, until AstraZeneca made its determination in December 2006 to proceed with further development of AZD3480. 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.

AstraZeneca's December 2006 determination to proceed with further development of AZD3480 triggered a $20.0 million milestone payment to us. Based on the criteria of Topic 13, 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 TC-5619 following our completion of Phase 1 clinical development and a planned 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 achieve 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 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, 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.

In May 2008, we received a $200,000 payment from AstraZeneca and, in December 2008, we received a $2.0 million payment from AstraZeneca. Each payment was made upon achievement of a milestone event related to the development of AZD1446. We recognized the full amount of each payment as revenue upon achievement of the milestone event because the event met each of the conditions required for immediate recognition under our revenue recognition policy.

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.

In May 2008, we received a $500,000 payment from GlaxoSmithKline upon achievement of a milestone event related to progress in our smoking cessation program. In November 2008, we received $1.0 million in payments from GlaxoSmithKline upon the achievement of milestone events related to progress in our smoking cessation program and in our preclinical pain program. We recognized the full amount of each payment as revenue upon achievement of the milestone event because the event met each of the conditions required for immediate recognition under our revenue recognition policy.

Accrued Expenses

In the normal course of our business, we contract with research institutions and contract research organizations that conduct or manage clinical trials or other research and development activities on our behalf and with contract manufacturers that produce drug substance or drug product for us. 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 agreements depend on factors such as the achievement of specified events, the production of drug substance or drug product, the successful recruitment of subjects, the completion of portions of a non-clinical study or clinical trial or similar conditions.

As part of the process of preparing financial statements, we are required to estimate accrued expenses with the objective of matching the recording of expenses in our financial statements to the actual services received and efforts expended. This process involves reviewing open contracts and purchase orders, communicating with our applicable personnel to identify services that have been performed on our behalf, estimating level of services performed and the associated cost incurred for the services when we have not yet been invoiced or otherwise notified of actual cost and reviewing invoices received that have not yet become due and payable. 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. 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. Examples of estimated accrued expenses include:

- fees for services performed by contract research organizations in connection with preclinical studies and clinical trials;
- fees for services performed by clinical trial sites in connection with clinical trials;
- fees for services performed by contract manufacturers in connection with the production of clinical trial materials and Inversine; and
- professional service fees.

Stock-Based Compensation

We record expense related to the issuance of stock-based awards in accordance with the terms of 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 awards 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 use the modified-prospective-transition method permitted by SFAS 123R, which requires us to record compensation expense for the non-vested portion of previously issued awards that were outstanding at January 1, 2005, and any awards issued or modified after January 1, 2005, taking into account projected forfeitures. We recorded stock-based compensation expense related to stock options granted to employees and directors of $2.1 million for the year ended December 31, 2008, $2.7 million for the year ended December 31, 2007, and $919,000 for the year ended December 31, 2006. As of December 31, 2008, we had $3.5 million in total unrecognized compensation cost related to non-vested stock-based compensation arrangements, which we expect to record over a weighted average period of 1.3 years. On January 9, 2009, we granted to employees stock options with an estimated grant-date fair value of $1.3 million, which we expect to record, after adjusting for estimated forfeitures, as stock-based compensation expense on a straight line basis over a period of 16 quarters.

Results of Operations

Years ended December 31, 2008 and December 31, 2007

Net Operating Revenues

	Year ended December 31,		
	2008	2007	Change
		(in thousands)	
Operating revenues:			
Collaboration research and development	$ 8,967	$ 7,288	$1,679
Milestones and license fees from collaborations	10,179	3,548	6,631
Product sales, net	718	518	200
Grant revenue	221	222	(1)
Net operating revenues	$20,085	$11,576	$8,509

Net operating revenues for the year ended December 31, 2008 increased by $8.5 million as compared to the year ended December 31, 2007. The higher net operating revenues were principally attributable to an increase of $6.6 million in milestones and license fees from collaborations and to an increase of $1.7 million in collaboration research and development revenue. The increase in milestones and license fees from collaborations reflected $2.2 million in aggregate payments received from AstraZeneca upon the achievement of milestone events related to the progression of AZD1446 and $1.5 million in aggregate payments received from GlaxoSmithKline upon the achievement of milestone events related to progress in our smoking cessation and preclinical pain programs. The increase in milestones and license fees from collaborations also reflected recognition of an additional $2.9 million of deferred license fee revenue from payments received from GlaxoSmithKline and AstraZeneca in the second half of 2007 to $4.2 million for 2008, from $1.3 million for 2007. The increase in collaboration research and development revenue was primarily attributable to an increase of $2.0 million in research fees to $8.9 million for 2008, from $6.9 million for 2007, resulting from additional services rendered by us in the preclinical research collaboration that we and AstraZeneca are conducting as contemplated by the research plan. Based on the objectives and budget for the preclinical research collaboration with AstraZeneca for 2009, we anticipate that our collaboration research and development revenue generated under the collaboration will decrease in 2009 as compared to 2008.

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 elects to conduct further development of AZD3480, 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. The likelihood that we will achieve any particular milestone event in 2009 or any future period is uncertain.

Net sales of Inversine for the year ended December 31, 2008 increased by $200,000 as compared to the year ended December 31, 2007. The increase resulted from a 62% increase in the sales price of Inversine made effective at the beginning of 2008, partially offset by a reduction in the volume of sales of Inversine. We instituted a 19% price increase for Inversine effective at the beginning of 2009. As of December 31, 2008, the effect of the 2009 price increase on net sales of Inversine was not determinable. We expect that we may discontinue sales of Inversine as soon as the second half of 2009. Even if we do not elect to discontinue sales of Inversine, we do not expect that sales of Inversine will increase substantially in the future.

Research and Development Expenses

	Year ended December 31, 2008	2007	Change
		(in thousands)	
Research and development expenses	$40,981	$34,620	$6,361

Research and development expenses for the year ended December 31, 2008 increased by $6.4 million as compared to the year ended December 31, 2007. The higher research and development expenses were principally attributable to an increase of $4.3 million in salary and benefit expenses and temporary personnel, supply and infrastructure costs and an increase of $2.2 million in costs incurred for third-party preclinical research and development services. These increases resulted principally from greater activities in the therapeutic focus areas of the alliance with GlaxoSmithKline, which was formed in July 2007, and greater activities in the preclinical research collaboration with AstraZeneca as product candidates progressed to later stages of research. A greater number of clinical-stage programs and progression of these programs during 2008 also contributed to the increase in salary and benefit expenses and temporary personnel, supply and infrastructure costs. These increases were partially offset by a decrease of $136,000 in costs incurred for third-party services in connection with research and development of clinical-stage product candidates, including costs for clinical trial activities, formulation activities, production of clinical trial materials, and pharmacology, toxicology and other non-clinical studies, to $11.1 million for 2008, from $11.2 million for 2007. The costs that we incurred for the years ended December 31, 2008 and 2007 for third-party services in connection with research and development of clinical-stage product candidates are shown in the table below:

	Year ended December 31, 2008	2007	Change
		(in thousands)	
TC-5214	$ 4,826	$ 3,926	$ 900
TC-5619	3,151	2,937	214
TC-6499	2,291	1,566	725
TC-2216	549	1,687	(1,138)
AZD3480	322	—	322
	$11,139	$10,116	$ 1,023

In addition to the product candidates shown in the table above, we incurred expenses for third party-services in connection with TC-2696, a product candidate that we have since ceased developing, of $1.1 million for the year ended December 31, 2007. We did not incur any expenses in connection with the development of TC-2696 during 2008.

The reported amount for TC-2216 for the year ended December 31, 2008 includes costs with respect to non-clinical studies conducted to characterize TC-2216 and its constituent enantiomers further and costs with respect to our completed Phase 1 single rising dose clinical trial.

General and Administrative Expenses

	Year ended December 31, 2008	2007	Change
		(in thousands)	
General and administrative expenses	$6,499	$8,013	$(1,514)

General and administrative expenses for the year ended December 31, 2008 decreased by $1.5 million as compared to the year ended December 31, 2007. The lower general and administrative expenses were principally attributable to a decrease of $627,000 in employee bonuses and a decrease of $967,000 in stock-based compensation expense.

Cost of Product Sales

	Year ended December 31,		
	2008	2007	Change
	(in thousands)		
Cost of product sales	$749	$715	$ 34

Our cost of product sales are those costs related directly to the sale of Inversine. Cost of product sales for the year ended December 31, 2008 increased by $34,000 as compared to the year ended December 31, 2007. The increase was primarily attributable to an increase in product and establishment fees assessed by the FDA.

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 some or all of the FDA fees with respect to Inversine.

The waiver of some or all of the FDA fees that we had historically received with respect to Inversine prior to 2007 resulted in lower cost of product sales. In March 2007, we received notice that the FDA, citing our revenue and cash assets, had denied our request for a waiver of product and establishment fees that were assessed by the FDA and paid by us in 2006.

The amount of product and establishment fees for the twelve months beginning October 1, 2008 was $284,000. We have not applied and do not plan to apply for a waiver of these fees. Accordingly, we expect that the FDA fees will impact our cost of product sales for 2009 and any applicable future periods. We instituted a 19% price increase for Inversine effective at the beginning of 2009 and a 62% price increase for Inversine effective at the beginning of 2008, with the objective of offsetting the impact of the FDA fees.

Interest Income and Interest Expense

	Year ended December 31,		
	2008	2007	Change
	(in thousands)		
Interest income	$2,734	$3,837	$(1,103)
Interest expense	251	138	113

Interest income for the year ended December 31, 2008 decreased by $1.1 million as compared to the year ended December 31, 2007. The decrease was primarily attributable to lower short-term interest rates.

Interest expense for the year ended December 31, 2008 increased by $113,000 as compared to the year ended December 31, 2007. The increase was attributable to higher average principal balance under loan facilities used to finance equipment, furnishings, software and other fixed assets. We borrowed $4.8 million under a loan agreement with a bank entered into in March 2008 and an additional $489,000 under the same loan facility in September 2008. We used $1.7 million of the proceeds from the March 2008 loan to refinance the principal and interest outstanding on two tranches of a previous loan facility.

Years ended December 31, 2007 and December 31, 2006

Net Operating Revenues

	Year ended December 31,		
	2007	2006	Change
	(in thousands)		
Operating revenues:			
Collaboration research and development	$ 7,288	$ 5,019	$ 2,269
Milestones and license fees from collaborations	3,548	21,146	(17,598)
Product sales, net	518	585	(67)
Grant revenue	222	787	(565)
Net operating revenues	$11,576	$27,537	$(15,961)

Net operating revenues for the year ended December 31, 2007 decreased by $16.0 million as compared to the year ended December 31, 2006. The lower net operating revenues were primarily attributable to a reduction of $17.6 million in milestones and license fees from collaborations. The lower milestones and license fees from collaborations for 2007 was attributable to our recognition of the $20.0 million milestone payment triggered by AstraZeneca's December 2006 determination to proceed with further development of AZD3480, 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 were achieved during 2007.

The lower net operating revenues were also attributable to a reduction of $565,000 in grant revenue. 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 in collaboration research and development revenues for the year ended December 31, 2007 of $2.3 million as compared to the year ended December 31, 2006. The higher collaboration research and development revenues were primarily attributable to an increase of $2.2 million in research fees to $6.9 million for the year ended December 31, 2007, from $4.7 million for the year ended December 31, 2006, resulting from additional services rendered by us in our preclinical research collaboration with AstraZeneca.

Net sales of Inversine for the year ended December 31, 2007 decreased by $67,000 as compared to the year ended December 31, 2006. The decrease resulted from a reduction in the volume of sales of Inversine.

Research and Development Expenses

	Year ended December 31,		
	2007	2006	Change
	(in thousands)		
Research and development expenses	$34,620	$21,788	$12,832

Research and development expenses for the year ended December 31, 2007 increased by $12.8 million as compared to the year ended December 31, 2006. The higher research and development expenses reflect increases in costs for third-party research and development services, including clinical trial activities, formulation activities, production of clinical trial materials, and pharmacology, toxicology and other non-clinical studies. The

costs that we incurred for the years ended December 31, 2007 and 2006 for third-party services in connection with research and development of clinical-stage product candidates are shown in the table below:

	Year ended December 31,		
	2007	2006	Change
	(in thousands)		
TC-5214	$ 3,926	$ —	$3,926
TC-5619	2,937	903	2,034
TC-6499	1,566	—	1,566
TC-2216	1,687	1,691	(4)
AZD3480	—	209	(209)
	$10,116	$2,803	$7,313

In addition to the product candidates shown in the table above, we incurred expenses for third party-services in connection with mecamylamine hydrochloride and TC-2696 of $0 and $1.1 million for the year ended December 31, 2007 and $555,000 and $891,000 for the year ended December 31, 2006, respectively.

The higher research and development expenses for 2007 also reflect an increase of $4.8 million in salary and benefits, occupancy costs and third-party service, supply and infrastructure costs incurred in connection with activities under the preclinical research collaboration with AstraZeneca and our other preclinical programs, including those in the therapeutic focus areas of our alliance with GlaxoSmithKline, to $21.2 million for the year ended December 31, 2007, from $16.4 million for the year ended December 31, 2006.

General and Administrative Expenses

	Year ended December 31,		
	2007	2006	Change
	(in thousands)		
General and administrative expenses	$8,013	$5,696	$2,317

General and administrative expenses for the year ended December 31, 2007 increased by $2.3 million as compared to the year ended December 31, 2006. The higher general and administrative expenses were principally attributable to an increase in stock-based compensation expense 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

	Year ended December 31,		
	2007	2006	Change
	(in thousand)		
Cost of product sales	$715	$457	$ 258

Cost of product sales for the year ended December 31, 2007 increased by $258,000 as compared to the year ended December 31, 2006. The increase primarily reflects the FDA's denial in 2007 of our request for a waiver of establishment fees for Inversine that had been granted in 2006. In both periods, the FDA denied our request for a waiver of product fees for Inversine.

Interest Income and Interest Expense

	Year ended December 31,		
	2007	2006	Change
	(in thousands)		
Interest income	$3,837	$2,584	$1,253
Interest expense	138	83	55

Interest income for the year ended December 31, 2007 increased by $1.3 million as compared to 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 for the year ended December 31, 2007 increased by $55,000 as compared to 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 interest free grace period under a loan from the City of Winston-Salem.

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 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. In January 2008, we completed another public offering of our common stock, consisting of 4.4 million shares at a price of $7.07 per share, the closing bid price of our common stock on the date that the offering was priced. After deducting underwriting discounts and commissions and offering expenses payable by us, our net proceeds from the offering were $29.1 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 expect that we may discontinue sales of Inversine as soon as the second half of 2009.

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. During 2008, we received $1.5 million in payments from GlaxoSmithKline upon the achievement of milestone events related to progress in our smoking cessation and preclinical pain programs. In December 2007, we received a $6.0 million payment from GlaxoSmithKline upon the initiation of a Phase 1 clinical trial of TC-6499. As of December 31, 2008, we had received $42.5 million in aggregate payments under our alliance agreement with GlaxoSmithKline.

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 and $20.0 million in January 2007 triggered

by achievement of a milestone event related to AZD3480. In November 2007, AstraZeneca paid us $2.0 million to secure the future right to license TC-5619. In May 2008, we received a $200,000 payment from AstraZeneca upon achievement of a milestone event related to the development of AZD1446. In December 2008, we received a $2.0 million payment from AstraZeneca upon achievement of a milestone event related to the initiation of Phase 1 clinical development of AZD1446. As of December 31, 2008, we had received $34.2 million in aggregate upfront fees and milestone payments under our collaboration agreement with AstraZeneca and had recognized an additional $21.3 million in collaboration research and development revenue for research services that we provided in the preclinical research collaboration that we are conducting with AstraZeneca under the agreement.

As discussed above under the heading "—Overview," we are eligible to receive substantial additional payments from AstraZeneca, contingent on the achievement of specified milestone events related to AZD3480, AZD1446 and, if TC-5619 achieves clinical proof of concept and AstraZeneca elects to license it, TC-5619, and from GlaxoSmithKline, contingent on the achievement of specified milestone events in the five therapeutic focus areas of the alliance. There is no assurance that we will achieve any particular milestone event in 2009 or in any future period.

In March 2008, we entered into a loan agreement with a bank that provided borrowing capacity of $5.3 million to fund the purchase of equipment, furnishings, software and other fixed assets and enabled the refinancing of our loan facility with R.J. Reynolds Tobacco Holdings, Inc., or RJRT. We borrowed $4.8 million upon entering into the loan agreement and borrowed the remaining $489,000 in September 2008. Pursuant to the loan agreement, we granted a first priority security interest in favor of the bank in the assets acquired with the proceeds of the loan facility. The March 2008 loan bears interest at a fixed rate of 5.231% per annum and is repayable in equal monthly installments of $112,000 beginning April 1, 2008 and continuing through the maturity date of March 1, 2012. We used $1.7 million of the proceeds from the March 2008 loan to pay and satisfy in full the principal and interest outstanding on two of the tranches under the loan facility with RJRT and granted a first priority security interest in favor of the bank in assets previously acquired with the proceeds of those tranches. The September 2008 loan bears interest at a fixed rate of 6.131% per annum and is repayable in equal monthly installments of $11,000 beginning October 1, 2008 and continuing through the maturity date of September 1, 2012. As of December 31, 2008, the outstanding principal balance under the loan facility was $4.4 million. There is no additional borrowing capacity remaining available to us under the loan agreement.

We had a loan facility with R.J. Reynolds Tobacco Holdings, Inc., or RJRT that we entered into originally in May 2002 and that was subsequently amended. All borrowings under the facility were secured by specified tangible fixed assets determined sufficient by the lender at the time of disbursement. As of December 31, 2008, the outstanding principal balance under the loan facility was $23,000. The outstanding balance was paid in full on the maturity date of January 1, 2009.

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 of the loan. 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, 2008, the outstanding principal balance under the loan was $337,000.

Our cash, cash equivalents and short-term investments were $88.4 million as of December 31, 2008 and $87.0 million as of December 31, 2007. As of December 31, 2008, substantially all of our cash, cash equivalents and short-term investments were invested in bank depository accounts, certificates of deposit, and institutional money market funds at Branch Banking and Trust Company, RBC Bank and Evergreen Investments, an affiliated entity of Wells Fargo & Company (formerly Wachovia Corporation). Approximately 94% of the $20.6 million that we had invested in institutional money market funds as of December 31, 2008 were in funds that invest 100% in U.S. Treasury bills and notes. In addition, our investments in Evergreen money market funds are currently subject to the U.S. Treasury Department's Temporary Guarantee Program for Money Market Funds

initiated in September 2008. The program is expected to be in effect through April 30, 2009, at which time the Secretary of the Treasury is expected to review the need and terms for the program.

