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UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 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, 2011

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** **(Address of principal executive offices)**	**27101** **(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 Select 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 whether the registrant has submitted electronically and posted on its corporate Website, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). ☒ Yes ☐ No

Indicate by check mark if disclosure of delinquent filers pursuant to Rule 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of 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.

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, 2011, was approximately $606,111,272, based on the price at which the registrant's common stock was last sold on June 30, 2011 ($21.07).

As of February 29, 2012, the registrant had 33,396,259 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 2012 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, 2011, 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 statement contained in this annual report, other than statements of historical fact, regarding, among other things:

- the progress, scope or duration of the development of TC-5214, TC-5619, TC-6987, AZD3480 (TC-1734), AZD1446 (TC-6683), TC-6499 or any of our other product candidates or programs, such as the target indication(s) for development, the size, design, population, location, conduct, objective, duration or endpoints of any clinical trial, or the timing for initiation or completion of or availability of results from any clinical trial, for submission or approval of any regulatory filing (including a new drug application with the U.S. Food and Drug Administration, or FDA, for TC-5214), for interactions with regulatory authorities, or, where applicable, for a decision by AstraZeneca as to whether to conduct particular development;
- the benefits that may be derived from any of our product candidates or the commercial opportunity in any target indication;
- any payments that AstraZeneca may make to us;
- our operations, financial position, revenues, costs or expenses; or
- our strategies, prospects, plans, expectations or objectives

is a forward-looking statement 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 any forward-looking statement as a result of various important factors, including our critical accounting policies and risks and uncertainties relating, among other things, to:

- our dependence on the success of our collaborations with AstraZeneca;
- whether the favorable results of our Phase 2b trial of TC-5214 as an adjunct treatment for major depressive disorder will be replicated in the remaining Phase 3 clinical trials of TC-5214;
- whether we and AstraZeneca will receive the regulatory approvals required to market and sell TC-5214;
- whether TC-5214 will be eligible for treatment in the United States as a new chemical entity with a five-year statutory exclusivity period, either because we and AstraZeneca submit a new drug application for TC-5214 prior to October 1, 2012 or because the applicable statutory provision is re-authorized by the U.S. Congress;
- whether favorable findings from completed clinical trials of TC-5619 will be replicated in ongoing and any future clinical trials and whether the designs and endpoints of any such future clinical trials will be deemed by applicable regulatory authorities to be acceptable to support regulatory approval of TC-5619;
- the control or significant influence that AstraZeneca has over the development of TC-5214, AZD3480 and AZD1446, including as to the timing, scope and design of any future clinical trials and as to the conduct at all of further development of AZD1446 or of AZD3480 beyond our ongoing trial in mild to moderate Alzheimer’s disease;
- the impact of the restructuring announced by AstraZeneca in February 2012 on its plans to progress the development of AZD1446 or on any future development of TC-5214 or AZD3480;

- the conduct and results of clinical trials and non-clinical studies and assessments of TC-5214, TC-5619, TC-6987, AZD3480, AZD1446, TC-6499 or any of our other product candidates, including the performance of third parties engaged to execute them, delays resulting from any changes to the applicable protocols or difficulties and delays in subject enrollment and data analysis;
- our ability to establish additional strategic alliances, collaborations or licensing or other comparable arrangements on favorable terms;
- our ability to protect our intellectual property; 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 to which our business is subject, the results or events indicated by any forward-looking statement 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 later 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 novel NNR Therapeutics™ for the treatment of diseases and disorders of the nervous system. Our NNR Therapeutics selectively target neuronal nicotinic receptors, which we refer to as 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 nervous system activity by selectively affecting specific NNR subtypes.

We have multiple clinical-stage product candidates and preclinical programs in areas in which we believe there are significant medical need and commercial potential, as well as proprietary drug discovery technologies. We have entered into two significant collaborations with the global pharmaceutical company AstraZeneca to provide expertise and resources to assist in the global development and potential commercialization of many of our product candidates. One is a collaboration and license agreement focused on TC-5214 as a treatment for major depressive disorder, and we refer to that agreement in this annual report as our “TC-5214 agreement with AstraZeneca.” The other is a collaborative research and license agreement focused in cognitive disorders, and we refer to that agreement in this annual report as our “cognitive disorders agreement with AstraZeneca.” Our most advanced product candidates are described briefly below.

TC-5214

TC-5214 is a nicotinic channel modulator that we are co-developing under our TC-5214 agreement with AstraZeneca as an adjunct, or add-on, therapy for patients with major depressive disorder who do not respond adequately to initial antidepressant treatment. In the fourth quarter of 2011, we and AstraZeneca reported that neither of the first two Phase 3 clinical trials of TC-5214 met its primary endpoint. Two additional Phase 3 clinical trials designed to evaluate the efficacy and tolerability of TC-5214 as an adjunct therapy, a long-term study designed primarily to evaluate the safety of TC-5214 and a Phase 2b clinical trial of TC-5214 as a “switch” monotherapy are ongoing.

TC-5619

TC-5619 is a novel small molecule that modulates the activity of the a7 NNR. We are currently conducting two separate Phase 2 clinical trials of TC-5619—a Phase 2b study in negative symptoms and cognitive dysfunction in schizophrenia and a Phase 2 study in inattentive-predominant attention deficit/hyperactivity disorder, or ADHDi. We are also currently evaluating potential additional Phase 2 clinical development of TC-5619 in Alzheimer’s disease.