Cash Flows

	Year ended December 31,		
	2008	2007	Change
		(in thousands)	
Net cash (used in) provided by operating activities	$(28,261)	$ 24,838	$(53,099)
Net cash used in investing activities	(5,519)	(26,286)	20,767
Net cash provided by financing activities	31,579	13,107	18,472
Net (decrease) increase in cash and cash equivalents	$ (2,201)	$ 11,659	

	Year ended December 31,		
	2007	2006	Change
		(in thousands)	
Net cash provided by (used in) operating activities	$ 24,838	$ (9,892)	$ 34,730
Net cash used in investing activities	(26,286)	(13,268)	(13,018)
Net cash provided by financing activities	13,107	40,053	(26,946)
Net increase in cash and cash equivalents	$ 11,659	$ 16,893	

Net cash used in operating activities was $28.3 million for the year ended December 31, 2008 and net cash provided by operating activities was $24.8 million for the year ended December 31, 2007, a change of $53.1 million. The change in net cash (used in) provided by operating activities was principally due to:

- a decrease in net loss of $2.4 million in 2008 to $25.7 million, from $28.1 million for the year ended December 31, 2007;
- a decrease in our collaboration revenue and accounts receivable balance of (1) $19.2 million for 2007 as a result of our receipt of a $20.0 million milestone payment from AstraZeneca in January 2007 triggered by achievement of a milestone event related to AZD3480 and (2) $2.1 million for 2008, a difference of $17.1 million;
- the addition in 2007 of an aggregate of $31.5 million in our deferred license fee revenue liability balance resulting from our receipt of a $20.0 million initial payment from GlaxoSmithKline and an aggregate deemed premium of $3.5 million resulting from GlaxoSmithKline's purchase of common stock, in each case in connection with the formation of our alliance in July 2007, our receipt of a $6.0 million milestone payment from GlaxoSmithKline upon our initiation of a Phase 1 clinical trial of TC-6499 and our receipt of a $2.0 million payment from AstraZeneca to secure the future right to license TC-5619; and
- an increase of $2.9 million in deferred license fee revenue recognized for 2008, which includes $1.5 million greater recognition of the payments received from GlaxoSmithKline upon formation of our alliance, $635,000 greater recognition of the payment received from GlaxoSmithKline upon our initiation of a Phase 1 clinical trial of TC-6499 and $808,000 greater recognition of the payment received from AstraZeneca to secure the future right to license TC-5619.

Net cash provided by operating activities for the year ended December 31, 2007 was $24.8 million and net cash used in operating activities for the year ended December 31, 2006 was $9.9 million, a change of $34.7 million. Our net loss for the year ended December 31, 2007 increased by $30.2 million to $28.1 million, from net income of $2.1 million for the year ended December 31, 2006. The increased net loss was more than offset by (1) the addition of an aggregate of $31.5 million in our deferred license fee revenue liability balance for 2007 as

compared to the addition of $10.0 million for 2006, an increase of $21.5 million; and (2) a decrease in our collaboration revenue and accounts receivable balance of $19.2 million for 2007 as compared to an increase of $23.3 million for 2006, a difference of $42.5 million. The change in collaboration revenue and accounts receivable for both 2007 and 2006 was primarily due to our receipt in January 2007 of the $20.0 million milestone triggered by AstraZeneca's December 2006 determination to proceed with further development of AZD3480.

Net cash used in investing activities for the year ended December 31, 2008 decreased by $20.8 million as compared to the year ended December 31, 2007. Net cash used in investing activities for the year ended December 31, 2007 increased by $13.0 million as compared to the year ended December 31, 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 investments. Additionally, we purchased $2.1 million of property and equipment for the year ended December 31, 2008, a decrease of $2.8 million from $4.9 million in property and equipment purchases for the year ended December 31, 2007. The $4.9 million of property and equipment purchases for the year ended December 31, 2007 reflected an increase of $3.8 million from $1.1 million in property and equipment purchases for the year ended December 31, 2006. Purchases of property and equipment for each of 2008, 2007 and 2006 were primarily for equipment required to support our research and development operations. The higher purchases in 2007 as compared to 2008 and 2006 were a result of furniture and equipment purchases in connection with the 2007 expansion of our leased facilities.

Net cash provided by financing activities for the year ended December 31, 2008 increased by $18.5 million as compared to the year ended December 31, 2007. The increase was principally attributable to our receipt of $29.1 million in net proceeds from a public stock offering that we completed in January 2008 and incremental net borrowings of $1.0 million under our loan facilities for the year ended December 31, 2008, partially offset by our receipt of $11.5 million, net of the deemed premium, from GlaxoSmithKline for the purchase of common stock in July 2007. Net cash provided by financing activities for the year ended December 31, 2007 decreased by $26.9 million as compared to 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, net of the deemed premium, from GlaxoSmithKline for the purchase of common stock in July 2007 and $2.0 million in incremental net borrowings under our loan facility for the year ended December 31, 2007.

Funding Requirements

As of December 31, 2008, we had an accumulated deficit of $189.9 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 results of the ongoing exploratory Phase 2 trial of AZD3480 in adults with ADHD and the decision by AstraZeneca whether to conduct additional development of AZD3480 in either or both of Alzheimer's disease and ADHD;
- 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 extent to which we retain development and commercialization rights or responsibilities for our product candidates that are not subject to our collaboration with AstraZeneca or our alliance with

GlaxoSmithKline and incur associated development and manufacturing costs and costs to establish sales and marketing functions;

- our ability to establish strategic alliances, collaborations and licensing or other arrangements on terms favorable to us;
- the costs, timing and outcomes of regulatory reviews or other regulatory actions;
- 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 manufacturing-related services for our product candidates in clinical and late preclinical development;
- the rate of technological advancements for the indications that we target;
- 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 additional capital 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 to be sufficient to fund our operations at least through the first half of 2011, without taking into account amounts that we would be entitled to receive if clinical development milestone events are achieved under our agreement with AstraZeneca or our agreement with GlaxoSmithKline. 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 years. To the extent our capital resources are insufficient to meet future capital requirements, we will need to finance future cash needs through alliances, collaborations or licensing arrangements, public or private equity or debt offerings or other financings. The global credit and financial markets have recently experienced a period of unusual volatility and illiquidity. This, coupled with other factors, may dramatically limit our access to additional equity or debt financing in the future on acceptable terms or at all. Also, additional alliances, collaborations or licensing arrangements may not be available on acceptable terms or 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 accurately determine the completion dates and related costs of our 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 establish strategic alliances or collaborations 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, 2008:

Contractual Obligation	Payments Due by Period				
	Total	Less Than 1 Year	1-3 Years	3-5 Years	More Than 5 Years
			(in thousands)		
Long-term debt obligations	$ 4,798	$ 1,390	$2,963	$ 445	$ —
Operating lease obligations	7,737	2,159	4,318	1,260	—
Purchase obligations	13,000	12,420	577	3	—
	$25,535	$ 15,969	$7,858	$1,708	$ —

The amounts of purchase 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 purchase obligations for 2009 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 purchase obligations in the above table after 2009. The amounts of purchase obligations for all periods reflected in the above table exclude contingent royalty payments that we may become required to make 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.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Recent Accounting Pronouncements

In December 2007, the Financial Accounting Standards Board, or FASB issued SFAS No. 141(R), *Business Combinations-a replacement of FASB Statement No. 141*, or SFAS 141(R), which significantly changes the principles and requirements for how the acquirer of a business recognizes and measures in its financial statements the identifiable assets acquired, the liabilities assumed, and any noncontrolling interest in the acquiree. SFAS 141(R) also provides guidance for recognizing and measuring the goodwill acquired in the business combination and determines what information to disclose to enable users of the financial statements to evaluate the nature and financial effects of the business combination. The provisions of SFAS 141(R) are effective prospectively, except for certain retrospective adjustments to deferred tax balances, for the fiscal years beginning after December 15, 2008. We do not expect SFAS 141(R) to have a material impact on our financial results.

In December 2007, the FASB issued SFAS No. 160, *Noncontrolling Interests in Consolidated Financial Statements-an amendment of ARB No. 51*, or SFAS 160. SFAS 160 establishes accounting and reporting standards for the noncontrolling interest in a subsidiary and for the deconsolidation of a subsidiary. The provisions of SFAS 160 are effective prospectively, except for certain retrospective disclosure requirements, for fiscal years beginning after December 15, 2008. We do not expect SFAS 160 to have a material impact on our financial results.

In April 2008, the FASB issued FASB Staff Position No. 142-3, *Determination of the Useful Lives of Intangible Assets*, FSP 142-3. FSP 142-3 amends the factors that should be considered in developing renewal or extension assumptions used to determine the useful life of an intangible asset. FSP 142-3 is effective for financial

statements issued for fiscal years beginning after December 15, 2008 and interim periods within those years. We do not expect FSP 142-3 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 investments in a variety of securities that are expected to be of high credit quality. Our investments are typically short-term in nature. As of December 31, 2008, we had cash, cash equivalents and short-term investments of $88.4 million. 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, 2008 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, clinical trial sites and contract 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 corresponding exchange rate as of December 31, 2008, 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.

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, 2008 and 2007, 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, 2008. 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, 2008 and 2007, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2008, 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, 2008, 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, 2009 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Greensboro, North Carolina
March 12, 2009

TARGACEPT, INC.

BALANCE SHEETS
(in thousands, except par value amounts)

	December 31, 2008	December 31, 2007
ASSETS		
Current assets:		
Cash and cash equivalents	$ 51,202	$ 53,403
Short-term investments	37,161	33,637
Collaboration revenue and accounts receivable	2,073	4,198
Inventories	100	140
Prepaid expenses	1,430	1,035
Total current assets	91,966	92,413
Property and equipment, net	6,401	6,115
Intangible assets, net of accumulated amortization of $112 and $205 at December 31, 2008 and 2007, respectively	184	437
Total assets	$ 98,551	$ 98,965
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,500	$ 2,296
Accrued expenses	4,381	5,461
Current portion of long-term debt	1,390	918
Current portion of deferred rent incentive	42	42
Current portion of deferred license fee revenue	6,479	6,479
Total current liabilities	13,792	15,196
Long-term debt, net of current portion	3,408	1,686
Deferred rent incentive, net of current portion	109	151
Deferred license fee revenue, net of current portion	23,869	30,348
Total liabilities	41,178	47,381
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.001 par value, 100,000 shares authorized; 24,964 and 20,503 shares issued and outstanding at December 31, 2008 and 2007, respectively	25	20
Capital in excess of par value	247,244	215,799
Accumulated deficit	(189,896)	(164,235)
Total stockholders' equity	57,373	51,584
Total liabilities and stockholders' equity	$ 98,551	$ 98,965

See accompanying notes.

TARGACEPT, INC.

STATEMENTS OF OPERATIONS
(in thousands, except per share amounts)

	Year ended December 31,		
	2008	2007	2006
Operating revenues:			
Collaboration research and development	$ 8,967	$ 7,288	$ 5,019
Milestones and license fees from collaborations	10,179	3,548	21,146
Product sales, net	718	518	585
Grant revenue	221	222	787
Net operating revenues	20,085	11,576	27,537
Operating expenses:			
Research and development (including stock-based compensation of $1,130, $845 and $644 in 2008, 2007 and 2006, respectively)	40,981	34,620	21,788
General and administrative (including stock-based compensation of $935, $1,902 and $275 in 2008, 2007 and 2006, respectively)	6,499	8,013	5,696
Cost of product sales	749	715	457
Total operating expenses	48,229	43,348	27,941
Loss from operations	(28,144)	(31,772)	(404)
Other income (expense):			
Interest income	2,734	3,837	2,584
Interest expense	(251)	(138)	(83)
Total other income (expense)	2,483	3,699	2,501
Net (loss) income	(25,661)	(28,073)	2,097
Preferred stock accretion	—	—	(3,333)
Net loss attributable to common stockholders	$(25,661)	$(28,073)	$ (1,236)
Basic and diluted net loss attributable to common stockholders per share	$ (1.04)	$ (1.42)	$ (0.09)
Weighted average common shares outstanding—basic and diluted	24,664	19,721	13,596

See accompanying notes.

TARGACEPT, INC.

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

	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, 2005	$ 31,837	$ 41,760	$ 110,031	270	$ —	$ 12,288	$ 214	$ (174,983)	$ (162,481)
Issuance of 30 shares of common stock related to exercise of stock options	—	—	—	30	—	62	—	—	62
Stock-based compensation	—	—	—	—	—	919	—	—	919
Accreted redemption value for Series A, Series B, and Series C redeemable convertible preferred stock	484	635	2,214	—	—	—	—	(3,333)	(3,333)
Net proceeds from initial public offering	—	—	—	5,000	5	40,770	—	—	40,775
Conversion of redeemable convertible preferred stock	(32,321)	(42,395)	(112,245)	13,832	14	147,103	—	39,843	186,960
Expiration of common stock warrants	—	—	—	—	—	—	(214)	214	—
Net income and comprehensive income	—	—	—	—	—	—	—	2,097	2,097
Balances at December 31, 2006	$ —	$ —	$ —	19,132	$ 19	$ 201,142	$ —	$ (136,162)	$ 64,999
Issuance of 96 shares of common stock related to exercise of stock options	—	—	—	96	—	432	—	—	432
Stock-based compensation	—	—	—	—	—	2,747	—	—	2,747
Net proceeds from sale of 1,275 shares of common stock to GlaxoSmithKline	—	—	—	1,275	1	11,478	—	—	11,479
Net loss and comprehensive loss	—	—	—	—	—	—	—	(28,073)	(28,073)
Balances at December 31, 2007	$ —	$ —	$ —	20,503	$ 20	$ 215,799	$ —	$ (164,235)	$ 51,584
Issuance of 91 shares of common stock related to exercise of stock options	—	—	—	91	—	271	—	—	271
Stock-based compensation	—	—	—	—	—	2,065	—	—	2,065
Net proceeds from public stock offering	—	—	—	4,370	5	29,109	—	—	29,114
Net loss and comprehensive loss	—	—	—	—	—	—	—	(25,661)	(25,661)
Balances at December 31, 2008	$ —	$ —	$ —	24,964	$ 25	$ 247,244	$ —	$ (189,896)	$ 57,373

See accompanying notes.

TARGACEPT, INC.

STATEMENTS OF CASH FLOWS
(in thousands)

	Year ended December 31,		
	2008	2007	2006
Operating activities			
Net (loss) income	$ (25,661)	$ (28,073)	$ 2,097
Adjustments to reconcile net (loss) income to net cash (used in) provided by operating activities:			
Depreciation and amortization	1,800	907	821
Recognition of deferred license fee revenue	(6,479)	(3,548)	(1,146)
Impairment of intangible asset	220	—	—
Stock-based compensation expense	2,065	2,747	919
Recognition of deferred rent incentive	(42)	(42)	(403)
Changes in operating assets and liabilities:			
Collaboration revenue and accounts receivable	2,125	19,171	(23,250)
Inventories	40	33	(132)
Prepaid expenses and accrued interest receivable	(453)	237	(646)
Accounts payable and accrued expenses	(1,876)	1,885	1,848
Deferred license fee revenue	—	31,521	10,000
Net cash (used in) provided by operating activities	(28,261)	24,838	(9,892)
Investing activities			
Purchase of investments	(104,800)	(151,751)	(41,192)
Proceeds from sale of investments	101,334	130,409	29,000
Purchase of property and equipment	(2,053)	(4,944)	(1,076)
Net cash used in investing activities	(5,519)	(26,286)	(13,268)
Financing activities			
Proceeds from issuance of long-term debt	5,300	2,000	407
Principal payments on long-term debt	(3,106)	(805)	(1,191)
Proceeds from issuance of common stock	29,385	11,912	40,837
Net cash provided by financing activities	31,579	13,107	40,053
Net (decrease) increase in cash and cash equivalents	(2,201)	11,659	16,893
Cash and cash equivalents at beginning of year	53,403	41,744	24,851
Cash and cash equivalents at end of year	$ 51,202	$ 53,403	$ 41,744

See accompanying notes.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS
DECEMBER 31, 2008

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 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

Use of Estimates and Reclassifications

The preparation of financial statements in conformity with U.S. generally accepted accounting principles, or GAAP, requires management to make estimates and assumptions that affect the amounts of assets, liabilities, revenues and expenses reported in the financial statements and accompanying notes. Actual results could differ from these estimates.

Certain reclassifications have been made to the financial statements for the year ended December 31, 2007 to conform to the presentation in the financial statements for the year ended December 31, 2008. These reclassifications had no impact on net loss.

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

Consistent with the Company's investment policy, cash is invested with prominent financial institutions in bank depository accounts, certificates of deposit, and institutional money market funds. 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 owned during 2008 and 2007 were classified as available for sale. Interest and dividend 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.

Through July 2008, the Company had also invested surplus cash in student loan auction rate securities, or ARS. In June and July 2008, all of the Company's student loan ARS were redeemed by the issuers of the underlying securities at full par value. As of December 31, 2008, the Company did not own any student loan ARS.

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.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

2. Summary of Significant Accounting Policies—(continued)

During 2008, 2007 and 2006, the Company recognized revenue of $19,146,000, $10,836,000 and $26,165,000, respectively, or 95%, 94% and 95% of net operating revenues, 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 laboratory 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. Laboratory 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 rights assigned from Layton Bioscience, Inc. The intangible assets are being amortized to research and development expense on a straight-line basis over the useful life of the patents, 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 estimated fair value. An impairment analysis conducted by the Company of its intangible assets is discussed in Note 6.

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.

Accrued Expenses

The Company records accruals based on estimates of the services received, efforts expended and amounts owed pursuant to contracts with clinical trial sites, contract research organizations and other service providers. In

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

2. Summary of Significant Accounting Policies—(continued)

the normal course of business, the Company contracts with third parties to perform various clinical trial and other research 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 non-clinical study or 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.

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 each of 2008 and 2007, and recognized $403,000 of the incentive during 2006.

Fair Value of Financial Instruments

The carrying amounts of cash and cash equivalents, short-term investments, accounts receivable, accounts payable, accrued expenses and long-term debt are considered to be representative of their respective fair values due to the short-term nature of cash and cash equivalents, short-term investments, accounts receivable, accounts payable and accrued expenses and the market interest rates of short-term investments and long-term debt.

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 has established guidelines for investment of its excess cash designed to emphasize safety, liquidity and preservation of capital. The Company places its cash and cash equivalents with prominent financial institutions. At December 31, 2008 and 2007, the Company had deposits in excess of federally insured limits of $50,452,000 and $53,200,000, respectively.

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, which are referred to together as SEC Topic 13, *Revenue Recognition*, or Topic 13.

In determining the accounting for collaboration and alliance 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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

2. Summary of Significant Accounting Policies—(continued)

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 an initial payment 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 or where our collaborator has substantially all research and development responsibility, over the estimated research and development period.

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 research and development 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 2008, 2007 and 2006, $204,000, $215,000 and $191,000 of shipping and handling costs, respectively, were included in cost of product sales.

Income Taxes

The Company uses the liability method in accounting for income taxes as required by Statement of Financial Accounting Standard, or SFAS, No. 109, *Accounting for Income Taxes*, or SFAS 109. The Company follows Financial Accounting Standards Interpretation No. 48, *Accounting for Uncertainty in Income Taxes*, or FIN 48, which clarifies the accounting for uncertainty in income taxes recognized in an enterprise's financial statements in accordance with SFAS 109. Under SFAS 109, deferred tax assets and liabilities are recognized for operating loss and tax credit carryforwards and for the future tax consequences attributable to the differences

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

2. Summary of Significant Accounting Policies—(continued)

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. 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.

Net Loss Attributable to Common Stockholders Per Share

The Company computes net loss attributable to common stockholders per share 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 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.

Public Offerings of Common Stock 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.

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 for 2006 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.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

2. Summary of Significant Accounting Policies—(continued)

On January 23, 2008, the Company completed a public offering of 4,370,000 shares of its common stock at a price of $7.07 per share. The Company's net proceeds from the offering, after deducting underwriters' discounts and commissions and offering expenses payable by the Company, were $29,114,000.

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

	Year ended December 31,		
	2008	2007	2006
	(in thousands, except per share amounts)		
Historical			
Numerator:			
Net loss attributable to common stockholders	$(25,661)	$(28,073)	$(1,236)
Denominator:			
Weighted-average common shares outstanding	24,664	19,721	13,596
Basic and diluted net loss per share attributable to common stockholders	$ (1.04)	$ (1.42)	$ (0.09)
Pro forma (unaudited)			
Numerator:			
Net income attributable to common stockholders			$ 2,097
Denominator:			
Shares used above			13,596
Pro forma adjustments to reflect assumed conversion of preferred stock and shares issued upon completion of IPO, on a weighted average basis			4,055
Shares used to compute pro forma basic net (loss) income per share attributable to common stockholders			17,651
Pro forma adjustments to reflect effects of dilutive stock options outstanding, on a weighted average basis			905
Shares used to compute pro forma diluted net (loss) income per share attributable to common stockholders			18,556
Pro forma basic and diluted net income per share attributable to common stockholders:			
Basic			$ 0.12
Diluted			$ 0.11

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

2. Summary of Significant Accounting Policies—(continued)

The Company has excluded all outstanding stock options and warrants from the historical calculation of net loss attributable to common stockholders per share for 2008, 2007 and 2006 because such securities are antidilutive. For 2006, the Company recognized pro forma net income attributable to common stockholders. As a result certain outstanding stock options were dilutive for 2006 on a pro forma basis, and have been included in the pro forma calculation of Diluted EPS. Total potentially dilutive securities, which include those reflected in the pro forma calculation for 2006, consist of the following on a weighted average basis:

	December 31,		
	2008	2007	2006
		(in thousands)	
Outstanding stock options	3,123	2,628	1,925
Redeemable convertible preferred stock	—	—	4,055
Outstanding warrants	—	—	63
Total	3,123	2,628	6,043

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.

The Company has 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.

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*, which 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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

2. Summary of Significant Accounting Policies—(continued)

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 FSP No. FAS 123(R)-3.

Non-refundable Advance Payments

The Company adopted EITF 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, on January 1, 2008. 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 non-refundable advance payments should be charged to expense. Application of the provisions of EITF 07-3 resulted in an increase in total assets and a decrease in net loss of $428,000, or $0.02 per share, for the year ended December 31, 2008.

Recent Accounting Pronouncements

In December 2007, the FASB issued SFAS No. 141(R), *Business Combinations-a replacement of FASB Statement No. 141*, or SFAS 141(R), which significantly changes the principles and requirements for how the acquirer of a business recognizes and measures in its financial statements the identifiable assets acquired, the liabilities assumed, and any non-controlling interest in the acquiree. SFAS 141(R) also provides guidance for recognizing and measuring the goodwill acquired in the business combination and determines what information to disclose to enable users of the financial statements to evaluate the nature and financial effects of the business combination. The provisions of SFAS 141(R) are effective prospectively, except for certain retrospective adjustments to deferred tax balances, for business combinations for which the acquisition date is on or after the beginning of a fiscal year that begins after December 15, 2008. The Company does not expect SFAS 141(R) to have a material impact on its financial results.

In December 2007, the FASB issued SFAS No. 160, *Noncontrolling Interests in Consolidated Financial Statements-an amendment of ARB No. 51*, or SFAS 160. SFAS 160 establishes accounting and reporting standards for the non-controlling interest in a subsidiary and for the deconsolidation of a subsidiary. The provisions of SFAS 160 are effective prospectively, except for certain retrospective disclosure requirements, for fiscal years beginning after December 15, 2008. The Company does not expect SFAS 160 to have a material impact on its financial results.

In April 2008, the FASB issued FASB Staff Position No. 142-3, *Determination of the Useful Lives of Intangible Assets*, or FSP 142-3. FSP 142-3 amends the factors that should be considered in developing renewal or extension assumptions used to determine the useful life of an intangible asset. The provisions of FSP 142-3 are effective for financial statements issued for fiscal years beginning after December 15, 2008 and interim periods within those years. The Company does not expect FSP 142-3 to have a material impact on its financial results.

Fair Value Accounting

Effective January 1, 2008, the Company adopted SFAS No. 157, *Fair Value Measurements*, or SFAS 157, for application to financial assets. SFAS 157 defines fair value, provides a consistent framework for measuring

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

2. Summary of Significant Accounting Policies—(continued)

fair value under GAAP and expands fair value financial statement disclosure requirements. SFAS 157 does not require any new fair value measurements. SFAS 157 applies only to accounting pronouncements that already require or permit fair value measures, except for standards that relate to share-based payments such as SFAS 123R and related interpretations.

The valuation techniques of SFAS 157 are based on both observable and unobservable inputs. Observable inputs reflect readily obtainable data from independent sources, and unobservable inputs reflect the Company's market assumptions. SFAS 157 classifies these inputs into the following hierarchy:

Level 1 Inputs—Quoted prices for identical instruments in active markets.

Level 2 Inputs—Quoted prices for similar instruments in active markets; quoted prices for identical or similar instruments in markets that are not active; and valuations whose inputs are observable or whose significant value drivers are observable.

Level 3 Inputs—Instruments with primarily unobservable value drivers.

As of December 31, 2008, the Company had $37,000,000 invested in available-for-sale marketable securities, comprised entirely of certificates of deposit. The Company determines fair value for certificates of deposit through quoted market prices, or Level 1 inputs. The Company has also previously invested in student loan auction rate securities, or ARS. All of the Company's previously owned ARS were redeemed by the issuers of the underlying securities at full par value in June and July 2008. Prior to January 1, 2008, the Company determined fair value for student loan ARS based on quoted market prices in active markets for identical assets. However, based on failures of student loan ARS to settle at auction, the Company determined fair value for student loan ARS based on a discounted cash flow model for a portion of the year ended December 31, 2008. This model considered, among other things, the expected timing for successful auctions or refinancings in the future, the composition and quality of the underlying collateral and the creditworthiness of the issuer. Because these inputs were not observable, they were classified as Level 3 inputs under SFAS 157. The adoption of SFAS No. 157 had no effect on the valuation of the Company's available-for-sale marketable securities as of December 31, 2008.

The table below provides a reconciliation of the Company's fair value measurements that used Level 3 inputs for the year ended December 31, 2008:

	Year Ended December 31, 2008 (in thousands) Available for Sale Marketable Securities
Level 3 balance at beginning of period	$ —
Transfers into Level 3	16,750
Transfers out of Level 3	—
Fair value adjustments	—
Redemptions	(16,750)
Level 3 balance at end of period	$ —

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

2. Summary of Significant Accounting Policies—(continued)

The Company values non-financial assets, such as the intangible asset measured at fair value for an impairment assessment (see Note 6), using previously issued FASB standards in accordance with FASB Staff Position No. FAS 157-2, *Effective Date of FASB Statement No. 157*.

3. Short-term Investments

As of the respective dates shown, the Company's short-term investments consisted of:

	December 31,	
	2008	2007
	(in thousands)	
Certificates of deposit	$ 37,000	$ 10,534
Student loan auction rate securities	—	23,000
Accrued interest	161	103
	$ 37,161	$ 33,637

4. Inventories

As of the respective dates shown, inventories consisted of the following:

	December 31,	
	2008	2007
	(in thousands)	
Raw materials	$ 52	$ 52
Finished goods	48	88
	$100	$140

5. Property and Equipment

As of the respective dates shown, property and equipment consisted of the following:

	December 31,	
	2008	2007
	(in thousands)	
Laboratory equipment	$10,268	$ 8,941
Office furniture and fixtures	3,232	2,659
Leasehold improvements	1,133	1,030
	14,633	12,630
Less: accumulated depreciation	(8,232)	(6,515)
Property and equipment, net	$ 6,401	$ 6,115

The Company recorded $1,767,000, $869,000 and $783,000 of depreciation expense for 2008, 2007 and 2006, respectively.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

6. Intangible Assets

As of the respective dates shown, intangible assets consisted of the following:

	December 31,	
	2008	2007
	(in thousands)	
Patents	$ 296	$ 642
Less: accumulated amortization	(112)	(205)
Total	$ 184	$ 437

Intangible assets consist of rights assigned from Layton Bioscience, Inc., which include licensed patent rights and rights related to the Inversine trademark and product technology. The Company recognized a net loss on sales of Inversine in each of 2008 and 2007 and does not expect to recognize net income from sales of Inversine in future periods. The history of losses on sales of Inversine and the forecast for future periods indicate the carrying value of the intangible asset may not be recoverable. The Inversine trademark and product technology intangible asset had an original value to the Company of $346,000. During the fourth quarter of 2008, as part of its processes for preparation of its financial statements, the Company performed an impairment analysis of the Inversine trademark and product technology intangible asset using a discounted cash flow model that is based on estimated future net product sales and cost of product sales and considers assumptions such as, among other things, estimated future product sales volumes and estimated future sales price increases. The Company determined that the Inversine trademark and product technology intangible asset had no fair value. As a result, the Company recorded an impairment charge for the full amount of the unamortized balance of the Inversine trademark and product technology intangible asset as of the valuation date, or $220,000, to research and development expense in the fourth quarter of 2008. The impairment charge has no effect on the Company's prospective amortization of the licensed patent rights intangible asset to research and development expenses on a straight-line basis over the remaining useful life of the patents.

The Company recorded amortization expense of $33,000 during 2008, which includes $16,000 of amortization expense related to the Inversine trademark and product technology for the period from January 1, 2008 through September 30, 2008. The Company recognized amortization expense of $38,000 for each of 2007 and 2006 and expects to recognize $17,000 of amortization expense for each of the next five years.

7. Accrued Expenses

As of the respective dates shown, accrued expenses consisted of the following:

	December 31,	
	2008	2007
	(in thousands)	
Clinical trial costs	$ 2,618	$ 2,830
Employee compensation	1,484	2,332
Other	279	299
Total	$ 4,381	$ 5,461

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

8. Long-term debt

During 2002, the Company entered into an agreement to borrow $500,000 from the City of Winston-Salem. The note payable to the City of Winston-Salem matures on April 19, 2012 and was non-interest bearing until April 2007 when it began to bear interest 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%.

During 2002, the Company entered into an agreement to borrow $2,500,000 from R.J. Reynolds Tobacco Holdings, Inc., or RJRT. The note payable to RJRT was subsequently amended and the Company borrowed an aggregate additional amount of $2,000,000 in 2004. The note payable to RJRT was further amended in 2006 and the Company borrowed an aggregate additional amount of $2,000,000 in two tranches in June 2007. All borrowings under the note payable to RJRT were used to fund the purchase of equipment, furnishings, software and other fixed assets and were repayable over 48-month terms from the respective borrowing dates. The Company used $1,679,000 of the proceeds from the March 2008 loan discussed below to pay and satisfy in full the principal and interest outstanding on the June 2007 borrowings. At December 31, 2008, the Company had $23,000 remaining outstanding under its note payable to RJRT, accruing interest at an annual rate of 6.89%. The outstanding balance was paid in full on the maturity date of January 1, 2009. As of January 1, 2009, the Company had no outstanding long-term debt to RJRT.

In March 2008, the Company entered into a loan agreement with a bank that provided borrowing capacity of $5,300,000 to fund the purchase of equipment, furnishings, software and other fixed assets and enable the refinancing of its loan facility with RJRT. The Company borrowed $4,811,000 upon entering into the loan agreement and borrowed the remaining $489,000 in September 2008.

The Company's March 2008 loan bears interest at a fixed rate of 5.231% per annum and is repayable in equal monthly installments of $112,000 beginning April 1, 2008 through the maturity date of March 1, 2012. The Company used $1,679,000 of the proceeds from the March 2008 loan to pay and satisfy in full the principal and interest outstanding on the two June 2007 tranches under its loan facility with RJRT and granted a first priority security interest in favor of the bank in assets previously acquired with the proceeds of those tranches. The Company's September 2008 loan bears interest at a fixed rate of 6.131% per annum and is repayable in equal monthly installments of $11,000 beginning October 1, 2008 through the maturity date of September 1, 2012.

The Company paid $244,000, $128,000 and $81,000 in interest under notes payable during 2008, 2007 and 2006, respectively. Maturities of long-term debt were as follows at December 31, 2008 (in thousands):

2009	$1,390
2010	1,442
2011	1,521
2012	445
2013	—
	$4,798

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

9. Redeemable Convertible 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 shares 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 the 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 the 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 the Series C and received cash of $612,000, net of offering costs.

All outstanding shares of the Series A, the Series B and the Series C automatically converted into shares of common stock upon completion of the IPO. Based on the terms of the redeemable convertible preferred stock, accrued dividends totaling $39,830,000 were forfeited in connection with the conversion.

Common stock issued upon automatic conversion of the redeemable convertible preferred stock upon completion of the IPO was as follows (in thousands, except conversion ratios):

Series	Shares Outstanding	Carrying Amount	Conversion Ratio	Shares of Common Stock Issued
A	5,000	$ 32,321	0.133	667
B	6,568	42,395	0.318 or 0.133	2,082
C	76,938	112,245	0.144	11,083
	88,506	$ 186,961		13,832

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

10. Stockholders' Equity (Deficit)

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.

In conjunction with the issuance of Series A, the Company issued a warrant to purchase 215,054 shares of the Company's common stock. The fair value of the warrant was estimated at the grant date to be $214,000 or $0.99 per share. The warrant expired unexercised upon completion of the IPO.

The Company had 3,119,000 and 3,125,000 shares of common stock reserved for future issuance upon the exercise of outstanding stock options at December 31, 2008 and 2007, respectively.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

11. Income Taxes

For the years ended December 31, 2008 and 2007, there was no provision (benefit) for federal or state income taxes, as the Company incurred operating losses. 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 incurred operating losses from inception through the year ended December 31, 2005.

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

	Year Ended December 31,		
	2008	2007	2006
Expected federal income tax benefit/expense at statutory rate	34%	34%	34%
Increase (decrease) resulting from:			
Research and development credits	4	3	(32)
Stock-based compensation	(1)	(1)	11
State income tax expense, net of federal benefit	4	4	6
Change in valuation allowance	(41)	(40)	(20)
Other	—	—	1
	— %	— %	— %

At December 31, 2008, 2007 and 2006, the Company had net operating loss carryforwards for federal income tax purposes of $113,648,000, $113,093,000 and $94,571,000, respectively, and for state income tax purposes of $113,493,000, $113,083,000 and $94,566,000, respectively, and research and development federal income tax credits of $6,118,000, $3,910,000 and $2,799,000, 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.

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 principally to its net operating loss carryforwards and recognition of deferred license fees from collaborations. A valuation allowance has been recognized to offset the deferred tax assets. 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, 2008 and 2007, the valuation allowance increased $10,574,000 and $10,619,000, respectively. For the year ended December 31, 2006, the valuation allowance decreased $410,000.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

11. Income Taxes—(continued)

As of the respective dates shown, significant components of the Company's deferred tax assets (liabilities) were as follows:

	December 31, 2008	December 31, 2007
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforward	$ 40,951	$ 40,830
Research and development tax credit	4,240	3,128
Collaboration revenue	11,701	2,546
Patents	1,605	1,368
Stock-based compensation	1,129	791
Total gross deferred tax assets	59,626	48,663
Valuation allowance	(59,130)	(48,556)
Net deferred tax asset	496	107
Deferred tax liabilities		
Equipment and other	(496)	(107)
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 (in thousands):

Balance at January 1, 2007	$ 720
Additions based on tax positions related to the current year	222
Balance at December 31, 2007	942
Additions based on tax positions related to the current year	278
Balance at December 31, 2008	$ 1,220

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 for any of the years ended December 31, 2008, 2007 or 2006. The Company believes it is reasonably possible that unrecognized tax benefits may increase in the range of $200,000 to $300,000 during 2009 as a result of additional research and development credits that the Company may become able to claim. Since the Company has incurred cumulative operating losses since inception, all tax years remain open to examination by major jurisdictions.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

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. 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, 2008, the number of shares authorized for issuance under the Plans was 4,362,078, of which 1,028,894 shares remained available for grant.

Awards may be made with respect to the 2006 Plan, or may have been made with respect to both 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.

Under SFAS 123R, the Company recognizes 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 to sixteen benchmark biotechnology companies that have been identified as comparable public entities. The expected term of options granted during 2006 is derived from the simplified method allowable under Staff Accounting Bulletin No. 107 because the Company did not have sufficient historical information regarding its options to derive the expected term. 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 2008 and 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.

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 as of the respective dates shown:

	Year ended December 31,		
	2008	2007	2006
Dividend yield	—	—	—
Risk-free interest rate	3.4%	4.0%	4.7%
Volatility	0.7	0.7	0.7
Expected life	6.43 years	6.55 years	6.25 years

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

12. Stock-Based Incentive Plans—(continued)

A summary of option activity and changes during each of the years ended December 31, 2008, 2007 and 2006 is presented below:

	Options (in thousands)	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2005	1,610	$ 2.88		
Granted	936	5.55		
Forfeited	(39)	3.07		
Exercised	(30)	2.07		
Outstanding at December 31, 2006	2,477	3.89		
Granted	789	8.83		
Forfeited	(45)	4.75		
Exercised	(96)	4.52		
Outstanding at December 31, 2007	3,125	5.11		
Granted	106	6.71		
Forfeited	(21)	6.73		
Exercised	(91)	2.98		
Outstanding at December 31, 2008	3,119	$ 5.21	6.82	$ 1,568
Vested and exercisable at December 31, 2008	2,335	$ 4.61	6.26	$ 1,562

The weighted average grant date fair value of options granted during 2008, 2007 and 2006 was $4.38, $6.02 and $3.80, respectively. The total intrinsic value of options exercised during the years ended December 31, 2008, 2007 and 2006 was $489,000, $461,000 and $141,000, respectively.