AZD3480 (TC-1734)

AZD3480 (TC-1734) is a novel small molecule that modulates the activity of the a4ß2 NNR and is subject to our cognitive disorders agreement with AstraZeneca. We or AstraZeneca have conducted several clinical studies of AZD3480 in various cognitive disorders, and we are currently conducting a Phase 2b clinical trial of the product candidate as a treatment for mild to moderate Alzheimer’s disease.

AZD1446 (TC-6683)

AZD1446 (TC-6683) is a novel small molecule that modulates the activity of the a4ß2 NNR. We discovered and advanced AZD1446 as part of a now completed preclinical research collaboration conducted under our cognitive disorders agreement with AstraZeneca. AstraZeneca has completed various early-stage clinical studies of AZD1446, and, in January 2012, we announced that we had been informed that AstraZeneca plans to progress the development of AZD1446 as a treatment for Alzheimer's disease.

TC-6987

TC-6987 is a novel small molecule that modulates the activity of the a7 NNR. We are currently conducting two separate Phase 2 clinical trials of TC-6987 that are designed to guide the selection of indications for which TC-6987 is best suited for later-stage development. One of the ongoing studies is in asthma and the other is in Type 2 diabetes.

TC-6499

TC-6499 is a novel small molecule that modulates the activity of the a4ß2 and a3ß4 NNRs. The a3ß4 NNR is located in the gastrointestinal tract, and we believe TC-6499 may have potential as a treatment for one or more gastrointestinal disorders. In an exploratory four-week study of TC-6499 that we completed at a single site in 2011 in 24 subjects with constipation-predominant irritable bowel syndrome, TC-6499 outperformed placebo on an objective secondary efficacy outcome measure, the number of spontaneous bowel movements per week, but not on the primary efficacy outcome measure (a subjective subject rating of global symptom relief).

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 25 years. We refer to these technologies collectively as Pentad.

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.

Pfizer's smoking cessation product Chantix, which acts on several NNR subtypes as well as other molecular targets in the body and is known outside of the United States as Champix, is currently the only product marketed in the United States that is believed to act predominantly by affecting NNRs. Beyond Chantix, many published studies have described beneficial effects of nicotine in humans and animals and the higher prevalence of diseases such as Alzheimer's disease and Parkinson's disease in non-smokers as compared to smokers, suggesting 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 mission is to provide superior treatment options for complex diseases and disorders to improve the lives of patients by developing innovative new medicines that exploit the unique role of NNRs. To achieve our mission, our goal is to leverage our experience and expertise in the biology of NNRs and the discovery and development of novel drugs that selectively target them to become a leader in the commercialization of NNR Therapeutics for diseases and disorders where there is significant medical need and commercial potential. To achieve this goal, we are pursuing the following strategies:

- *Continue to pursue NNR Therapeutics.* 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 progress compounds that selectively target specific NNR subtypes as potential treatments for diseases and disorders of the nervous system.
- *Collaborate selectively.* We have two collaborations with AstraZeneca, one focused on TC-5214 as a treatment for major depressive disorder and one focused in cognitive disorders. 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 a potential collaborator has unique 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 the future, other markets. Under our agreements with AstraZeneca, we have the option to co-promote TC-5214 and AZD3480, as well as AZD1446 and any other licensed compounds that arose out of the preclinical research collaboration that we conducted with AstraZeneca, to specified classes of physicians in the United States.
- *Seek a collaboration partner to provide funding to support research.* For several years prior to 2011, we received funding from AstraZeneca and GlaxoSmithKline that supported various of our research programs designed to identify new product candidates or to progress existing preclinical product candidates towards the clinic. The term of our preclinical research collaboration under our cognitive

disorders agreement with AstraZeneca expired in January 2010, and a product development and commercialization agreement that we had with GlaxoSmithKline terminated in May 2011. We are actively seeking a collaborator to fund or substantially support one or more of our research programs. If we do not enter into such a collaboration, we may scale back or eliminate some research activities.

- *Maintain leadership position in NNR space.* We have established ourselves as a leader in NNR research over more than 25 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.
- *Prioritize target indications.* 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 to use our capital efficiently and to apply our product pipeline to indications where we believe there is a significant medical need and commercial potential.

Our Product Development Pipeline

The following table summarizes our most advanced clinical-stage product candidates.

Product Candidate	Planned Target Indication(s)	Status of Development	Commercial Rights
TC-5214	Major depressive disorder (adjunct therapy, “switch” monotherapy)	Two Phase 3 clinical trials as an adjunct therapy completed and three others ongoing; Phase 2b clinical trial as a “switch” monotherapy ongoing	AstraZeneca
TC-5619	Negative symptoms and cognitive dysfunction in schizophrenia, ADHDi and Alzheimer’s disease	Phase 2b clinical trial in negative symptoms and cognitive dysfunction in schizophrenia and separate Phase 2 clinical trial in ADHDi in adults ongoing; potential additional Phase 2 clinical development in Alzheimer’s disease under consideration	Targacept
AZD3480 (TC-1734)	Mild to moderate Alzheimer’s disease	Phase 2b clinical trial ongoing	AstraZeneca
AZD1446 (TC-6683)	Mild to moderate Alzheimer’s disease	AstraZeneca expected to conduct Phase 2 clinical trial	AstraZeneca
TC-6987	One or more disorders characterized by inflammation	Separate Phase 2 clinical trials in asthma and Type 2 diabetes ongoing	Targacept

Information regarding our research and development expenses for the fiscal years ended December 31, 2011, 2010 and 2009 is included under the caption “Management’s Discussion and Analysis of Financial Condition and Results of Operations” in this annual report. All of our long-lived assets are located in the United States.