A summary of the status of non-vested stock options granted under the Plans as of December 31, 2008 and changes during the year ended December 31, 2008 is presented below:

	Options (in thousands)	Weighted Average Grant-Date Fair Value Per Share
Non-vested at January 1, 2008	1,239	$ 4.48
Granted	106	4.38
Vested	(549)	4.04
Forfeited	(12)	4.87
Non-vested at December 31, 2008	784	$ 4.76

As of December 31, 2008, there was $3,454,000 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 recorded over a weighted average period of 1.3 years. The total fair value of shares subject to stock-based compensation arrangements granted under the Plans that vested during the year ended

12. Stock-Based Incentive Plans—(continued)

December 31, 2008, 2007 and 2006 was $2,217,000, $2,612,000 and $2,825,000, respectively. On January 9, 2009, the Company granted to employees 700,250 stock options with a Black-Scholes-Merton fair value of $1,275,000, which the Company expects to record, after adjusting for estimated forfeitures, as stock-based compensation on a straight line basis over a period of 16 quarters.

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 $2,159,000, $2,176,000 and $1,500,000 for the years ended December 31, 2008, 2007 and 2006, 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 (in thousands):

2009	$2,159
2010	2,159
2011	2,159
2012	1,260
2013	—
	$7,737

Employment Arrangements

The Company has entered into employment agreements with 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 $558,000, $559,000 and $539,000 to the plan for the years ended December 31, 2008, 2007 and 2006, respectively.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

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 specified conditions characterized by cognitive impairment, including Alzheimer's disease, cognitive dysfunction in schizophrenia and attention deficit/hyperactivity disorder, or ADHD. The collaboration agreement also provides for a multi-year preclinical research collaboration between the Company and AstraZeneca. The Company is eligible to receive 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, first commercial sale and first detail 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 license grants, until December 2006, when AstraZeneca made a determination to proceed with further development of AZD3480 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 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). The Company recognized $2,250,000 of the initial fee as revenue for each of the years ended December 31, 2008 and 2007 and $1,146,000 of the initial fee as revenue for the year ended December 31, 2006.

The Company would 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 Topic 13. 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 $197,000,000, contingent upon the achievement of development, regulatory, first commercial sale and first detail milestones for AZD3480 for two indications, as well as stepped 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. The Company recorded $758,000 in license fees paid to UKRF in 2006. No fees were paid to UKRF in 2008 or 2007.

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. As a result of AstraZeneca's

15. Strategic Alliance and Collaboration Agreements—(continued)

decision to proceed with further development of AZD3480, 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 $8,921,000, $6,888,000 and $4,672,000 for the years ended December 31, 2008, 2007 and 2006, respectively. The Company recognized additional collaboration research and development revenue of $46,000, $400,000 and $347,000 for the years ended December 31, 2008, 2007 and 2006, respectively, for clinical trial material purchased by AstraZeneca from the Company and other research and development costs reimbursable under the collaboration.

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 AstraZeneca 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 Phase 2 proof of concept. Accordingly, the Company recognized $923,000 and $115,000 of the payment as revenue for the years ended December 31, 2008 and 2007, respectively.

In May 2008, the Company received a $200,000 payment from AstraZeneca and, in December 2008, the Company received a $2,000,000 payment from AstraZeneca. Each payment was made upon achievement of a milestone event related to the development of a product candidate under the parties' preclinical research collaboration. The Company recognized the full amounts of both payments as revenue upon achievement of the respective milestone events because the events met each of the conditions required for immediate recognition under the Company's revenue recognition policy (see Note 2).

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 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

15. Strategic Alliance and Collaboration Agreements—(continued)

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 contingent milestone payments from GlaxoSmithKline as product candidates subject to the alliance advance 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 $3,521,000, 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 as deferred license fee revenue 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. The Company recognized $2,613,000 and $1,125,000 of the initial payment and deemed premium as revenue for the years ended December 31, 2008 and 2007, respectively.

The Company is also eligible to receive up to $1.5 billion 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 stepped double-digit royalties dependent on sales achieved following regulatory approval for any product licensed by GlaxoSmithKline. The Company would 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 Topic 13. 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.

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 within the meaning of the Company's revenue recognition policy. Therefore, the Company recorded the payment as deferred license fee revenue and is recognizing it into revenue on a straight-line basis over the estimated term of the Company's research and early development obligations under the agreement. Accordingly, the Company recognized $692,000 and $58,000 of the payment as revenue for the years ended December 31, 2008 and 2007, respectively.

In May 2008, the Company received a $500,000 payment from GlaxoSmithKline upon achievement of a milestone event related to progress in the Company's smoking cessation program. In November 2008, the Company received $1,000,000 in payments from GlaxoSmithKline upon the achievement of milestone events

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
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15. Strategic Alliance and Collaboration Agreements—(continued)

related to progress in the Company's program in smoking cessation and preclinical program in pain. The Company immediately recognized the full amount of each of these payments as revenue upon achievement of the respective milestone events because the events met each of the conditions required for immediate recognition under the Company's revenue recognition policy (see Note 2).

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 completion of the IPO, RJRT no longer beneficially owned more than 5% of the Company's outstanding shares of common stock. 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. 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, 2008 and 2007, the Company owed RJRT $23,000 and $909,000, respectively, under the note payable. The Company paid $49,000, $112,000 and $81,000 in interest on the note payable to RJRT during 2008, 2007 and 2006, respectively.

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 to RJRT, the Company recognized compensation expense of $1,000 for the year ended December 31, 2006. The Company did not recognize any compensation expense in connection with the issuance of the stock options for the years ended December 31, 2008 and 2007.

17. Selected Quarterly Financial Data (unaudited)

	2008 Quarter			
	First	Second	Third	Fourth
	(in thousands, except per share amounts)			
Net operating revenues	$ 4,276	$ 5,156	$ 4,135	$ 6,518
Gross (loss) profit on product sales	(16)	22	(20)	(17)
Operating loss	(6,700)	(7,433)	(8,162)	(5,849)
Net loss attributable to common stockholders	(5,781)	(6,803)	(7,648)	(5,429)
Basic and diluted net loss per share attributable to common stockholders(1)(2)	$ (0.24)	$ (0.27)	$ (0.31)	$ (0.22)
Weighted average common shares outstanding—basic and diluted(2)	23,834	24,906	24,946	24,964

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2008

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

	2007 Quarter			
	First	Second	Third	Fourth
	(in thousands, except per share amounts)			
Net operating revenues	$ 2,051	$ 2,842	$ 3,126	$ 3,556
Gross loss on product sales	(25)	(1)	(72)	(99)
Operating loss	(5,643)	(9,071)	(8,403)	(8,655)
Net loss attributable to common stockholders	(4,793)	(8,263)	(7,371)	(7,646)
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)	19,137	19,147	20,097	20,484

(1) Per common share amounts for the quarters and full years have been calculated separately. Accordingly, the sum of quarterly amounts may not equal the annual amount because of differences in the weighted average common shares outstanding during each period, principally due to the effect of share issuances by the Company during the year.

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

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, 2008 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, 2008, 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, 2008. 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, 2008, 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, 2008, based on the COSO criteria.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of Targacept, Inc. as of December 31, 2008 and 2007, 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, 2008 and our report dated March 12, 2009 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Greensboro, North Carolina
March 12, 2009

(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, 2008 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 2009 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 by reference in this Item 10.

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 2009 Annual Meeting of Stockholders to be filed with the SEC under the headings “Executive Compensation” and “Corporate Governance” and is incorporated by reference in this Item 11.

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 2009 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 by reference in this Item 12.

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 2009 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 by reference in this Item 13.

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 2009 Annual Meeting of Stockholders to be filed with the SEC under the heading “Independent Registered Public Accounting Firm Fee Information and Audit Committee Pre-Approval Policy” and is incorporated by reference in this Item 14.

PART IV

Item 15. Exhibits, Financial Statement Schedules.

(a)(1) *Financial Statements.* For a list of the financial statements included in this annual report, see “Index to the Financial Statements” on page 84.

(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 by reference in this Item 15(a)(3).

(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 13, 2009

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 13, 2009
/s/ ALAN A. MUSSO **Alan A. Musso**	Vice President, Chief Financial Officer and Treasurer (principal financial officer and principal accounting officer)	March 13, 2009
/s/ MARK SKALETSKY **Mark Skaletsky**	Chairman of the Board of Directors	March 13, 2009
/s/ M. JAMES BARRETT **M. James Barrett**	Director	March 13, 2009
/s/ CHARLES A. BLIXT **Charles A. Blixt**	Director	March 13, 2009
/s/ JULIA R. BROWN **Julia R. Brown**	Director	March 13, 2009
/s/ G. STEVEN BURRILL **G. Steven Burrill**	Director	March 13, 2009
/s/ ERROL B. DE SOUZA **Errol B. De Souza**	Director	March 13, 2009
/s/ ALAN W. DUNTON **Alan W. Dunton**	Director	March 13, 2009
/s/ JOHN P. RICHARD **John P. Richard**	Director	March 13, 2009
/s/ RALPH SNYDERMAN **Ralph Snyderman**	Director	March 13, 2009

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, as amended and restated January 9, 2009
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	Loan Agreement, dated March 7, 2008, by and between the Company and Branch Banking and Trust Company (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K filed March 12, 2008)
10.6(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))
10.6(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))
10.6(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))
10.6(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))
10.7(a)*	Targacept, Inc. 2006 Stock Incentive Plan, amended and restated as of November 28, 2007 (incorporated by reference to Exhibit 10.6(a) to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2007)
10.7(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))
10.7(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))
10.7(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))
10.7(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))
10.8(a)*	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(b)*	Amendment No. 1, dated March 13, 2008, to Employment Agreement, dated as of August 22, 2000, by and between the Company and J. Donald deBethizy (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2008)

Exhibit Number	Description
10.9(a)*	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(b)*	Amendment No. 1, dated March 13, 2008, to Employment Agreement, dated as of August 22, 2000, by and between the Company and Merouane Bencherif (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2008)
10.10(a)*	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(b)*	Amendment No. 1, dated March 13, 2008, to Employment Agreement, dated as of August 22, 2000, by and between the Company and William S. Caldwell (incorporated by reference to Exhibit 10.5 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2008)
10.11(a)*	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(b)*	Amendment No. 1, dated March 13, 2008, to Employment Agreement, dated as of April 24, 2001, by and between the Company and Geoffrey C. Dunbar (incorporated by reference to Exhibit 10.6 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2008)
10.12(a)*	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))
10.12(b)*	Amendment No. 1, dated March 13, 2008, to Employment Agreement, dated as of February 8, 2002, by and between the Company and Alan A. Musso (incorporated by reference to Exhibit 10.7 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2008)
10.13(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))
10.13(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 (incorporated by reference to Exhibit 10.12(b) to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2007)
10.13(c)*	Amendment No. 2, dated March 13, 2008, to Employment Agreement, dated as of September 1, 2003, by and between the Company and Jeffrey P. Brennan (incorporated by reference to Exhibit 10.4 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2008)
10.14*	Employment Agreement, dated as of March 13, 2008, by and between the Company and Peter A. Zorn (incorporated by reference to Exhibit 10.8 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2008)
10.15	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. (incorporated by reference to Exhibit 10.13 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2007)

Exhibit Number	Description
10.16+	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))
10.17(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))
10.17(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))
10.18(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)
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	Supply Agreement, dated July 23, 2001, between the Company (as assignee of Layton Bioscience, Inc.), Interchem Corporation and Poli Industria Chimica, SPA
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)

Exhibit Number	Description
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 3.2

BYLAWS

OF

TARGACEPT, INC.

(as amended and restated January 9, 2009)

BYLAWS
OF
TARGACEPT, INC.

ARTICLE I

Offices

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

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

ARTICLE II

Meetings of Stockholders

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

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

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

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

Section 5. Notice of Meetings. Written or printed notice shall be given not less than ten (10) or more than sixty (60) days before the date of the meeting, to each stockholder of record entitled to vote at the meeting by delivering a written notice thereof to such stockholder personally or by depositing such notice in the United States mail, postage prepaid, directed to such stockholder at his last address as it appears on the stock records of the Corporation. The notice shall state the time and place of the meeting, the means of remote communications, if any, by which stockholders and proxy holders may be deemed to be present in person and vote at such meeting (if authorized by the Board in its sole discretion pursuant to the Delaware General Corporation Law, as may be amended from time to time the "**DGCL**") and, in the case of a special meeting, briefly describing the purpose or purposes of the meeting. It shall be the primary responsibility of the Secretary to give the notice, but notice may be given by or at the direction of the President or other person or persons calling the meeting. Notice of any adjourned meeting of the stockholders shall not be required to be given, except where expressly required by law.

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

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

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

Section 7. Proxies. Each stockholder entitled to vote at a meeting of stockholders may authorize another person or persons to act for such stockholder by proxy, but no such proxy shall be voted or acted upon after three (3) years from its date, unless the proxy provides for a longer period. A proxy may be granted in writing or otherwise as permitted under Section 212(c) or any other provision of the DGCL. A duly executed proxy shall be irrevocable if it so states and it is coupled with an interest sufficient in law to support an irrevocable power.

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

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

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

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

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

Section 13. Proposals by Stockholders at Annual Meeting.

(a) At an annual meeting of stockholders, only such business shall be conducted as shall have been properly brought before the meeting. To be properly brought before an annual meeting, business must be: (i) specified in the notice of meeting (or any supplement thereto) given by or at the direction of the Board in accordance with these Bylaws; (ii) brought before the meeting by or at the direction of the Board; or (iii) properly brought before the meeting by a stockholder that: (A) is a stockholder of record (and, with respect to any beneficial owner, if different, on whose behalf such business is proposed, only if such beneficial owner was the beneficial owner of shares of the Corporation) both on the date of the giving of notice provided for in this Article II, Section 13 and on the date of the annual meeting; (B) is entitled to vote at such annual meeting; and (C) complies with the notice procedures set forth in this Article II, Section 13. Except for proposals properly made in accordance with Rule 14a-8 under the Securities Exchange Act of 1934 (as amended and inclusive of the rules and regulations thereunder, the "**Exchange Act**") and included in the notice of meeting given by or at the direction of the Board, the foregoing clause (iii) shall be the exclusive means for a stockholder to propose business to be brought before an annual meeting of stockholders. Stockholders shall not be permitted to propose business to be brought before a special meeting of the stockholders, and the only matters that may be brought before a special meeting are the matters specified in the notice of meeting given by or at the direction of the person calling the meeting pursuant to Article II, Section 3. Stockholders seeking to nominate persons for election to the Board must comply with Article II, Section 14 and, except as expressly provided in Article II, Section 14, this Article II, Section 13 shall not be applicable to nominations.

(b) Without qualification, for business to be properly brought before an annual meeting by a stockholder, the stockholder must (i) provide Timely Notice (as defined below) thereof in writing and in proper form required by this Article II, Section 13 to the Secretary of the Corporation, and (ii) provide all updates and supplements to such notice at the times and in the forms required by this Article II, Section 13. As used in these Bylaws, the term "**Timely Notice**" shall mean notice delivered to or mailed and received at the principal executive offices of the Corporation not fewer than ninety (90) and not more than one hundred twenty (120) calendar days in advance of the date that is the one year anniversary of the preceding year's annual meeting of stockholders; provided, however, that in the event that no annual meeting was held in the preceding year or the date of the annual meeting has been advanced by more than thirty (30) days or delayed by more than sixty (60) days from the one year anniversary of the previous year's annual meeting of stockholders, notice by a stockholder, to be considered a "Timely Notice," must be so delivered, or mailed and received, not later than the close of business on the ninetieth (90th) day prior to such annual meeting or, if the first public disclosure of the date of such annual meeting is less than one hundred (100) days prior to such annual meeting, the close of business on the tenth (10th) day following such first public disclosure. In no event will adjournment of an annual meeting or public disclosure thereof commence a new time period for the giving of such notice by a stockholder.

(c) To be in proper form for purposes of this Article II, Section 13, a stockholder's notice must set forth (in addition to any information required by applicable law):

(i) as to each item of business:

(A) a description of the business desired to be brought before the annual meeting and the reasons for conducting such business at the annual meeting; and

(B) the text of the proposal or business (including the text of any resolutions proposed for consideration);

(ii) as to each Proposing Person (as defined below):

(A) the name and address, as they appear on the Corporation's books, of the Proposing Person; and

(B) the class or series and number of shares of the Corporation which are owned of record or beneficially owned by the Proposing Person (the disclosures to be made pursuant to this clause (ii) are collectively referred to as "**Stockholder Information**");

(iii) as to each Proposing Person:

(A) any derivative, swap or other transaction or series of transactions engaged in, directly or indirectly, by such Proposing Person, the purpose or effect of which is to give such Proposing Person economic risk similar to ownership of shares of any class or series of the Corporation, including due to the fact that the value of such derivative, swap or other transactions are determined by reference to the price, value or volatility of any shares of any class or series of the Corporation, or which derivative, swap or other transactions provide, directly or indirectly, the opportunity to profit from any increase in the price or value of shares of any class or series of the Corporation ("**Synthetic Equity Interests**"), which Synthetic Equity Interests shall be disclosed without regard to whether (x) the derivative, swap or other transactions convey any voting rights in such shares to such Proposing Person, (y) the derivative, swap or other transactions are required to be, or are capable of being, settled through delivery of such shares or (z) such Proposing Person may have entered into other transactions that hedge or mitigate the economic effect of such derivative, swap or transactions;

(B) any proxy (other than a revocable proxy or consent given in response a solicitation made pursuant to, and in accordance with, Section 14(a) of the Exchange Act by way of a solicitation statement filed on Schedule 14A), agreement, arrangement, understanding or relationship pursuant to which such Proposing Person has or shares a right to vote any shares of any class or series of the Corporation;

(C) any agreement, arrangement, understanding or relationship, including any repurchase or similar so-called "stock borrowing" agreement or arrangement, engaged in, directly or indirectly, by such Proposing Person, the purpose or effect of which is to mitigate loss to, reduce the economic risk (of ownership or otherwise) of shares of any class or series of the Corporation by, manage the risk of share price changes for, or increase or decrease voting power of, such Proposing Person with respect to the shares of any class or series of the Corporation, or which provides, directly or indirectly, the opportunity to profit from any decrease in the price or value of the shares of any class or series of the Corporation ("**Short Interests**");

(D) any rights to dividends on the shares of any class or series of the Corporation owned beneficially by such Proposing Person that are separated or separable from the underlying shares of the Corporation;

(E) any performance related fees (other than an asset based fee) that such Proposing Person is entitled to based on any increase or decrease in the price or value of shares of any class or series of the Corporation, or any Synthetic Equity Interests or Short Interests, if any;

(F) a reasonably detailed description of all agreements, arrangements and understandings (x) between or among any of the Proposing Persons or (y) between or among any Proposing Person and any other record or beneficial holder of the shares of any class or series of the Corporation (including their names) in connection with the proposal of such business by such stockholder;

(G) any other material interest, direct or indirect, of the Proposing Person in the business being proposed; and

(H) any other information relating to such Proposing Person that would be required to be disclosed in a proxy statement or other filing required to be made in connection with solicitations of proxies or consents by such Proposing Person in support of the business proposed to be brought before the meeting pursuant to Section 14(a) of the Exchange Act (the disclosures to be made pursuant to this clause (iii) are collectively referred to as "**Disclosable Interests**"); provided, however, that Disclosable Interests shall not include any such disclosures with respect to the ordinary course business activities of any broker, dealer, commercial bank, trust company or other nominee who is a Proposing Person solely as a result of being the stockholder directed to prepare and submit the notice required by these Bylaws on behalf of a beneficial owner; and

(iv) a representation that the stockholder providing the notice of business proposed to be brought before the annual meeting is a holder of record of shares of the Corporation entitled to vote at the meeting and intends to appear in person or by proxy at the meeting to present the proposal.