TC-5214

TC-5214 is a nicotinic channel modulator that is in development as a treatment for major depressive disorder. TC-5214 is one of the two enantiomers of the racemate 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.

Clinical Program in Major Depressive Disorder

We are co-developing TC-5214 under our TC-5214 agreement with AstraZeneca. The clinical program for TC-5214 includes development both as an adjunct, or add-on, therapy and as a "switch" monotherapy, in each case in adults with major depressive disorder who do not respond adequately to initial therapy with a medication from one of two drug classes—selective serotonin reuptake inhibitors, or SSRIs, and serotonin/norepinephrine reuptake inhibitors, or SNRIs. We and AstraZeneca refer to the Phase 3 program as the RENAISSANCE Program. The RENAISSANCE Program includes four multi-center, double blind, parallel group clinical trials to evaluate the efficacy and tolerability of TC-5214 as an adjunct to continued SSRI or SNRI treatment, two with a fixed dose design and two with a flexible dose design. In the fixed dose trials, each subject who receives TC-5214 receives a set dosing regimen throughout the dosing period. In the flexible dose trials, each subject who received TC-5214 initially received a particular dosage, which could be increased at various times during the trial by the applicable investigator based on how the subject tolerated and responded to the then-current dosage. The term "double blind" means that neither the subjects nor the investigators know which subjects receive the investigational drug and which subjects receive placebo. The RENAISSANCE Program also includes a double blind, placebo controlled, long-term study designed primarily to evaluate safety. The trial design for the long-term study provides for subjects to receive TC-5214 or placebo for one year.

Both of the flexible dose trials in the RENAISSANCE Program were completed in 2011, and neither met its primary endpoint—change from double blind baseline on the Montgomery-Asberg Depression Rating Scale, or MADRS, total score after eight weeks of adjunct treatment with TC-5214 as compared to adjunct placebo. MADRS is a scale on which the clinician evaluates the subject's depressed mood and other symptoms of depression and anxiety. We expect the two fixed dose trials, as well as the long-term study, to complete in the first half of 2012. Following completion of these ongoing trials, we and AstraZeneca plan to present more detailed results from the RENAISSANCE Program studies at a future scientific meeting.

We and AstraZeneca are also conducting a Phase 2b clinical trial of TC-5214 as a "switch" monotherapy in subjects who do not respond adequately to initial therapy with an SSRI or SNRI, and we expect the study to complete in the second half of 2012. The primary outcome measure in the two fixed dose adjunct therapy trials, as well as in the "switch" monotherapy trial, is the same as the primary outcome measure in the flexible dose trials. As used in this annual report, the terms "endpoint" and "outcome measure" have the same meaning.

In addition to the RENAISSANCE Program, we and AstraZeneca are conducting multiple Phase 1 clinical trials of TC-5214, including a QTc study, which is designed to confirm that various doses of TC-5214 do not disturb the electrical activity of the heart, an abuse liability study, which is designed to assess whether TC-5214 induces craving and its excessive use in humans, and a drug-drug interaction study designed to assess the safety of TC-5214 when used together with particular drugs.

AstraZeneca is responsible for 80% and we are responsible for 20% of the costs of the clinical program for TC-5214, except that AstraZeneca is responsible for 100% of development costs that are required only to obtain or maintain regulatory approval in countries outside the United States and the European Union. We have the right to terminate our obligation to fund our share of the costs of the program once we have funded a specified amount. If we fund the specified amount and terminate our obligation to fund our share of further costs of the program, any future milestones and royalties payable to us under the agreement would be reduced by the amount of our unfunded share plus interest at a specified rate, subject to a maximum reduction that may be applied to any one payment.

Completed Phase 2b Clinical Trial in Major Depressive Disorder

In 2009, we completed a Phase 2b clinical trial of TC-5214 as an adjunct, or add-on, therapy in subjects with major depressive disorder who did not respond well to initial treatment with citalopram hydrobromide. Citalopram is an SSRI used to treat major depressive disorder, and it is marketed in the United States as Celexa.

The Phase 2b clinical trial was a multi-center, double blind, parallel group, flexible dose study conducted primarily in India and also in the United States. The primary outcome measure in the trial was change from double blind baseline on the Hamilton Rating Scale for Depression-17, or HAM-D, after eight weeks of adjunct treatment with TC-5214 as compared to adjunct placebo. HAM-D is another scale on which the clinician evaluates the subject's depressed mood and other symptoms of depression and anxiety. The result in the trial on HAM-D was statistically significant in favor of TC-5214 ($p < 0.0001$) on an intent to treat basis.

TC-5619

TC-5619 is a novel small molecule that modulates the activity of the a7 NNR. We are currently conducting a Phase 2b clinical trial of TC-5619 in negative symptoms and cognitive dysfunction in schizophrenia. Examples of the negative symptoms of schizophrenia include anhedonia (inability to experience pleasure), affective flattening (lack of emotional expressiveness), avolition (lack of motivation or drive), social withdrawal and alogia (lack of unprompted comment that occurs in normal speech). Cognitive functions often impaired in schizophrenia include executive function (ability to organize cognitive processes, including the ability to plan, prioritize, stop and start activities, shift from one activity to another activity and monitor one's own behavior), attention, vigilance, memory and learning. In a survey of 46 cognitive neuroscientists and neuropharmacologists conducted in 2004 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 a target of interest in the development of treatments for cognitive dysfunction in schizophrenia.