(d) For purposes of this Article II, Section 13, the term "**Proposing Person**" shall mean: (i) the stockholder providing the notice of business proposed to be brought before an annual meeting; (ii) the beneficial owner or beneficial owners, if different, on whose behalf the notice of the business proposed to be brought before the annual meeting is made; and (iii) any affiliate or associate (each within the meaning of Rule 12b-2 under the Exchange Act for purposes of these Bylaws) of such stockholder or beneficial owner.

(e) A stockholder providing notice of business proposed to be brought before an annual meeting shall further update and supplement such notice, if necessary, so that the information provided or required to be provided in such notice pursuant to this Article II, Section 13 shall remain true and correct as of the record date for the annual meeting and as of the date that is ten (10) business days prior to the annual meeting or any adjournment or postponement thereof, and such update and supplement shall be delivered to, or mailed and received by, the Secretary at the principal executive offices of the Corporation not later than five (5) business days after the record date for the annual meeting (in the case of the update and supplement required to be made as of the record date), and not later than eight (8) business days prior to the date of the annual meeting, if practicable (or, if not practicable, on the earliest practicable date prior to the date of the annual meeting), or any adjournment or postponement thereof (in the case of the update and supplement required to be made as of ten (10) business days prior to the annual meeting or any adjournment or postponement thereof).

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

(g) This Article II, Section 13 is expressly intended to apply to any business proposed to be brought before an annual meeting of stockholders other than any proposal made pursuant to Rule 14a-8 under the Exchange Act. In addition to the foregoing provisions of this Article II, Section 13, a stockholder shall also comply with all applicable requirements of the Exchange Act and the DGCL with respect to matters set forth in this Article II, Section 13. Nothing in this Article II, Section 13 shall be deemed to affect any rights of stockholders to request inclusion of proposals in the Corporation's proxy statement pursuant to Rule 14a-8 under the Exchange Act.

(h) For purposes of these Bylaws, "**beneficially own**" has the meaning provided in Rules 13d-3 and 13d-5 under the Exchange Act, and "**beneficial owner**" and "**beneficial holder**" mean a person or entity that beneficially owns the relevant securities. A person shall in all events be deemed to beneficially own shares of any class or series of the Corporation as to which such person has a right to acquire beneficial ownership at any time in the future.

(i) For purposes of these Bylaws, "**public disclosure**" shall mean disclosure via press release reported by a national news service or via a filing with the Securities and Exchange Commission pursuant to the Exchange Act.

(j) For purposes of these Bylaws, "**close of business"** shall mean, on any particular day, 5:00 p.m. Winston-Salem, North Carolina time or, if such day is not a business day, on the business day immediately preceding such day.

Section 14. Nominations by Stockholders at Meeting of Stockholders.

(a) Only persons who are nominated in accordance with the procedures set forth in this Article II, Section 14 shall be eligible for election as directors at a meeting of stockholders, except as otherwise may be provided in the Charter with respect to the right of holders of any series of preferred stock then outstanding. Nominations of persons for election to the Board may be made at an annual meeting (or at a special meeting, but only if the election of directors is a matter specified in the notice of meeting given by or at the direction of the person calling such special meeting in accordance with Article II, Section 3) only as follows: (i) by or at the direction of the Board (or any committee thereof); or (ii) by any stockholder of the Corporation that (A) is a stockholder of record (and, with respect to any beneficial owner, if different, on whose behalf such nomination is proposed to be made, only if such beneficial owner

was the beneficial owner of shares of the Corporation) both on the date of the giving of notice provided for in this Article II, Section 14 and on the date for the meeting; (B) is entitled to vote at such meeting; and (C) complies with the notice procedures set forth in this Article II, Section 14. The foregoing clause (ii) shall be the exclusive means for a stockholder to make any nomination of a person or persons for election to the Board.

(b) Without qualification, for a stockholder to make any nomination of a person or persons for election to the Board at an annual meeting, the stockholder must (i) provide Timely Notice (as defined in Article II, Section 13(b)) thereof in writing and in proper form required by this Article II, Section 14 to the Secretary of the Corporation, and (ii) provide all updates and supplements to such notice at the times and in the forms required by this Article II, Section 14. Without qualification, if the election of directors is a matter specified in the notice of meeting given by or at the direction of the person calling such special meeting in accordance with Article II, Section 3, then, for a stockholder to make any nomination of a person or persons for election to the Board at a special meeting, the stockholder must have (A) given timely notice thereof in writing and in proper form required by this Article II, Section 14 to the Secretary of the Corporation and (B) provided all updates and supplements to such notice at the times and in the forms required by this Article II, Section 14. To be timely, a stockholder's notice for nominations to be made at a special meeting must be delivered to, or mailed and received at, the principal executive offices of the Corporation not earlier than the one hundred twentieth (120^{th}) day prior to such special meeting and not later than the close of business on the ninetieth (90^{th}) day prior to such special meeting or, if the first public disclosure of the date of such special meeting is less than one hundred (100) days prior to such special meeting, the close of business on the tenth (10^{th}) day following the day of such first public disclosure. In no event shall any adjournment of an annual meeting or special meeting or the announcement thereof commence a new time period for the giving of a stockholder's notice as described above.

(c) To be in proper form for purposes of this Article II, Section 14, a stockholder's notice to the Secretary shall set forth:

(i) as to each person that a Nominating Person (as defined below) proposes to nominate for election or re-election as a director:

(A) the name, age, business address and residence address of such person;

(B) the principal occupation or employment of such person;

(C) all information with respect to such proposed nominee that would be required to be set forth in a stockholder's notice pursuant to this Article II, Section 14 if such proposed nominee were a Nominating Person;

(D) any other information relating to such proposed nominee that is required to be disclosed in solicitations of proxies for elections, or is otherwise required, in each case pursuant to Regulation 14A under the Exchange Act (including without limitation such person's written consent to being named in the proxy statement, if any, as a nominee and to serving as a director if elected);

(E) a description of all direct and indirect compensation and other material monetary agreements, arrangements and understandings during the past three years, and any other material relationships, between or among any Nominating Person, on the one hand, and each proposed nominee, his or her respective affiliates and associates, on the other hand, including, without limitation, all information that would be required to be disclosed pursuant to Item 404 under Regulation S-K if such Nominating Person were the "registrant" for purposes of such rule and the proposed nominee were a director or executive officer of such registrant; and

(F) a completed and signed questionnaire, representation and agreement as described in Article II, Section 14(g);

(ii) as to each Nominating Person, the Stockholder Information (as defined in Article II, Section 13(c)(ii), except that for purposes of this Article II, Section 14, the term "Nominating Person" shall be substituted for the term "Proposing Person" in all places it appears in Section 13(c)(ii));

(iii) as to each Nominating Person, any Disclosable Interests (as defined in Article II, Section 13(c)(iii), except that for purposes of this Article II, Section 14, the term "Nominating Person" shall be substituted for the term "Proposing Person" in all places it appears in Section 13(c)(iii) and the disclosure in clause H of Section 13(c)(iii) shall be made with respect to the election of directors at the meeting);

(iv) such other information (A) as may reasonably be required by the Corporation to determine the eligibility of such proposed nominee to serve as an independent director or financial expert on the Board or any committee thereof in accordance with the Corporation's Corporate Governance Guidelines and the various rules and standards applicable to the Corporation, or (B) that could be material to a reasonable stockholder's understanding of the independence, financial expertise, or lack of independence or financial expertise of such proposed nominee.

(d) For purposes of this Article II, Section 14, the term "**Nominating Person**" shall mean: (i) the stockholder providing the notice of the nomination proposed to be made at the meeting; (ii) the beneficial owner or beneficial owners, if different, on whose behalf the notice of the nomination proposed to be made at the meeting is made; and (iii) any affiliate or associate of such stockholder or beneficial owner.

(e) A stockholder providing notice of any nomination proposed to be made at the meeting shall further update and supplement such notice, if necessary, so that the information provided or required to be provided in such notice pursuant to this Article II, Section 14 shall be true and correct as of the record date for the meeting and as of the date that is ten (10) business days prior to the meeting or any adjournment or postponement thereof, and such update and supplement shall be delivered to, or mailed and received by, the Secretary at the principal executive offices of the Corporation not later than five (5) business days after the record date for the meeting (in the case of the update and supplement required to be made as of the record date), and not later than eight (8) business days prior to the date of the meeting, if practicable (or, if not practicable, on the earliest practicable date prior to the date of the meeting), or any adjournment or postponement thereof (in the case of the update and supplement required to be made as of ten (10) business days prior to the meeting or any adjournment or postponement thereof).

(f) No stockholder nominee shall be eligible for election as a director of the Corporation unless nominated in accordance with this Article II, Section 14. The officer presiding at such meeting shall, if the facts warrant, determine and declare at the meeting that a nomination was not made in accordance with the procedures prescribed by these Bylaws and that the defective nomination shall be disregarded.

(g) To be eligible to be a nominee for election as a director of the Corporation, the proposed nominee must deliver (in accordance with the time periods prescribed for delivery of notice under this Article II, Section 14) to the Secretary at the principal executive offices of the Corporation a written questionnaire with respect to the background and qualifications of such proposed nominee (which questionnaire shall be in form provided by the Secretary to the proposed nominee upon written request) and a written representation and agreement (in form provided by the Secretary to the proposed nominee upon written request) that such proposed nominee:

(i) is not and will not become a party to (A) any agreement, arrangement or understanding with, and has not given any commitment or assurance to, any person or entity as to how such proposed nominee, if elected as a director of the Corporation, will act or vote on any issue or question (a "**Voting Commitment**") that has not been disclosed to the Corporation, or (B) any Voting Commitment that could limit or interfere with such proposed nominee's ability to comply, if elected as a director of the Corporation, with such proposed nominee's fiduciary duties under applicable law;

(ii) is not, and will not become a party to, any agreement, arrangement or understanding with any person or entity other than the Corporation with respect to any direct or indirect compensation, reimbursement or indemnification in connection with service or action as a director that has not been disclosed to the Corporation; and

(iii) in such proposed nominee's individual capacity and on behalf of the stockholder (or the beneficial owner, if different) on whose behalf the nomination is made, would be in compliance, if elected as a director of the Corporation, and will comply with all publicly disclosed corporate governance, conflict of interest, confidentiality and stock ownership and trading policies and guidelines of the Corporation, if any.

(h) In addition to the foregoing provisions of this Article II, Section 14, a stockholder shall also comply with all applicable requirements of the Exchange Act and the DGCL with respect to matters set forth in this Article II, Section 14.

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

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

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

Section 16. Notice by Electronic Transmission. Without limiting the manner by which notice otherwise may be given effectively to stockholders, any notice to stockholders given by the Corporation under any provision of the DGCL, the Charter or these Bylaws shall be effective if given by a form of electronic transmission consented to by the stockholder to which the notice is given. Any such consent shall be revocable by the stockholder by written notice to the Corporation and shall be deemed revoked if (i) the Corporation is unable to deliver by electronic transmission two (2) consecutive notices given by the Corporation in accordance with such consent and (ii) such inability becomes known to the Secretary or an Assistant Secretary of the Corporation, the transfer agent or other person responsible for the giving of notice; provided, however, the failure to treat such inability as a revocation shall not invalidate any meeting or other action. This Article II, Section 16 shall not apply to those situations in which notice by electronic transmission is not permitted in accordance with Section 232 of the DGCL.

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

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

ARTICLE III

Board of Directors

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

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

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

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

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

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

ARTICLE IV

Meetings of Directors

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

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

Section 3. Notice of Special Meetings. The Secretary or other person or persons calling a meeting for which notice is required shall give notice of each special meeting of the Board to each director personally, by telephone or by mail, electronic transmission, overnight mail, courier service or telegram, postage or charges prepaid, at his or her address as shown on the records of the Corporation. If the notice is: (i) given by telephone, electronic transmission, facsimile or hand delivery, it shall be deemed adequate if given at least twelve (12) hours prior to the time set for the meeting; (ii) mailed, it shall be deemed adequate if deposited in the United States mail at least four (4) calendar days before the date of the meeting; (iii) delivered by overnight mail, courier service or telegram, it shall be deemed adequate if delivered to the overnight mail or courier service company or telegraph company at least forty-eight (48) hours before such meeting. Any oral notice given personally or by telephone may be communicated either to the director or to a person at the office of the director who the person giving the notice has reason to believe will promptly communicate it to the director. The notice need not specify the purpose or the place of the meeting, if the meeting is to be held at the principal executive office of the Corporation. Whenever notice is required to be given under any provision of the DGCL, the Charter or these Bylaws, a written waiver thereof, signed by the director entitled to notice, or a waiver by electronic transmission by the director entitled to notice, whether before or after the time stated therein, shall be deemed equivalent to notice. Attendance of a director at a meeting shall constitute a waiver of notice of such meeting, except when the director attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of, any regular or special meeting of the directors need be specified in any written waiver of notice, or any waiver by electronic transmission, unless so required by the Charter or these Bylaws.

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

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

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

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

ARTICLE V

Committees

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

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

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

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

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

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

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

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

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

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

ARTICLE VI

Officers

Section 1. Titles. The officers of the Corporation shall be elected by the Board and shall consist of a President, a Secretary and a Treasurer. The Board may also elect a Chairman of the Board, a Vice Chairman of the Board, a Chief Executive Officer, a Chief Financial Officer, one or more Vice Presidents, a Controller, one or more Assistant Secretaries, one or more Assistant Treasurers, one or more Assistant Controllers and such other officers as may be elected in accordance with Section 3 of this Article VI. Except as otherwise provided in these Bylaws, officers shall have the authority and perform the duties as from time to time may be prescribed by the Board or the officer electing such officer in accordance with Section 3 of this Article VI. Any two or more offices may be held by the same individual, but no officer may act in more than one capacity where action of two or more officers is required.

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

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

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

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

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

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

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

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

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

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

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

Section 13. Secretary. The Secretary shall keep or cause to be kept accurate records of the acts and proceedings of all meetings of stockholders and of the Board and of all committees of the Board and shall give or cause to be given all notices required by law and by these Bylaws. The Secretary shall have general charge of the corporate books and records and of the corporate seal and shall affix the corporate seal to any lawfully executed instrument requiring it. The Secretary shall have general charge of the stock transfer books of the Corporation and shall keep at the principal office of the Corporation (or at the office of the Corporation’s transfer agent or registrar) a record of stockholders, showing the name and address of each stockholder and the number and class of the shares held by each. The Secretary shall have such other powers and duties as the Board or the Chief Executive Officer shall designate or as may be provided by applicable law or prescribed by these Bylaws.

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

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

ARTICLE VII

Capital Stock

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

Section 2. Transfer of Shares. Transfer of shares shall be made on the stock transfer books of the Corporation only upon surrender of the certificate for the shares sought to be transferred by the record holder or by a duly authorized agent, transferee or legal representative to the Corporation or its transfer agent, duly endorsed or accompanied by proper evidence of succession, assignment or authority to transfer. All certificates surrendered for transfer shall be cancelled before new certificates for the transferred shares shall be issued.

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

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

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

ARTICLE VIII

INDEMNIFICATION

Section 1. Right to Indemnification in Proceedings other than those by or in the Right of the Corporation. The Corporation shall indemnify any person who was or is a party or threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (a "**proceeding**") (other than an action by or in the right of the Corporation) by reason of the fact that such person is or was a director or officer of the Corporation, or is or was serving at the request of the Corporation as a director, officer or trustee of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement actually and

reasonably incurred by such person in connection with such action, suit or proceeding to the fullest extent permitted by the DGCL, as the same exists or as may be amended (but, in the case of any amendment, only to the extent such amendment permits broader indemnification rights than such law permitted the Corporation provided prior to such amendment). Such indemnification shall, unless otherwise provided when authorized or ratified, continue as to an indemnitee who has ceased to be a director, officer or trustee and shall inure to the benefit of the indemnitee's heirs, executors and administrators; provided that, except as provided in Section 3 of this Article VIII with respect to proceedings to enforce rights to indemnification, the Corporation shall indemnify any such indemnitee in connection with a proceeding (or part thereof) initiated by such indemnitee only if such proceeding (or part thereof) was authorized by the Board. The right to indemnification conferred in this Section shall be a contract right and shall include the right to be paid by the Corporation the expenses (including attorneys' fees) incurred in defending any such proceeding in advance of its final disposition (hereinafter, an "**advancement of expenses**"); provided, however, that if the DGCL so requires, an advancement of expenses incurred by an indemnitee in his or her capacity as a director or officer (and not in any other capacity in which service was or is rendered by such indemnitee, including without limitation, service to an employee benefit plan) shall be made only upon delivery to the Corporation of an undertaking, by or on behalf of such indemnitee, to repay all amounts so advanced if it shall ultimately be determined that such indemnitee is not entitled to be indemnified by the Corporation under this Section or otherwise (hereinafter an "**undertaking**").

Section 2. Right to Indemnification in Proceedings by or in the Right of the Corporation. The Corporation shall indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the Corporation to procure a judgment in its favor by reason of the fact that such person is or was a director or officer of the Corporation, or is or was serving at the request of the Corporation as a director, officer or trustee of another corporation, partnership, joint venture, trust, employee benefit plan or other enterprise, against expenses (including attorneys' fees) actually and reasonably incurred by such person in connection with the defense or settlement of such action or suit to the fullest extent permitted by the DGCL, as the same exists or as may be amended (but, in the case of any amendment, only to the extent such amendment permits broader indemnification rights than such law permitted the Corporation provided prior to such amendment).