We are also currently conducting a Phase 2 clinical trial of TC-5619 in ADHDi in adults. ADHDi is one of three subtypes of ADHD included in the Diagnostic and Statistical Manual of Mental Disorders, fourth edition, or DSM-IV, along with hyperactive-impulsive-predominant ADHD and combined-type ADHD where both inattentive symptoms and hyperactive-impulsive symptoms are present. The specific subtype diagnosed for a particular patient is based on an assessment of the respective numbers of inattention and hyperactivity/impulsivity criteria met by the patient.

In addition to our ongoing development, we are currently evaluating potential Phase 2 clinical development of TC-5619 in Alzheimer's disease.

Ongoing Phase 2b Clinical Trial in Negative Symptoms and Cognitive Dysfunction in Schizophrenia

Our ongoing Phase 2b clinical trial of TC-5619 in negative symptoms and cognitive dysfunction in schizophrenia is a double blind, placebo controlled, parallel group study. The study is planned to enroll approximately 450 subjects with stable schizophrenia who are taking a fixed dose of one of several marketed drugs from the class known as atypical antipsychotics at sites in the United States and Eastern Europe. The target for the study is to enroll 80% tobacco users and 20% non-tobacco users. The study design provides for a four-week screening period, followed by a 24-week treatment period during which subjects receive either one of two daily doses of TC-5619 (5mg or 50mg) or placebo, randomized in a ratio of 2:1:1 (placebo, low dose, high dose). The primary outcome measure in the study is change from baseline on the Scale for the Assessment of Negative Symptoms, or SANS, at the end of the treatment period with TC-5619 as compared to placebo. SANS is an investigator assessment of improvement on the negative symptoms of schizophrenia. The composite score on the CogState Schizophrenia Battery, or CSB, a computerized battery of neuropsychiatric tests that assess specific cognitive domains, and the University of California, San Diego Performance-Based Skills Assessment, brief version, are identified as key secondary outcome measures in the study.

Ongoing Phase 2 Clinical Trial in Adults with ADHDi

Our ongoing Phase 2 clinical trial of TC-5619 in ADHDi is a double blind, placebo controlled, parallel group study. The study is planned to enroll approximately 152 adult subjects with ADHDi at sites in the United States. The study design provides for a four-week screening period, followed by a four-week treatment period during which subjects receive either one of two daily doses of TC-5619 (5mg or 25mg) or placebo, randomized in a ratio of 2:1:1 (placebo, low dose, high dose). The primary outcome measure in the study is change from baseline on the inattention subscale of the Conners' Adult ADHD Rating Scale—Investigator-Rated, or CAARS-INV, after four weeks of treatment with TC-5619 as compared to placebo. CAARS-INV is a multimodal questionnaire assessment of symptoms and behaviors associated with ADHD in adults. The study is powered to demonstrate a statistically significant difference between TC-5619 and placebo on the primary outcome measure using a one-sided test and a significance level of 10% (p ☐ 0.10). Efficacy assessments will also be made after two weeks and after six weeks of treatment.

Completed Phase 2 Clinical Trial in Cognitive Dysfunction in Schizophrenia

We have completed a Phase 2 clinical trial of TC-5619 in cognitive dysfunction in schizophrenia. The trial was a double blind, placebo controlled, forced titration, multi-center study conducted in the United States and India. In the trial, 185 subjects with schizophrenia who had stable psychotic symptoms were randomly assigned to receive either TC-5619 or placebo, together with continued treatment with an atypical antipsychotic (either quetiapine, marketed as Seroquel, or risperidone, marketed as Risperdal), for 12 weeks. Approximately half of the subjects were users of tobacco products. Subjects who received TC-5619 received a 1mg daily dose for the first four weeks, a 5mg daily dose for the next four weeks and a 25mg daily dose for the last four weeks.

The primary outcome measure of the trial was change from baseline on the Groton Maze Learning task of the CSB on each of three measurement dates for TC-5619 as compared to placebo. The Groton Maze Learning task is designed to assess executive function. The trial protocol defined a positive outcome on the Groton Maze Learning task as superiority (one-sided p-value < 0.10) for the TC-5619 dose group as compared to the placebo dose group after adjusting statistically to account for multiple comparisons.

In the trial, the results on the Groton Maze Learning task met the pre-defined success criteria (adjusted p-value = 0.054), as well as at two of the trial's three measurement dates (at 4 weeks, unadjusted p-value = 0.018; and at 12 weeks, unadjusted p-value = 0.041), and were favorable for tobacco users as compared to non-tobacco users (where there was no activity) and for subjects at study sites in the United States as compared to subjects at study sites in India. Estimates of the precise prevalence of smoking amongst schizophrenia patients vary, with many studies indicating a prevalence between 70% and 85%. Each of the p-values noted above was derived after data log transformation, a commonly utilized statistical technique where the data does not follow a normal distribution.

In addition, we observed encouraging signals (one-sided p-value < 0.10 on one of the measurement dates) in the trial on several secondary efficacy outcome measures, including SANS, Clinical Global Impression—Global Improvement, an investigator assessment of overall response, Subject Global Impression—Cognition scale, a subject self-assessment of cognitive change, and two of six computer-based items of the CSB. Other secondary efficacy outcome measures of the trial, including a composite measure of the CSB and Clinical Global Impression—Severity of Illness, an investigator assessment of severity of illness based on total clinical experience, did not demonstrate a drug effect in the dataset that included all subjects and occasionally statistically favored placebo over TC-5619 (including on the verbal memory item of the CSB after four weeks).

TC-5619 exhibited a favorable tolerability profile in the trial. There were two serious adverse events reported in the trial, one in the TC-5619 dose group and one in the placebo dose group. Both were considered by the applicable investigator as not drug related.

As a result of a process that we had previously initiated under our cognitive disorders agreement with AstraZeneca and a related election previously made by AstraZeneca, AstraZeneca had the right to license TC-5619 based on the outcome of the trial. In 2011, AstraZeneca elected not to exercise its license right.

Completed Phase 2 Clinical Trial in Adults with ADHD

We have also completed a Phase 2 clinical trial of TC-5619 in adults with ADHD. The trial was a double blind, placebo controlled, forced titration, multi-center study conducted in the United States. In the trial, 135 non-tobacco-using adults with ADHD were randomly assigned to receive either TC-5619 or placebo for 12 weeks. Subjects who received TC-5619 received a 1mg daily dose for the first four weeks, a 5mg daily dose for the next four weeks and a 25mg daily dose for the last four weeks. There were 84 subjects who completed the trial. TC-5619 did not meet the primary outcome measure of the trial—change from baseline on CAARS-INV total score after four, eight and 12 weeks of treatment with TC-5619 as compared to placebo. Analysis of the full dataset showed encouraging signals (one-sided p-value < 0.10 on at least one of the measurement dates) in the subpopulation of the subjects with ADHDi on some of the trial's other efficacy measures, including CAARS-INV total score, the CAARS-INV inattention subscale and the CAARS—Subject-Rated ADHD Index. TC-5619 exhibited a favorable tolerability profile in the trial, and there were no serious adverse events reported.

AZD3480 (TC-1734)

AZD3480 (TC-1734) is a novel small molecule that modulates the activity of the a4ß2 NNR and is subject to our cognitive disorders agreement with AstraZeneca. We are currently conducting a Phase 2b clinical trial of AZD3480 as a treatment for mild to moderate Alzheimer's disease. We are responsible for funding the study, but have received $6.2 million in payments from AstraZeneca in connection with events associated with the study. Our ongoing study is the second clinical trial of AZD3480 in mild to moderate Alzheimer's disease. The first was conducted by AstraZeneca, and its outcome was inconclusive.

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

Our ongoing Phase 2b clinical trial of AZD3480 in mild to moderate Alzheimer's disease is a potential registration study that is the subject of a Special Protocol Assessment agreement with the FDA. It is a double blind study designed to evaluate AZD3480 head-to-head against donepezil, the marketed medication most often prescribed for Alzheimer's disease. The trial design provides for approximately 300 subjects diagnosed with probable Alzheimer's disease classified as mild or moderate in severity to be randomly assigned to receive donepezil or a fixed 30mg dose of AZD3480 daily over 12 months. We are conducting the study at sites predominantly in Eastern Europe and also in the United States. The study has co-primary outcome measures, change from baseline after 12 months of treatment with AZD3480 as compared to donepezil on the Alzheimer's Disease Assessment Scale-cognitive subscale, or ADAS-Cog, and on a functional measure. The functional measure at European sites is the Alzheimer's Disease Cooperative Study—Activities of Daily Living Inventory, and the functional measure at U.S. sites is the Clinician's Interview Based Impression of Change Plus Caregiver Input, each of which assesses subjects' ability to perform typical day-to-day activities. Following completion of the study, further development of AZD3480 will be in the discretion of AstraZeneca, subject to the terms of our cognitive disorders agreement with AstraZeneca.

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

In 2008, AstraZeneca completed a Phase 2b double blind, placebo controlled, dose finding, multi-center clinical trial of AZD3480 in mild to moderate Alzheimer's disease, known as the "Sirocco" trial. The Sirocco trial was conducted at sites in Western Europe, Eastern Europe and Canada. In the trial, 567 subjects 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 primary outcome measure of the trial was change from baseline on ADAS-Cog after 12 weeks of

treatment with AZD3480 as compared to placebo. 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 in that neither donepezil nor AZD3480 met the trial's criteria for statistical significance versus placebo on the primary outcome measure. However, in an analysis conducted post hoc in which the most mildly impaired subjects (MMSE = 25 or 26) were excluded, the middle dose of AZD3480 tested achieved statistical significance (one-sided p-value = 0.04) and donepezil showed a strong trend (one-sided p-value = 0.065).

Subjects dosed with AZD3480 showed an improvement on ADCS-CGIC and the MMSE, two of the trial's secondary outcome measures, 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.

Completed Clinical Trials in Other Indications

In addition to the previous trial in Alzheimer's disease, we or AstraZeneca have completed Phase 2 clinical trials of AZD3480 in various other indications characterized by cognitive impairment. These studies have generated a range of efficacy results, including: (1) achievement of the primary outcome measure(s) (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 in adults with ADHD); (2) encouraging signals (in early-stage trials in AAMI and mild cognitive impairment, or MCI); and (3) failure to achieve the primary outcome measures (in cognitive dysfunction in schizophrenia). These trials are summarized below.