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

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

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

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

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

Section 8. Severability. If any provision or provisions of this Article VIII shall be held to be invalid, illegal or unenforceable for any reason whatsoever: (i) the validity, legality and enforceability of the remaining provisions of this Article VIII (including, without limitation, each portion of any Section of this Article VIII containing any such provision held to be invalid, illegal or unenforceable, that is not itself held to be invalid, illegal or unenforceable) shall not in any way be affected or impaired thereby; and (ii) to the fullest extent possible, the provisions of this Article VIII (including, without limitation, each such portion of any Section of this Article VIII containing any such provision held to be invalid, illegal or unenforceable) shall be construed so as to give effect to the intent manifested by the provision held invalid, illegal or unenforceable.

ARTICLE IX

General Provisions

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

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

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

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

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

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

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

Exhibit 10.24

SUPPLY AGREEMENT

THIS AGREEMENT, is made and entered into on and as of 23 July, 2001 by and between INTERCHEM CORPORATION, a corporation of the State of New Jersey, having offices at 120 Route 17 North, Paramus, New Jersey 07852 (INTERCHEM) and POLI INDUSTRIA CHIMICA, SPA, a corporation of the country Italy, having offices at Via Volturno 48-20089, Quinto De Stampi, Rozzano, Milano, Italy (POLI), and LAYTON BIOSCIENCE INC., a corporation of the State of Delaware, having offices at 709 E. Evelyn Ave, Sunnyvale, CA. 94086 (LAYTON BIOSCIENCE).

WHEREAS POLI INDUSTRIA CHIMICA is in the business of producing bulk pharmaceuticals, and in particular expert in producing MECAMYLAMINE HYDROCHLORIDE and its ISOMERS;

WHEREAS INTERCHEM is the exclusive United States agent for POLI INDUSTRIA CHIMICA for the sales of MECAMYLAMINE HYDROCHLORIDE (PRODUCT) and ISOMERS (ISOMERS);

WHEREAS LAYTON BIOSCIENCE INC. wishes to secure a predictable and reliable source of bulk MECAMYLAMINE HYDROCHLORIDE and ISOMERS;

WHEREAS POLI INDUSTRIA CHIMICA desires to provide bulk pharmaceutical PRODUCT and ISOMERS worldwide;

WHEREAS POLI, INTERCHEM and LAYTON BIOSCIENCE desire to cooperate to achieve these objectives; and

NOW, THEREFORE, in consideration of the promises, covenants and representations of the PARTIES set forth herein, and other good and sufficient consideration receipt of which is hereby acknowledged, LAYTON BIOSCIENCE, POLI, and INTERCHEM agree as follows:

1. DEFINITIONS

PARTIES shall mean INTERCHEM CORPORATION, POLI INDUSTRIA CHIMICA and LAYTON BIOSCIENCE INC., collectively.

LAYTON BIOSCIENCE shall mean LAYTON BIOSCIENCE INC., the signatory to this Agreement, and all affiliates and successors of LAYTON BIOSCIENCE INC.

POLI shall mean POLI INDUSTRIA CHIMICA and its affiliates, the signatory to this agreement, and all successors in interest.

INTERCHEM shall mean INTERCHEM CORPORATION and its affiliates, the signatory to this Agreement, and all successors in interest.

PRODUCT shall mean the pharmaceutical PRODUCT identified as MECAMYLAMINE HYDROCHLORIDE.

ISOMERS shall mean ISOMERS of MECAMYLAMINE that are patented by and the exclusive property of LAYTON BIOSCIENCE.

AFFILIATE shall mean and include any individual, corporation, business association, or entity that controls, is controlled by, or is under common control with the specified PARTY. For purposes of this definition, control shall mean direct or indirect beneficial ownership of more than fifty percent (50%) of the voting stock or other ownership or more than fifty percent (50%) or more interest in the income of, such entity. Notwithstanding the foregoing, for purposes of this Agreement, INTERCHEM CORPORATION shall be deemed an affiliate of POLI INDUSTRIA CHIMICA.

2. REQUIREMENTS CONTRACT

LAYTON BIOSCIENCE agrees to purchase its requirements for the PRODUCT and ISOMERS exclusively from POLI through INTERCHEM. POLI and INTERCHEM agree to supply the PRODUCT to LAYTON BIOSCIENCE for its exclusive use in marketing pharmaceutical products that are indicated for hypertension, neurological disorders, or psychiatric disorders, and to supply the PRODUCT to LAYTON BIOSCIENCE for its non-exclusive use in marketing pharmaceutical products indicated for any and all other indications. POLI and INTERCHEM agree to supply the ISOMERS to LAYTON BIOSCIENCE for its exclusive use in marketing pharmaceutical products indicated for any and all indications. LAYTON BIOSCIENCE acknowledges that POLI and INTERCHEM are cooperating with another company for the use of the PRODUCT to be combined with another active ingredient in a pharmaceutical product for the indication of smoking cessation, and that this grant of exclusivity in no way impairs the rights of POLI and INTERCHEM to continue such cooperation and to sell the PRODUCT for use in combination with another active ingredient in a pharmaceutical product for the indication of smoking cessation. POLI and INTERCHEM therefore reserve the right to contract with third parties in order to combine PRODUCT with another active ingredient and market the resulting pharmaceutical product for the indication of smoking cessation.

INTERCHEM agrees to supply and fill all orders from LAYTON BIOSCIENCE with PRODUCT and ISOMERS from PRODUCT and ISOMERS manufactured by POLI upon order from LAYTON BIOSCIENCE except as provided herein or otherwise as agreed to in writing between LAYTON BIOSCIENCE and either of the other two PARTIES. Pursuant to the provisions of this Agreement, POLI agrees to manufacture a sufficient quantity of the PRODUCT and ISOMERS to meet LAYTON BIOSCIENCE's requirements for the same.

a. Volume

To assist INTERCHEM and POLI in meeting their obligations under this contract, LAYTON BIOSCIENCE will provide an annual forecast of its needs for the PRODUCT to INTERCHEM which forecast will be updated at least semi-annually. LAYTON BIOSCIENCE will purchase over the life of this Agreement the minimum total volume of PRODUCT specified in Exhibit A. In addition, each year LAYTON BIOSCIENCE will purchase the minimum yearly volume of PRODUCT specified in Exhibit A.

Upon initiation of scale-up of batches for LAYTON BIOSCIENCE ISOMERS, LAYTON BIOSCIENCE will enter good faith negotiations with POLI and INTERCHEM to determine minimum total volume requirements for such ISOMERS for the period of time remaining in the term of this Agreement.

b. Orders

LAYTON BIOSCIENCE shall place written orders for the PRODUCT and to the extent applicable, ISOMERS with INTERCHEM at least twelve (12) weeks in advance of the earliest delivery date required hereunder. Each order shall specify the delivery dates and quantity of the PRODUCT and/or ISOMERS ordered. INTERCHEM shall promptly convey to POLI the quantity of PRODUCT and/or ISOMERS and delivery dates specified in the LAYTON BIOSCIENCE orders. POLI agrees to manufacture and ship to Siegfried CMS Ltd in Zofingen, Switzerland sufficient PRODUCT and/or ISOMERS in a timely fashion so as to comply with LAYTON BIOSCIENCE's orders. POLI shall ship PRODUCT and/or ISOMERS in accordance with such orders (provided such orders are within +/- 10% of LAYTON BIOSCIENCE's forecast for any PRODUCT or ISOMERS over the twelve (12) month period preceding the order) to Siegfried CMS Ltd F.O.B. in Zofingen, Switzerland. Title and risk of loss shall be POLI and INTERCHEM's responsibility until delivered to LAYTON BIOSCIENCE or its agent Siegfried CMS Ltd. in Zofingen, Switzerland. POLI or INTERCHEM may decline to accept orders for any of the PRODUCT or ISOMERS if either POLI or INTERCHEM has received the opinion of patent counsel that the production or sale of the PRODUCT or ISOMERS would infringe on the patent rights of others in either the United States or the country in which POLI's manufacturing facility is located. Pursuant to the requirements of Paragraph 3.d. of this Agreement, POLI or INTERCHEM will promptly notify LAYTON BIOSCIENCE in such a circumstance, and provide LAYTON BIOSCIENCE with a reasonable opportunity to resolve such an issue.

Within thirty (30) days from the date of this Agreement, and at any other time during this Agreement, POLI will advise if there are any existing patents in the country where POLI's manufacturing facility is located which would preclude POLI from providing the PRODUCT or ISOMERS to LAYTON BIOSCIENCE and advise as to the first date when POLI may lawfully supply the PRODUCT or ISOMERS.

c. Modification of Orders

Orders may be modified only upon six (6) weeks written notice to INTERCHEM. LAYTON BIOSCIENCE agrees to accept and pay for all PRODUCT and ISOMERS scheduled for delivery less than six (6) weeks prior to INTERCHEM's receipt of such written notice on the terms and conditions previously agreed to. INTERCHEM shall promptly notify POLI of any such modifications. ill no event may the volume of PRODUCT purchased in any calendar year be less than the yearly minimum specified in Exhibit A.

d. Acceptance and Rejection

If LAYTON BIOSCIENCE determines that any PRODUCT and/or ISOMERS is defective in material or workmanship, not in conformance with the specifications in Exhibit B or current Good Manufacturing Practices (cGMP) as determined by the United States Food and Drug Administration (FDA), is adulterated or misbranded, or is otherwise not in conformity with this Agreement (Defective Product), then LAYTON BIOSCIENCE, in addition to any other rights it may have under this Agreement, may reject

and return any such PRODUCT and/or ISOMERS to POLI and INTERCHEM. At the time of such rejection, LAYTON BIOSCIENCE shall provide INTERCHEM with a written notice describing in detail the circumstances surrounding the rejection and LAYTON BIOSCIENCE's reasons therefor. If LAYTON BIOSCIENCE rejects any PRODUCT and/or ISOMERS it will, at POLI and INTERCHEM's option, either return them to POLI or INTERCHEM, destroy or dispose of them in the least expensive and most environmentally sound manner, or take other actions as POLI and INTERCHEM may request, within reason. In any event, POLI and INTERCHEM shall be responsible for all costs of any such return, destruction, disposal, or any other action.

LAYTON BIOSCIENCE or its agent shall promptly inspect each shipment of the PRODUCT and/or ISOMERS and notify INTERCHEM of any deficiencies. It shall be the responsibility of INTERCHEM and POLI to promptly remedy any such deficiency. LAYTON BIOSCIENCE will make available samples of any allegedly defective PRODUCT and ISOMERS and, if requested, return the same to INTERCHEM at INTERCHEM's expense by the means specified by INTERCHEM. LAYTON BIOSCIENCE shall be deemed to have accepted a PRODUCT and/or ISOMERS shipment if written notice of any alleged deficiency is not received within sixty (60) days from delivery to LAYTON BIOSCIENCE or its agent in Zofingen, Switzerland.

In the event LAYTON BIOSCIENCE receives Defective Product from POLI or INTERCHEM, LAYTON BIOSCIENCE may avail itself, but is not limited to, the following remedies: (i) the replacement by POLI and INTERCHEM of rejected PRODUCT and/or ISOMERS that have either been returned or destroyed with PRODUCT and ISOMERS that are not Defective Product; or (ii) a full refund of any amount paid hereunder by LAYTON BIOSCIENCE for such Defective Product.

If POLI and INTERCHEM replace such Defective Product with PRODUCT and ISOMERS that are not Defective Product within thirty (30) days from their rejection, there will be no alteration of the minimum total volume of PRODUCT requirement for the life of this Agreement as specified in Exhibit A. If after receiving allegedly defective PRODUCT INTERCHEM/POLI disagree with LAYTON BIOSCIENCE as to the existence of a defect, then INTERCHEM/POLI shall have the right to investigate the nature and existence of the defect in a commercially reasonable time. If after this time frame a disagreement between the parties continues to exist then INTERCHEM/POLI will submit the samples to a mutually acceptable independent testing laboratory to test for the alleged defect. Results from the testing laboratory will be binding on both INTERCHEM/POLI, and LAYTON BIOSCIENCE, and the costs for the independent testing will be borne by the Party against whom the laboratory decides.

The minimum total volume of PRODUCT required under this Agreement as specified in Exhibit A will be reduced if and only if LAYTON BIOSCIENCE is forced, for a legitimate reason, to go to a third-party manufacturer for its PRODUCT or ISOMER needs. A legitimate reason includes four circumstances: 1) if POLI and INTERCHEM are unable to supply PRODUCT or ISOMERS for any reason; 2) if POLI and INTERCHEM are unwilling to produce the PRODUCT or ISOMERS for any reason; 3) if POLI and INTERCHEM consistently fail to meet regulatory specifications, including but not limited to U.S. Food and Drug Administration Current Good Manufacturing Practices, and any specifications listed under the terms of this agreement as specified at Exhibit B; or

4) termination or expiration of this Agreement. LAYTON BIOSCIENCE will determine when and if POLI and INTERCHEM have consistently failed to meet regulatory and product specifications. If a disagreement arises as to the existence of a consistent failure to meet regulatory specifications, related U.S. Food and Drug Administration action (including but not limited to issuance of Warning Letters or Form 483s) will serve as prima facie evidence thereof. In the absence of U.S. Food and Drug Administration action, the parties will submit the issue to a mutually acceptable third party arbitrator, whose decision will be final in accordance with Paragraph 26 of this Agreement. The costs of the arbitration will be borne by the party against whom the arbitrator decides.

e. Term

The term of the Agreement is five (5) years from the date of Food and Drug Administration approval of Product or the effective date of this Agreement, whichever is later. It shall be thereafter automatically extended by a term of one (2) years except any PARTY may provide written notice at least twelve (12) months prior to the expiration of any term that it does not wish the Agreement to be renewed for an additional one (2) year period.

3. PATENTS AND PATENT INFRINGEMENT

a. Validity of PARTIES Patents

INTERCHEM and POLI, both independently and collectively, hereby represent and warrant that pursuant to its manufacturing and supply of PRODUCT and ISOMERS that to the best of their knowledge and belief the Patents they will utilize in the furtherance of the manufacturing and supply of PRODUCT and ISOMERS have not been declared invalid or unenforceable, they have good title to such Patents and they are not aware of any application pending in relation to the same that in any way affects these Patents, has not encumbered these Patents or taken any action whereby their title may be impugned or encumbered, or knowledge that these Patents infringe the claims of any third-party patent or other third-party property rights.

LAYTON BIOSCIENCE hereby represents and warrants that pursuant to its use of PRODUCT and ISOMERS, as described at Paragraph 2 of this Agreement, that to the best of its knowledge and belief the Patents it will utilize in the furtherance of the use of PRODUCT and ISOMERS have not been declared invalid or unenforceable, it has good title to such Patents and it is not aware of any application pending in relation to the same that in any way affects these Patents, has not charged or encumbered these Patents or taken any action whereby their title may be impugned or encumbered, or knowledge that these Patents infringe the claims of any third-party patent or other third-party property rights.

b. Patent and Know-How Rights Gained During Agreement

The PARTIES recognize that in the course of work under this Agreement, a PARTY may independently make or otherwise acquire rights to inventions (including without limitation, processes, methods, and improvements to the manufacturing materials, equipment, procedure, or LAYTON BIOSCIENCE patents or other technology during the term of this Agreement) or know-how useful in the manufacture of PRODUCT or ISOMERS. In such event, the PARTY independently making or acquiring the invention or know-how shall be the sole owner of that invention or know-how.

With respect to any such inventions or know-how for which POLI or INTERCHEM are the sole owner, POLI and/or INTERCHEM will grant to LAYTON BIOSCIENCE or any acquiring entity of LAYTON BIOSCIENCE a non-exclusive, royalty-free license, with a right to sublicense, any know-how and patents or patent applications for such inventions under four circumstances: 1) if POLI and INTERCHEM are unable to produce the PRODUCT or ISOMERS for any reason; 2) if POLI and INTERCHEM are unwilling to produce the PRODUCT or ISOMERS for any reason; 3) if POLI and INTERCHEM consistently fail to meet regulatory and product specifications, including but not limited to U.S. Food and Drug Administration Current Good Manufacturing Practices, and any specifications listed under the terms of this agreement at Exhibit B; or 4) termination or expiration of this Agreement. LAYTON BIOSCIENCE will determine in its sole discretion when and if POLI and INTERCHEM have consistently failed to meet regulatory and product specifications. If a disagreement arises as to the existence of a consistent failure to meet regulatory specifications, related U.S. Food and Drug Administration action (including but not limited to issuance of Warning Letters or Form 483s) will serve as prima facie evidence thereof. In the absence of U.S. Food and Drug Administration action, the parties will submit the issue to a mutually acceptable third party arbitrator, whose decision will be final in accordance with Paragraph 26 of this Agreement. The costs of the arbitration will be borne by the party against whom the arbitrator decides.

To the extent that LAYTON BIOSCIENCE or any acquiring entity of LAYTON BIOSCIENCE sublicenses any POLI or INTERCHEM inventions or know-how under these provisions, the licensees of such sublicenses are limited to entities manufacturing pharmaceutical products on behalf of LAYTON BIOSCIENCE or any acquiring entity of LAYTON BIOSCIENCE, and any such sublicenses must state that the use of the POLI or INTERCHEM inventions or know-how are limited to manufacturing pharmaceutical products for the direct benefit of LAYTON BIOSCIENCE or any acquiring entity of LAYTON BIOSCIENCE.

With respect to any inventions that are jointly made by the PARTIES (i.e., inventions in which one or more inventors from each PARTY have made an inventive contribution as determined by the laws of inventorship), including any inventions made by a PARTY's employee or third-party contractor obliged to assign such invention to a PARTY, concerning PRODUCT or ISOMERS or processes or methods relating to PRODUCT or ISOMERS, the PARTIES shall own such inventions (and any patent applications filed on such inventions and any patents issued on such inventions) jointly as co-owners of equal, undivided shares without right of accounting for any act carried out in accordance with the invention, and agree to cooperate and assist one another in filing any patent applications and undertaking all other reasonable and appropriate protection for such patentable joint inventions, including provision of powers of attorney for this purpose.