AAMI (later study)	• a double blind, placebo controlled, multi-center study that we conducted in the United States • subjects were between the ages of 50 and 80 and classified with AAMI based on inclusion criteria reflecting both subjective and objective memory impairment • there were three co-primary endpoints, change from baseline on the Power of Attention and Episodic Memory factors of the CDR test battery and on the Subject Global Impression– Cognition scale at the end of 16 weeks of dosing with AZD3480 as compared to placebo • AZD3480 met all three co-primary endpoints ($p < 0.05$) at 50mg and met the Power of Attention endpoint at 25mg
Adults with ADHD	• a double blind, placebo controlled crossover design study that we and AstraZeneca conducted at a single site in the United States in which each subject served as his or her own control • two doses of AZD3480 tested • the primary outcome measure was change from baseline on the CAARS-INV total score after two weeks dosing with AZD3480 as compared to placebo, and the result was statistically significant in favor of one of the doses (50mg AZD3480, $p < 0.01$) on an intent to treat basis

AAMI (earlier study); MCI	• two double blind, placebo controlled, crossover design Phase 2 studies that we conducted, one in each indication, assessing the effects of multiple doses of AZD3480 at various time points using the CDR test battery • AZD3480 demonstrated positive effects in the AAMI study at some, but not all, dose levels and measures tested, with the results most favorable at 50mg • the results of the MCI trial were more favorable at 100mg AZD3480 and did not favor 50mg AZD3480 on any measure
Cognitive Dysfunction in Schizophrenia	• a double blind, placebo controlled, dose finding, multi-center study that AstraZeneca conducted in the United States and Canada • subjects were clinically stable schizophrenics who were active smokers and taking a marketed atypical antipsychotic • AZD3480 did not meet pre-defined success criteria on the primary endpoints, change from baseline 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 after 12 weeks of treatment with AZD3480 as compared to placebo

AZD1446 (TC-6683)

AZD1446 (TC-6683) is a novel small molecule that modulates the activity of the a4ß2 NNR. We discovered and advanced AZD1446 as part of a now completed preclinical research collaboration that we and AstraZeneca conducted under our cognitive disorders agreement. AstraZeneca is responsible for conducting and funding the development and potential future commercialization of AZD1446, and, in January 2012, we announced that we had been informed that AstraZeneca plans to progress the development of AZD1446 as a treatment for Alzheimer's disease. Based on feedback previously received from AstraZeneca, we expect the next clinical trial to be a Phase 2 study as an adjunct treatment to donepezil in patients with mild to moderate Alzheimer's disease. AstraZeneca has previously completed various early-stage clinical studies of AZD1446, including in particular:

- a trial in adults with ADHD in which AZD1446, as compared to placebo, did not improve core symptoms of ADHD, as measured by the trial's primary outcome measure (CAARS-INV), but showed signals of a drug effect in the subpopulation of non-nicotine using subjects at specific doses on two of five tasks of the CogState ADHD Battery, computerized tests used as secondary outcome measures to assess cognitive functions such as learning and memory (80mg of AZD1446 once daily, Groton Maze Learning Task ($p = 0.019$) and International Shopping List Task—Immediate Recall ($p = 0.055$); and 80mg of AZD1446 three times daily, International Shopping List Task—Immediate Recall ($p = 0.079$)—with all of such p-values statistically adjusted for multiplicity);
- a four-week trial designed primarily to evaluate the safety and tolerability of AZD1446 when administered with donepezil to subjects with Alzheimer's disease; in this study, AZD1446 exhibited a safety and tolerability profile acceptable for further development and, as expected with a short dosing period and small number of subjects, did not show an effect on surrogate measures of cognition and global function;
- a trial designed to explore the effects of a single dose of AZD1446 in healthy volunteers with drug-induced cognitive impairment; in this study, pro-cognitive signals were observed on various secondary outcome measures, but neither AZD1446 nor the positive comparator donepezil demonstrated a statistically significant effect on the primary outcome measure—an assessment of reversal of a drug-induced effect on brain waves associated with attention; and
- a trial designed to evaluate the effect of AZD1446 and donepezil on brain response in subjects with Alzheimer's disease as assessed by electroencephalography (EEG); in this study, AZD1446 showed greater activity than donepezil.

TC-6987

TC-6987 is a novel small molecule that modulates the activity of the a7 NNR. We are currently conducting two separate Phase 2 clinical trials of TC-6987 that are designed to guide the selection of indications for which the product candidate is best suited for later-stage development. One of the ongoing studies is in asthma and the other is in Type 2 diabetes. Both studies include a number of different measures designed to detect anti-inflammatory effects of TC-6987 and inform potential future development.

Ongoing Phase 2 Clinical Trial in Asthma

Our ongoing Phase 2 clinical trial in asthma is a multicenter, double blind, placebo controlled, parallel group study being conducted in the United States. There are 94 adult subjects with asthma mild to moderate in severity enrolled in the study. The study design provides for each subject to undergo a four-week wash-out period during which the subject receives a low-dose inhaled corticosteroid and ceases taking any asthma medication (other than permitted rescue medication) that he or she is currently taking before being randomly assigned to one of two cohorts. Subjects then receive either placebo or TC-6987 once daily, together with the low-dose inhaled corticosteroid, for four weeks. Subjects in the TC-6987 cohort receive a 100mg dose on the first day of dosing and then a 50mg dose for the remainder of the dosing period. The study includes several efficacy outcome measures, with change in forced expiratory volume from baseline to pre-dosing and two hours post-dosing on the last day of the dosing period for subjects receiving TC-6987 as compared to placebo designated as the primary outcome measures. The study also includes assessments of safety, tolerability and pharmacokinetics of TC-6987.

Ongoing Phase 2 Clinical Trial in Type 2 Diabetes

As in the asthma study described above, the Phase 2 clinical trial in Type 2 diabetes is a multicenter double blind, placebo controlled, parallel group trial being conducted in the United States. There are 112 adult subjects with Type 2 diabetes enrolled in the study. The study design includes a one-week screening period followed by a four-week washout period during which each subject ceases taking any medication for Type 2 diabetes that he or she is currently taking before being randomly assigned to one of two cohorts. Subjects then receive either TC-6987 or placebo once daily for four weeks. Subjects in the TC-6987 cohort receive a 20mg dose on the first day of dosing and then a 10mg dose for the remainder of the dosing period. The study includes several efficacy outcome measures, with change in fasting plasma glucose (which is a metabolic measurement used to expose problems with insulin function) from baseline to the last day of the dosing period for subjects receiving TC-6987 as compared to placebo designated as the primary outcome measure. The study also includes assessments of safety, tolerability and pharmacokinetics of TC-6987.

TC-6499

TC-6499 is a novel small molecule that modulates the activity of the a4ß2 and a3ß4 NNRs. The a3ß4 NNR is located in the gastrointestinal tract and, based on observations from previous Phase 1 development of TC-6499 in contemplation of later-stage development as a treatment for pain, we believe the product candidate may have potential as a treatment for one or more gastrointestinal disorders. In an exploratory four-week study of TC-6499 that we completed in 2011 in 24 subjects with constipation-predominant irritable bowel syndrome, TC-6499 outperformed placebo on an objective secondary efficacy outcome measure, the number of spontaneous bowel movements per week, but not on the primary efficacy outcome measure (a subjective subject rating of global symptom relief).

Medical Need and Commercial Opportunity in Our Target Indications

The indications for which our most advanced product candidates are currently in development include major depressive disorder, negative symptoms and cognitive dysfunction in schizophrenia, ADHDi, Alzheimer’s disease and inflammatory disorders (currently asthma and Type 2 diabetes).

Major depressive disorder is characterized by one or more depressive episodes without a history of manic, mixed or persistent elevated or irritable mood episodes. The essential feature of a major depressive episode is a period of at least two weeks during which there is depressed mood or the loss of interest or pleasure in nearly all activities. The disorder is disabling and can prevent a person from functioning normally. The biopharmaceutical market research firm Decision Resources estimated that approximately 42.3 million people suffered from major depressive disorder in the world's seven major pharmaceutical markets —the United States, France, Germany, Italy, Spain, the United Kingdom and Japan—in 2010. The Sequenced Treatment Alternatives to Relieve Depression, or STAR*D, study sponsored by the National Institute of Mental Health between 2001 and 2006 highlighted 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 the representative SSRI citalopram for 12 to 14 weeks. Only about one-third of the participants achieved "remission" (as defined in the study) and about 10-15 percent more responded, but did not reach remission.

Schizophrenia is a chronic, severe and disabling form of psychosis. The disease generally includes three domains, positive symptoms, negative symptoms and cognitive dysfunction. The negative symptoms and cognitive dysfunction play a primary role in the inability of many schizophrenic patients to function normally. Decision Resources estimated that there were approximately 4.6 million people with schizophrenia in the world's seven major pharmaceutical markets in 2010. Estimates as to the prevalence of schizophrenia patients who suffer from negative symptoms vary, and it has been estimated that up to 75% of persons with schizophrenia are cognitively impaired. There is currently no drug approved in the United States or Europe specifically for the treatment of negative symptoms of schizophrenia or cognitive dysfunction in schizophrenia.

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, with ADHDi characterized by predominantly inattentive symptoms. Decision Resources estimated that more than 60% of pediatric ADHD cases in the world's seven major pharmaceutical markets in 2010 were ADHDi, with an estimated total ADHD prevalence of 23.5 million adults and 23.9 million children. The most commonly used treatments for ADHD are from the drug class known as stimulants. Because stimulants have potential for abuse, they are scheduled and can therefore be burdensome for patients. All of the currently available treatments for ADHD have side effects, such as increased heart rate and blood pressure, loss of appetite, insomnia and behavioral changes like irritability.

Alzheimer's disease, the most common form of dementia, is a progressive, debilitating disorder that attacks neurons in the brain, resulting in loss of memory, thinking and language skills and behavioral changes. Decision Resources estimated that there were approximately 18 million people with Alzheimer's disease in the world's seven major pharmaceutical markets in 2010. Alzheimer's 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 increasing forgetfulness, failure to recognize friends and family, disorientation regarding time and place even in familiar locations and personality changes. Patients can exhibit the symptoms of moderate Alzheimer's disease for several 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.

Asthma is a chronic inflammatory disorder of the lungs and airways that is characterized by recurring periods of wheezing, chest tightness, shortness of breath and coughing that occurs most often at night or early in the morning. The disorder affects people of all ages, but most often starts in childhood and is one of the most common long-term diseases of childhood. Asthma attacks are triggered by various genetic and environmental factors, including family history, second-hand smoke, dust mites, air pollution and allergens. Decision Resources estimated that there were approximately 52.5 million people with asthma in the world's seven major pharmaceutical markets in 2010.