If any proceedings in bankruptcy or in reorganization, or for the appointment of a receiver or trustee for all or a substantial portion for the assets of any PARTY to this Agreement, or any other like proceedings, under any law for the relief of debtors shall be instituted by or against any PARTY hereto and are not dismissed within ninety (90) days, any patent or know-how rights gained during this Agreement shall pass to the successors in interest to the PARTIES.

c. Prosecution of Joint Patents

LAYTON BIOSCIENCE shall have the first right, but no obligation, to undertake joint patent filings and prosecution in one or more countries respecting jointly held inventions, subject to reimbursement from POLI and INTERCHEM for one-half of any reasonable out-of-pocket expenses LAYTON BIOSCIENCE incurs in such filing and prosecution. In the event LAYTON BIOSCIENCE fails to undertake the filing of such a patent application within ninety (90) days of a notice by LAYTON BIOSCIENCE to POLI or INTERCHEM that it believes the filing of such an application is appropriate, POLI and INTERCHEM may undertake such a filing at their own expense, in which event any subsequently issued patent application shall be owned solely by POLI or INTERCHEM. A PARTY may not assign its rights to any jointly owned invention, application or subsequently issued patent except on the written approval of the other PARTIES to this Agreement, which approval shall not be unreasonably withheld.

d. Patent Infringement and Third-Party Claims

Upon the occurrence of any infringement or suspected or threatened infringement of any PARTY's patents, or misappropriation or misuse of the know-how or confidential information related to such patents, any knowledgeable PARTY shall as soon as practicable consult with the remaining PARTIES to determine what steps should be taken to prevent or terminate such infringement.

If a third-party asserts that a patent or other right owned by it is infringed by the manufacture of PRODUCT or ISOMERS by POLI or INTERCHEM pursuant to this Agreement, the PARTY first obtaining knowledge of such a claim shall immediately provide the other PARTIES notice of such claim and the related facts in reasonable detail. Each PARTY agrees to investigate the situation fully in collaboration with the other two PARTIES, and the PARTIES agree to discuss how best to control the defense of any such claim. In the event the PARTIES cannot agree on the defense of any such claim, LAYTON BIOSCIENCE shall have the right, but not the obligation, to control such defense. POLI and INTERCHEM shall have the right to be represented separately by counsel of its own choice.

As to the enforcement of jointly owned patents, including actions against an infringer, the PARTIES shall consult with each other in good faith as to the best manner in which to proceed. The PARTIES agree as a basic principle that in the case of such actions against infringers, the expenses incurred and damages awarded shall be for the account of the PARTY or PARTIES undertaking such actions to the extent of their financial participation therein.

For the duration of this Agreement, and for any subsequent term of the same, LAYTON BIOSCIENCE hereby agrees not take any patent infringement or other like action against POLI and INTERCHEM related to their manufacture and supply of ISOMERS that are the subject of patents issued to LAYTON BIOSCIENCE.

For the duration of this Agreement and any subsequent term of the same, and pursuant to grants of POLI and/or INTERCHEM licenses for know-how or patents under the terms of this Agreement, POLI and INTERCHEM hereby agree not to take any patent infringement or other like action against LAYTON BIOSCIENCE or LAYTON BIOSCIENCE’s agents related to LAYTON BIOSCIENCE’s or its agents testing, manufacture, and/or use of PRODUCT or ISOMERS that are the subject of know-how or patents issued and/or owned by POLI and/or INTERCHEM.

4. PRICE AND PAYMENT

a. Price

The initial selling price to LAYTON BIOSCIENCE for the PRODUCT for deliveries is set forth in Exhibit C and shall be firm throughout the term of this Agreement.

Upon marketing approval of any LAYTON BIOSCIENCE ISOMERS by the United States Food and Drug Administration, LAYTON BIOSCIENCE will enter good faith negotiations with POLI and INTERCHEM to determine and agree upon an initial selling price for such ISOMERS to be firm throughout the subsequent twelve (12) months from the date an initial selling price for ISOMERS is agreed upon by the PARTIES.

b. Payment

At the time of shipment by INTERCHEM or POLI for eventual delivery to LAYTON BIOSCIENCE or its agent of any lot of PRODUCT or ISOMERS hereunder, INTERCHEM shall submit to LAYTON BIOSCIENCE an invoice setting forth the total amount of PRODUCT and/or ISOMERS being shipped to LAYTON BIOSCIENCE and the amount due to INTERCHEM and POLI with respect to such volume of PRODUCT and/or ISOMERS. Accompanying each such invoice shall also be a certification that the PRODUCT and/or ISOMERS for which LAYTON BIOSCIENCE is being billed has been produced fully in conformance with Exhibit B, cGMP, other requirements of this Agreement, and any other specifications the PARTIES agree upon regarding the quality of ISOMERS to be manufactured under this Agreement.

LAYTON BIOSCIENCE shall pay all undisputed invoices within thirty (30) days of receipt of invoice and acceptance of PRODUCT or ISOMERS. INTERCHEM's prices for the PRODUCT or ISOMERS do not include sales, use, excise, or similar taxes, which shall be the responsibility of LAYTON BIOSCIENCE. LAYTON BIOSCIENCE shall provide INTERCHEM with an appropriate tax exemption certificate acceptable to the taxing authorities imposing such taxes, if LAYTON BIOSCIENCE wishes not to make such payments on its own behalf.

c. INTERCHEM's Compensation

INTERCHEM's compensation on the sale of PRODUCT or ISOMERS shall be included in the selling price of the PRODUCT or ISOMERS.

5. PRODUCT QUALITY

All PRODUCT or ISOMERS supplied hereunder shall be manufactured and supplied by POLI and INTERCHEM strictly in accordance with the specifications set forth in Exhibit Band current Good Manufacturing Practices (cGMP) as determined by the United States Food and Drug Administration (FDA),and any other requirements the PARTIES mutually agree to in writing

concerning any LAYTON BIOSCIENCE ISOMERS approved for marketing by the United States FDA. In addition, all PRODUCT or ISOMERS supplied hereunder shall be manufactured and supplied by POLI and INTERCHEM strictly in accordance with all applicable rules and regulations of all applicable governmental regulatory authorities with jurisdiction over such manufacture and supply, including, but not limited to, the United States FDA and the United States Drug Enforcement Administration (DEA). POLI and INTERCHEM may not subcontract with any third-party to perform any of POLI or INTERCHEM's obligations under this Agreement without the prior written consent of LAYTON BIOSCIENCE, which consent shall not be unreasonably withheld.

The PRODUCT and ISOMERS shall conform to the specifications as set forth in Exhibit B attached hereto, except that any changes made pursuant to this Agreement and mutually agreed upon by all PARTIES in writing may modify these specifications. In addition to other warranties hereinafter set forth, POLI warrants that all PRODUCT and ISOMERS sold to LAYTON BIOSCIENCE pursuant to this Agreement shall comply with the specifications of Exhibit B, any modifications thereto agreed to by the PARTIES, and FDA cGMPs.

POLI and INTERCHEM will take all steps necessary to ensure that they have the facilities, equipment, instrumentation, resources, and trained personnel to provide all raw materials, manufacturing processes, in-process and product assays, analysis and other testing as compliance with cGMP standards may require in connection with POLI and INTERCHEM's supply of PRODUCT and ISOMERS hereunder. POLI and INTERCHEM shall provide a certificate of analysis for each lot of PRODUCT or ISOMERS supplied hereunder at the time of shipment.

POLI and INTERCHEM shall maintain complete and accurate documentation of all validation data, stability testing data, batch records, quality control and laboratory testing and any other data required under cGMP and other requirements of any relevant regulatory authorities in connection with the manufacturing and supply of PRODUCT and ISOMERS hereunder. POLI and INTERCHEM shall permit LAYTON BIOSCIENCE or its consultants to have access to any relevant records and data in connection with such manufacture, upon reasonable notice and during normal business hours.

POLI and INTERCHEM agree that they will not engage in any act which causes any PRODUCT or ISOMERS produced by POLI or INTERCHEM to become adulterated or misbranded within the meaning of the United States Federal Food, Drug, and Cosmetic Act, as amended.

a. Changes in Process

POLI reserves the right to modify or change the process by which it manufactures the PRODUCT or ISOMERS. POLI will not manufacture PRODUCT or ISOMERS prepared by any such modified or changed process until it has notified LAYTON BIOSCIENCE and LAYTON BIOSCIENCE, POLI, and INTERCHEM have received all necessary regulatory approvals. POLI further agrees to provide documentation concerning processing changes to the PRODUCT and ISOMERS and samples thereof produced by any such modified or changed process to LAYTON BIOSCIENCE within thirty (30) days of their first production so that LAYTON BIOSCIENCE may verify that the PRODUCT and/or ISOMERS meets or exceeds all applicable quality standards.

6. RECALL, WITHDRAWAL, OR FIELD CORRECTION

If LAYTON BIOSCIENCE initiates or is required to initiate a product recall, withdrawal, or field correction with respect to, or if there is any governmental seizure of, any of its products containing any PRODUCT or ISOMERS supplied hereunder which action is due, in whole or in part to the negligent or intentional wrongful act or omission of POLI or INTERCHEM in connection with the testing, manufacturing, release and control of PRODUCT or ISOMERS hereunder, LAYTON BIOSCIENCE will notify INTERCHEM or POLI promptly of the details regarding such action, including providing copies of all relevant documentation concerning such action. POLI and INTERCHEM will assist LAYTON BIOSCIENCE in investigating any such situation and all regulatory contacts and communications that are made and all activities concerning seizure, recall, withdrawal, or field correction will be jointly coordinated by LAYTON BIOSCIENCE, POLI, and, INTERCHEM, although the final decisions with respect to seizure, recall, withdrawal, field correction or regulatory contacts and communications will be with LAYTON BIOSCIENCE.

If any such recall, withdrawal, field correction, or seizure occurs due solely to the negligent or intentional wrongful act or omission of POLI or INTERCHEM in connection with the testing, manufacturing, release and control of PRODUCT or ISOMERS hereunder, then POLI and INTERCHEM shall bear the full cost and expense including reasonable attorney=s and consultant=s fees, of any such seizure, recall, withdrawal, or field correction. If any such recall, withdrawal, field correction, or seizure occurs due solely to the negligent or intentional wrongful act or omission of LAYTON BIOSCIENCE, including LAYTON BIOSCIENCE's failure to properly ascertain whether PRODUCT or ISOMERS meets regulatory and product specifications, then LAYTON BIOSCIENCE shall bear the full cost and expense of any such seizure, recall, withdrawal, or field correction. If more than one of the PARTIES contributes to the cause of a seizure, recall, withdrawal, or field correction, the cost and expenses thereof will be shared in proportion to each PARTY's contribution to the problem.

If any such recall, withdrawal, field correction, or seizure occurs due to a latent defect in the Product (i.e., a defect other than the failure of the product to meet the established specifications in Exhibit B for the PRODUCT or similar specifications established for ISOMERS), as delivered to LAYTON BIOSCIENCE, that affects its quality or functionality, then POLI/INTERCHEM and LAYTON shall equally share the cost and expense of any such seizure, recall, withdrawal, or field correction.

7. FORCE MAJEURE

Neither INTERCHEM, POLI, nor LAYTON BIOSCIENCE shall be liable or be in breach of any existing provision hereof for delays in delivery or failure to manufacture and deliver to the extent such delays are due to an event of force majeure; including: (1) causes beyond its reasonable control, (2) acts of God, acts of civil or military authority, government controls or regulations, fire, strikes, accidents, floods, epidemics, quarantine restrictions, war, or (3) inability to obtain necessary labor, materials, components or manufacturing facilities through regular channels due to causes beyond its reasonable control and only if the PARTY affected shall have used all reasonable efforts to avoid such occurrence and to remedy it promptly if it shall have occurred. In the event of any such delay that impacts the performance of POLI or INTERCHEM under this Agreement, the date of delivery of PRODUCT or ISOMERS shall be deferred to a period up to but not to exceed the time attributable to the delay. If an event of force majeure causes a failure or delay by POLI or INTERCHEM that exceeds forty-five (45) days, LAYTON BIOSCIENCE may, at its sole discretion, elect to obtain the PRODUCT or ISOMERS from another source for such period of time as such delay continues.

In the event that an act of force majeure causes a failure in the manufacture or delay in the delivery of PRODUCT or ISOMERS, once the direct effects of such an event are no longer present, POLI and INTERCHEM shall place priority on the manufacturing and supply of the deferred PRODUCT or ISOMERS for LAYTON BIOSCIENCE to the exclusion of all other manufacturing and supply activities.

If there is a failure in the manufacture or delay in the delivery of PRODUCT due to an event of force majeure, and the delivery of PRODUCT or ISOMERS is deferred by less than forty-five (45) days, there will be no alteration of the minimum total volume of PRODUCT requirement for the life of this Agreement as specified in Exhibit A, and any minimum total volume requirement for ISOMERS as agreed upon by the PARTIES. However, if an event of force majeure causes the delivery of PRODUCT or ISOMERS to be deferred by more than forty-five (45) days, and such a deferral occurs within the last sixty (60) days within a given yearly period as specified in Exhibit A, or any applicable twelve (12) month period per an agreed upon schedule for minimum total volume requirements for ISOMERS, the volume of PRODUCT or ISOMERS related to such a deferral shall be deducted from the yearly minimum total volume of PRODUCT requirement for the year in which the deferral occurred pursuant to the schedule in Exhibit A or any applicable twelve (12) month period per an agreed upon schedule for minimum total volume requirements for ISOMERS.

In the event that an act of force majeure causes a failure in the delay in the delivery of PRODUCT or ISOMERS that exceeds ninety (90) days, LAYTON BIOSCIENCE may terminate this Agreement at its sole discretion, and in such a circumstance shall not be responsible for meeting any and all of the minimum volume of PRODUCT or ISOMERS requirements as specified in Paragraph 2.a. and Exhibit A of this Agreement, or otherwise agreed upon by the PARTIES for ISOMERS.

Pursuant to the PARTIES good faith negotiations concerning minimum total volume requirements as discussed in Paragraph 2.a. of this Agreement, the PARTIES will specifically delineate the effects of an event of force majeure effecting the delivery of ISOMERS to LAYTON BIOSCIENCE on such minimum total volume requirements.

8. INTELLECTUAL PROPERTY AND TECHNOLOGY TRANSFER

a. Grants and Licenses

LAYTON BIOSCIENCE hereby grants POLI and INTERCHEM a non-exclusive license without right to sublicense under the LAYTON BIOSCIENCE Patents for ISOMERS for the sole purpose of manufacturing the ISOMERS during the term of this Agreement. This license may not be assigned or transferred without the prior written consent of LAYTON BIOSCIENCE.

POLI and/or INTERCHEM will hereby grant to LAYTON BIOSCIENCE or any acquiring entity of LAYTON BIOSCIENCE a non-exclusive, royalty-free license, with a right to sublicense, any know-how, Patents, or Patent applications for manufacturing or processing PRODUCT or ISOMERS, under four circumstances: 1) if POLI and INTERCHEM are unable to produce the PRODUCT

or ISOMERS for any reason; 2) if POLI and INTERCHEM are unwilling to produce the PRODUCT or ISOMERS for any reason; 3) if POLI and INTERCHEM consistently fail to meet regulatory and product specifications, including but not limited to U.S. Food and Drug Administrations Current Good Manufacturing Practices, and any specifications listed under the terms of this agreement at Exhibit B; or 4) termination or expiration of this Agreement. If a disagreement arises as to the existence of a consistent failure to meet regulatory and product specifications, related U.S. Food and Drug Administration action (including but not limited to issuance of Warning Letters or Form 483s) will serve as prima facie evidence thereof. In the absence of U.S. Food and Drug Administration action, the parties will submit to a mutually acceptable third party arbitrator, whose decision will be final in accordance with Paragraph 26 of this agreement. The costs of the arbitration will be borne by the party against whom the arbitrator decides.

To the extent that LAYTON BIOSCIENCE or any acquiring entity of LAYTON BIOSCIENCE sublicenses any POLI or INTERCHEM inventions, know-how, or Patents under this provision, the licensees of such sublicenses are limited to entities manufacturing pharmaceutical products on behalf of LAYTON BIOSCIENCE, and any such sublicenses must state that the use of the POLI or INTERCHEM inventions, know-how, or Patents are limited to manufacturing pharmaceutical products for the direct benefit of LAYTON BIOSCIENCE or any acquiring entity of LAYTON BIOSCIENCE.

b. Drug Master Files

POLI and/or INTERCHEM will file in a timely manner with the United States FDA, Type II Drug Master Files (DMF) regarding PRODUCT and ISOMERS, filed on behalf of POLI and/or INTERCHEM, relating to POLI and INTERCHEM's Type II DMFs regarding the processes and materials used to manufacture and supply PRODUCT and ISOMERS.

c. Continuing Access to POLI and INTERCHEM Know-How and Technology Improvements

Upon the natural expiration of this Agreement, or if this Agreement is terminated for cause by LAYTON BIOSCIENCE as a result of the actions of POLI or INTERCHEM, as provided for in Paragraphs 25 and 14 of this Agreement, POLI and INTERCHEM agree to provide technical advice and continuing access to the POLI and INTERCHEM intellectual property and know-how related to the manufacture and supply of PRODUCT and ISOMERS, including but not limited to providing full access to and a copy of the contents of any DMFs filed by POLI or INTERCHEM with the United States FDA concerning PRODUCT or ISOMERS, and any related improvements to the manufacturing materials, equipment, procedures, or LAYTON BIOSCIENCE patents or other technology.

Upon a material breach by LAYTON BIOSCIENCE of this Agreement commensurate with POLI and INTERCHEM's termination of the same, or a LAYTON BIOSCIENCE termination of this Agreement without cause (as described in Paragraph 25 of this Agreement) before the end of the initial term of this Agreement: (1) POLI and INTERCHEM agree to provide technical advice and continuing access to the POLI and INTERCHEM intellectual property and know-how related to the manufacture and supply of PRODUCT and ISOMERS, including but not limited to providing full access to and a copy of the contents of any DMFs filed by

POLI or INTERCHEM with the United States FDA concerning PRODUCT or ISOMERS, and any related improvements to the manufacturing materials, equipment, procedures, or LAYTON BIOSCIENCE patents or other technology, and (2) LAYTON BIOSCIENCE agrees to negotiate in good faith a reasonable fee or royalty rate, relative to the anticipated compensation to be paid to POLI and INTERCHEM under this Agreement and the manufacturing start-up costs of the same, to compensate POLI and INTERCHEM for their start-up expenditures in furtherance of this Agreement and the opportunity costs of performing hereunder, prior to such termination or expiration of this Agreement.

9. CONFIDENTIALITY

LAYTON BIOSCIENCE, POLI, and INTERCHEM shall maintain in confidence and not use or disclose to any third-party, except as is specifically contemplated herein or as is otherwise necessary to perform their respective obligations under this Agreement, and then only on a confidential basis, any information, including, without limitation, business and technical information, experience or data regarding any facility, programs, laboratories, processes, products, costs, equipment operation, or customers, relating to the manufacture, supply, and sale of PRODUCT hereunder.

LAYTON BIOSCIENCE, POLI, and INTERCHEM shall maintain in confidence and not use or disclose to any third-party, any information, including, without limitation, business and technical information, experience or data regarding any facility, programs, laboratories, processes, products, costs, equipment operation, or customers, relating to the manufacture, supply, and sale of ISOMERS hereunder.

Nothing herein shall prevent any PARTY to this Agreement from disclosing any information required by statute or governmental regulations to be disclosed in a judicial or administrative proceeding after all reasonable legal remedies for maintaining such information in confidence have been practically exhausted.

Each PARTY agrees to retain in confidence proprietary information of the other disclosed pursuant to this Agreement Disclosed information shall not be deemed confidential hereunder unless it is so identified and in written or graphic form, or reduced to written or graphic form within ten (10) days after disclosure; it is not now or later publicly known except through fault of the receiving PARTY; and it is not known to the receiving PARTY at the time of disclosure other than through a confidential communication from the disclosing PARTY. Confidentiality of disclosed proprietary information and the obligation of confidentiality hereunder shall survive termination of this Agreement for ten (10) years.

10. REGULATORY COMPLIANCE

POLI and INTERCHEM will comply in all material respects with all United States federal, state and local laws, regulations and standards applicable to production and supply by POLI and INTERCHEM and their performance of their obligations hereunder, including, but not limited to, obtaining and maintaining any and all required permits, licenses, and certifications required by the United States FDA and Drug Enforcement Administration, and will file, maintain, and keep current United States FDA Drug Master Files concerning the PRODUCT and ISOMERS.

POLI and INTERCHEM agree to promptly notify LAYTON BIOSCIENCE of any written or oral inquiries, notifications, or inspection activities by any regulatory authority, including but not limited to the United States or Italy, in regard to the PRODUCT or ISOMERS. POLI and INTERCHEM will promptly furnish LAYTON BIOSCIENCE with all FDA inspection reports and related correspondence directly related to and affecting their performance hereunder as and when such reports and correspondence become available to POLI or INTERCHEM. POLI and INTERCHEM will discuss with LAYTON BIOSCIENCE any regulatory authority comments directly related to and affecting POLI or INTERCHEM's performance hereunder and will give LAYTON BIOSCIENCE a reasonable opportunity to comment on POLI or INTERCHEM's proposed response to such comments. POLI and INTERCHEM agree to rectify promptly or resolve any deficiencies noted by a regulatory authority in a report or correspondence issued to the same, and which are based on POLI or INTERCHEM's performance under this Agreement. In addition, POLI and INTERCHEM shall promptly notify LAYTON BIOSCIENCE in the event of any communication from a regulatory authority, written or oral, which does not specifically relate to the PRODUCT or ISOMERS but which could reasonably be expected to result in a disruption of POLI or INTERCHEM's ability to supply PRODUCT or ISOMERS under this Agreement.

POLI and INTERCHEM will notify LAYTON BIOSCIENCE immediately of any warning (including any FDA Form 483), Warning Letter, citation, indictment, claim, lawsuit or proceeding issued or instituted against POLI or INTERCHEM or any of its affiliates or of any revocation of any license or permit issued to POLI or INTERCHEM or any of its affiliates, to the extent that any such occurrence relates directly to POLI or INTERCHEM's performance hereunder.

11. WARRANTIES

a. INTERCHEM and POLI represent and warrant that:

(l) they have full right and power to enter into this Agreement and perform in accordance with its terms;

(2) The PRODUCT will conform to the specifications in Exhibit B, FDA cGMPs, and with any and all other requirements and specifications the PARTIES mutually agree upon concerning ISOMERS;

(3) the PRODUCT and ISOMERS shall be in good and merchantable condition and fit for the purpose intended;

(4) the PRODUCT and ISOMERS shall be manufactured and delivered in compliance with all applicable United States state and federal laws and regulations and guidelines specifically without limitation, the provisions of the United States Federal Food, Drug, and Cosmetic Act (FFDCA), including cGMPs;

(5) they have good title to applicable patents as specified in-Paragraph 3 of this Agreement;

(6) there is no claim, suit, proceeding, or investigation pending or, to the knowledge of POLI or INTERCHEM, threatened against POLI or INTERCHEM or any of their collective affiliates which might prevent or interfere with POLI or INTERCHEM's performance under this Agreement;

(7) the PRODUCT and ISOMERS sold and supplied hereunder will not be: (i) adulterated or misbranded within the meaning of the United States FFDCA, as amended, or within the meaning of any applicable state or municipal law in which the definitions of adulteration and misbranding are substantially identical with those contained in the FFDCA, (ii) manufactured or sold in violation of the United States Federal Controlled Substances Act, as amended, or any applicable state law, (iii) manufactured or sold in violation of any of the provisions of the United States Fair Labor Standards Act of 1938, as amended, (iv) manufactured or sold in violation of the Occupational Safety and Health Act of 1970, as amended, (v) manufactured in violation of any applicable federal, state, or local environmental law or regulation, in either the United States or Italy, or (vi) manufactured in violation of any agreement, judgement, order, or decree to which POLI or INTERCHEM are a PARTY;

(8) they will file in a timely manner with the United States FDA, Type II Drug Master File (DMF) regarding PRODUCT and ISOMERS, maintain and keep current this DMF, and not interfere in any way with LAYTON BIOSCIENCE's references to this DMF pursuant to LAYTON BIOSCIENCE investigational new drug applications, new drug applications (NDAs), supplemental NDAs, or other applications and requests submitted to the United States FDA;

(9) neither POLI, INTERCHEM, nor their collective affiliates, nor any member of their respective staffs, have been disqualified or debarred by the FDA for any purpose;

(10) neither POLI, INTERCHEM, nor their collective affiliates, nor any member of their respective staffs have been charged with or convicted under United States federal law for conduct relating to the development or approval, or otherwise relating to the regulation of any drug product under the Generic Drug Enforcement Act of 1992 or any other relevant statute, law or regulation; and

(11) the execution and delivery of this Agreement has been duly authorized, and upon execution and delivery shall be a valid and binding obligation of POLI and INTERCHEM.

b. LAYTON BIOSCIENCE represents and warrants that it has the full right and power to enter into this Agreement and perform in accordance with its terms, and that the execution and delivery of this Agreement has been duly authorized, and upon execution and delivery shall be a valid and binding obligation of LAYTON BIOSCIENCE.

12. FACILITY ACCESS

LAYTON BIOSCIENCE, through its employees, consultants, or other representatives, will have the right during normal business hours and upon advance arrangement with POLI or INTERCHEM to inspect POLI and INTERCHEM's manufacturing operations to determine whether or not POLI and INTERCHEM are complying in all respects with their obligations hereunder. LAYTON BIOSCIENCE warrants that all such inspections and audits shall be carried out in a manner calculated not to unreasonably interfere with POLI or INTERCHEM's conduct of business and to insure the continued confidentiality of POLI and INTERCHEM's business and technical information. Further, LAYTON BIOSCIENCE agrees to comply with all of POLI and INTERCHEM's safety and security measures during any visits to the POLI or INTERCHEM facilities.

13. INDEMNIFICATION

POLI and INTERCHEM, on behalf of themselves and their respective affiliates, hereby agree to indemnify, defend, and hold harmless LAYTON BIOSCIENCE and its affiliates from and against any and all demands, claims, actions, causes of action, assessments, losses, damages, injuries, liabilities, costs and expenses, including without limitation, interest, penalties and reasonable attorneys fees and expenses (collectively Damages) asserted against, resulting to, imposed upon or incurred by LAYTON BIOSCIENCE, its employees or its affiliates, directly or indirectly related to, arising out of, or resulting from:

(i) any breach or failure of any of the representations, warranties, and covenants of POLI and INTERCHEM contained herein, including (without limitation) any breach or failure by POLI or INTERCHEM to perform any obligations contained hereunder;

(ii) the negligence or willful misconduct of POLI or INTERCHEM or their respective officers, employees, or agents;

(iii) any defect in the manufacture of the PRODUCT or ISOMERS, to the extent not caused by fault attributable to LAYTON BIOSCIENCE or its agents or third-party contractors; or

(iv) any failure of POLI or INTERCHEM to observe or comply in all material respects with any laws, rules, or regulations directly related to POLI or INTERCHEM's performance hereunder.

LAYTON BIOSCIENCE, on behalf of itself and its affiliates, hereby agrees to indemnify, defend, and hold harmless POLI and INTERCHEM and their collective affiliates from and against any and all Damages asserted against, resulting to, imposed upon or incurred by POLI or INTERCHEM or their collective employees or affiliates, directly or indirectly related to, arising out of, or resulting from:

(i) any breach or failure of any of the representations, warranties, and covenants of LAYTON BIOSCIENCE contained herein;

(ii) any failure of LAYTON BIOSCIENCE to observe or comply in all material respects with any laws, rules, or regulations directly related to LAYTON BIOSCIENCE's performance hereunder, including the failure to adequately inspect for deviations from the specifications set forth at Exhibit B of this Agreement, or agreed-upon specifications related to the ISOMERS; or

(iii) LAYTON BIOSCIENCE's, its agents, distributors, or customers use, processing, transportation, possession, disposal, or sale of any finished dosage product manufactured by LAYTON BIOSCIENCE, whether containing PRODUCT or ISOMERS or not, and whether used alone or in combination with any other material; *provided, however,* the foregoing shall not apply in circumstances which give rise to POLI or INTERCHEM's obligation to indemnify, defend, and hold harmless LAYTON BIOSCIENCE, its employees and affiliates pursuant to this Paragraph.

Each indemnitee hereunder shall notify the indemnitor in writing within ten (10) working days after receipt of written notice that the indemnitee has been sued or that suit is reasonably imminent, but no indemnitee shall lose indemnification rights hereunder by failing to give the indemnitor such a notice unless such failure materially and adversely affects the indemnitor's ability to defend.

The indemnitor shall have the sole right to select defense counsel and to direct the defense or settlement of any such claim or suit, as long as it bears the costs thereof. In the event that representation of both the indemnitor and the indemnitee by the same counsel would be a conflict of interest for such counsel, an indemnitee may select its own independent counsel without relieving the indemnitor of its obligations under this section. Under no circumstances, however, shall any indemnitee settle or otherwise compromise any suit or claim without either bearing the cost thereof or obtaining the indemnitor's prior written consent.

14. BANKRUPTCY

If any proceedings in bankruptcy or in reorganization, or for the appointment of a receiver or trustee for all or a substantial portion for the assets of any PARTY to this Agreement, or any other like proceedings, under any law for the relief of debtors shall be instituted by or against any PARTY hereto and are not dismissed within ninety (90) days, this Agreement shall immediately terminate. The PARTIES shall give each other immediate written notice of the institution of such proceedings as hereinafter set forth in Paragraph 16 of this Agreement.

15. ASSIGNMENT

Except in connection with the sale or transfer of all or substantially all of any PARTY's assets, by merger or otherwise, no PARTY shall assign this Agreement without the express written approval of the other PARTIES, which approval shall not be unreasonably withheld.

16. NOTICES

Any notice or request required or permitted to be given under or in connection with this Agreement shall be deemed to have been sufficiently given if in writing and sent by certified mail, return receipt requested; or prepaid telegram, to such PARTY, at the address set forth for such PARTY below. If a PARTY changes its address, written notice shall be shall be given promptly to the other PARTIES of the new address. Notice shall be deemed given on the day it is sent (in the case of delivery by method other than hand delivery) or the date of delivery (in the case of delivery by hand) in accordance with the provisions of this Paragraph. The addresses for the notices are as follows:

If to LAYTON BIOSCIENCE, INC.:	LAYTON BIOSCIENCE, INC. 709 East Evelyn Road Sunnyvale, California 94086 Attention: Gary L. Snable, President & CEO
If to INTERCHEM:	INTERCHEM CORPORATION 120 Route 17 North Paramus, New Jersey 07652 Attention: Ronald J. Mannino, Chairman
If to POLI INDUSTRIAL CHIMICA:	POLI INDUSTRIA CHIMICA Via Volturno 48-20089 Quinto DeStampi Rozzano, Milano Italy Attention: Dr. Alberto Mangia – Managing Director
With a copy to:	Stephen A. Janetta Morgan, Lewis & Bockius LLP 1701 Market Street Philadelphia, Pennsylvania 19103-2921

17. WAIVER

The failure by any PARTY to exercise its rights hereunder or to enforce any of the terms or conditions of this Agreement on any occasion shall not constitute or be deemed a waiver of that PARTY's rights thereafter to exercise any rights hereunder or to enforce each and every term and condition of this Agreement.

18. MODIFICATIONS

This Agreement may not be amended or modified except by a writing specifically referring to this Agreement and executed by duly authorized representative of all PARTIES. The obligations of the PARTIES are governed by the terms and conditions of this Agreement and none of the general terms and conditions of any LAYTON BIOSCIENCE purchase order or any POLI or INTERCHEM acknowledgment of any substantially similar documents of either PARTY will in any case be controlling or supersede the provisions hereof.

19. OTHER DOCUMENTS

Unless specifically agreed to the contrary by the PARTIES in writing, if there is any inconsistency between the provisions of the Agreement and any purchase order or other documents passing between the PARTIES, the provisions of this Agreement shall control.

20. GOVERNING LAW

This Agreement shall be governed and interpreted in accordance with the laws of the State of New Jersey.

21. SEVERABILITY

If and to the extent that any court of competent jurisdiction holds a provision or part of this Agreement to be invalid or unenforceable, such holding shall, to the extent possible, in no way affect the validity of the remainder of this Agreement.

In the event that any part of any of the covenants, sections, or provisions herein may determined by a court of law or equity to be overly broad or against applicable precedent or public policy, thereby making such covenants, sections or provisions invalid or unenforceable, the PARTIES shall attempt to reach agreement with respect to a valid and enforceable substitute for the deleted provisions, which shall be as close in its intent and effect as possible to the deleted provisions.

22. HEADINGS

Headings in this Agreement are included for ease of reference only and shall have no legal effect.

23. ENTIRE AGREEMENT

This Agreement sets' forth the entire Agreement and understanding between the PARTIES as to the subject matter hereof and merges all prior discussions and negotiations between them, and none of the PARTIES shall be bound by any conditions, definitions, warranties, understandings or representations with respect to such subject matter other than as expressly provided herein or as duly set forth on or subsequent to the date hereof in writing and signed by a proper and duly authorized officer or representative of the PARTY to be bound hereby.

24. PARTIES RELATIONSIDP

No PARTY shall hold itself out to third-parties as possessing any power or authority to enter into any contract or make any commitment on behalf of the other PARTY. It is not intended that this Agreement create any agency, partnership or joint employer relationship, and that POLI and INTERCHEM shall be deemed to be independent contractors of LAYTON BIOSCIENCE.

25. TERMINATION

Pursuant to Paragraph 2.e. of this Agreement, this Agreement shall remain in full force and effect for said term unless this Agreement is terminated. This Agreement may be terminated for a material breach which is not remedied within sixty (60) days of written notice of the breach. Written notice of the alleged material breach is a condition precedent to acting under the material breach provisions of this section. Pursuant to Paragraph 26 of this Agreement, the P ARTY accused of the material breach may request arbitration if the same issues a written notice to the other PARTIES to this Agreement. The arbitration may determine whether a breach has occurred or if the breach is material. The decision of the arbitrators shall be final. This Agreement may also be terminated pursuant to the bankruptcy provisions in Paragraph 14 of this Agreement, or any other provisions of this Agreement which explicitly provide for termination.

The representations and warranties of the PARTIES hereunder, covenants which by their terms have effect after the termination or expiration hereof, and the PARTIES' indemnification, confidentiality, intellectual property, and technology transfer obligations shall survive termination or expiration of this Agreement. Upon termination, the PARTIES, at the request of another PARTY, shall return promptly to an owner all technical and promotional material in its possession related to this Agreement and the manufacture and supply of PRODUCT or ISOMERS; all copies of such material shall remain confidential pursuant to Paragraph 9 of this Agreement.

In the event of any termination of this Agreement, for whatever reason, POLI and INTERCHEM shall, notwithstanding the effective date of any termination, complete any orders for PRODUCT or ISOMERS that were made by LAYTON BIOSCIENCE prior to such date, and LAYTON BIOSCIENCE shall pay POLI and INTERCHEM for any PRODUCT or ISOMERS produced in accordance with such orders at the then applicable PRODUCT or ISOMERS prices in effect on the effective date of the termination hereunder.

26. ARBITRATION

It is anticipated that during the existence of this contract issues may arise upon which the PARTIES may not agree. In the event of a disagreement, which cannot be resolved by negotiation, any PARTY may request arbitration. Arbitration shall be the exclusive means of resolving disputes under this Agreement' which cannot be resolved by mutual negotiation. The decision of the arbitrators shall be final and may not be appealed. Any arbitration hearing will be conducted in Philadelphia, Pennsylvania or New York, New York,

a. Number of Arbitrators

In the event of a dispute in which two (2) of the PARTIES have reached an agreement, there shall be three (3) arbitrators; one (1) selected by the two (2) PARTIES in agreement and one (1) by the other PARTY. These two arbitrators shall select a third arbitrator. If the arbitrators cannot agree on the third arbitrator, one shall be selected by the American Arbitration Association (AAA). In the event none of the PARTIES agree, there shall be five (5) arbitrators, one (1) selected by each PARTY and two (2) selected by the arbitrators. In the event the arbitrators cannot agree on the other two arbitrators, the AAA shall select the same.

b. Arbitration Rules

The arbitration shall be conducted by the AAA under its rules in effect at the time the arbitration is requested. The loser of the arbitration shall pay the cost of the arbitration but not the legal costs incurred by the other PARTIES. The arbitrators may apportion the costs as they may deem fair and equitable.

IN WITNESS THEREOF, the PARTIES hereto have executed this Agreement as of the date set forth above.

INTERCHEM CORPORATION

BY: /s/ Ronald J. Mannino
Ronald J. Mannino,
Chairman

DATE: July 18, 2001

POLI INDUSTRIA CHIMICA

BY: /s/ Alberto Mangia
Dr. Alberto Mangia,
Managing Director

DATE: July 20th, 2001

LAYTON BIOSCIENCE, INC.

BY: /s/ Robert Alonso
Robert Alonso
Vice President

DATE: July 11, 2001

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the following Registration Statements:

- Registration Statement (Form S-8 No. 333-133882) pertaining to the Targacept, Inc. 2000 Equity Incentive Plan
- Registration Statement (Form S-8 No. 333-133881) pertaining to the Targacept, Inc. 2006 Stock Incentive Plan
- Registration Statement (Form S-3 No. 333-143259) of Targacept, Inc.

of our reports dated March 12, 2009, with respect to the financial statements of Targacept, Inc. and the effectiveness of internal control over financial reporting of Targacept, Inc., included in this Annual Report (Form 10-K) for the year ended December 31, 2008.

/s/ Ernst & Young LLP

Greensboro, North Carolina
March 12, 2009

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 13, 2009

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 13, 2009

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, 2008 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 13, 2009

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, 2008 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 13, 2009

By: /S/ ALAN A. MUSSO
Alan A. Musso
Vice President, Chief Financial Officer and Treasurer