Diabetes is a chronic disease characterized by high blood sugar, either because the body does not produce enough of the blood sugar-regulating hormone insulin (Type 1 diabetes) or because the body fails to use insulin properly (Type 2 diabetes). High blood sugar, or hyperglycemia, can over time lead to serious damage to many of the body's systems, especially the nerves and blood vessels. Symptoms of diabetes include excessive excretion of urine, thirst, constant hunger, weight loss, vision changes and fatigue. Type 2 diabetes is the most common form of diabetes and is thought to result largely from excess body weight and physical inactivity. According to the World Health Organization, approximately 311 million people worldwide have Type 2 diabetes, representing about 90% of all diabetics. The World Health Organization also projects deaths related to complications from diabetes to double between 2005 and 2030.

Our Preclinical Research

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. 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. Our current research focus is on (1) nicotinic channel modulators, which we believe have potential therapeutic application for a number of indications, (2) compounds that act on the a7 NNR and (3) Parkinson's disease. We have been awarded three grants from The Michael J. Fox Foundation for Parkinson's Research—two to test the potential of compounds with novel NNR pharmacologies to address abnormal involuntary movements, or dyskinesias, that are a side effect of levodopa treatment and one to identify compounds that bind to specific NNRs and can be radiolabeled and used as imaging agents to better understand any relationship between those NNRs and Parkinson's disease. Levodopa is commonly used to treat the motor deficits of Parkinson's disease.

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 25 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 and pharmaceutical 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.

Discontinued Product

As a result of increased fees charged by the FDA and declining prescriptions, we discontinued the commercialization of Inversine, which is currently our only approved product, effective as of September 30, 2009. 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. Inversine was first approved for marketing in 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.

Strategic Alliances and Collaborations

AstraZeneca AB – TC-5214

On December 3, 2009, we entered into a collaboration and license agreement with AstraZeneca AB for the global development and commercialization of TC-5214. The agreement became effective later in December 2009. Pursuant to the agreement, we granted AstraZeneca an exclusive global license under patents and other technology owned or licensed by us to develop and commercialize TC-5214, as well as any other compounds of ours that meet specified structural and pharmacological criteria designed to reflect substantial similarity to TC-5214, for all fields of use except hypertension.

Payment Terms. In January 2010, AstraZeneca made a non-refundable upfront payment to us of $200 million, which was triggered upon the agreement becoming effective. The agreement provides for us to be eligible to receive up to an additional $540 million if specified development, regulatory and first commercial sale milestone events are achieved, up to an additional $500 million if specified sales-related milestones are achieved, and significant stepped double digit royalties on any future TC-5214 product sales. Under the terms of an existing license agreement, we paid $16 million to University of South Florida Research Foundation, or USFRF, based on our receipt of the upfront payment from AstraZeneca and, if we receive any milestone payments from AstraZeneca under the agreement, we would be required to pay a percentage of each such milestone payment, after deducting from the milestone payment the unexhausted portion of our projected share of the costs of the initial development program for TC-5214, as well as royalties on any future TC-5214 product sales, to USFRF. The percentage of each milestone payment, net of any deduction, that we would be required to pay would be at least 10% and could be greater in specified circumstances. Based on the terms of the license agreement with USFRF and the terms of another existing license agreement with Yale University, we expect to pay royalties at an effective worldwide rate in the low single digits and that such effective royalty rate could in some circumstances reach the mid single digits.

AstraZeneca's obligation to pay royalties to us for TC-5214 expires on a country-by-country basis on the later of expiration of the patent rights in each country licensed by us to AstraZeneca that have a specified scope or 12 years after the first commercial sale of TC-5214 in that country. The U.S. patent rights with respect to TC-5214 licensed by us to AstraZeneca expire between 2017 and 2020 and the corresponding licensed foreign patent rights licensed by us to AstraZeneca expire between 2017 and 2019. We have also licensed to AstraZeneca pending U.S. and foreign patent applications with respect to TC-5214 that, if issued as patents, would expire between 2019 and 2030. None of the foregoing years of expiration reflect any patent term extension that may be available in a particular country. It is uncertain whether any of the pending U.S. and foreign patent applications, even if issued as a patent, would be sufficient to extend our royalty term under the agreement for TC-5214 in any particular country. Royalty rates are subject to reduction under the agreement in specified circumstances, including in any country if TC-5214 is not subject to patent protection with a specified scope in that country or if AstraZeneca licenses patent rights from any third party under circumstances in which it is more likely than not that TC-5214 would infringe the third party's patent rights.

Development and Commercialization. The agreement provides for us and AstraZeneca to co-develop TC-5214 under the oversight of a committee comprised of representatives of each company. The clinical program for TC-5214 includes development as an adjunct, or add-on, to antidepressant therapy and as a "switch" monotherapy, in each case in adults with major depressive disorder who do not respond adequately to initial antidepressant treatment. AstraZeneca is responsible for 80% and we are responsible for 20% of the costs of the program, except that AstraZeneca is responsible for 100% of development costs that are required only to obtain or maintain regulatory approval in countries outside the United States and the European Union. We have the right to terminate our obligation to fund our share of the costs of the program once we have funded a specified amount. If we fund the specified amount and terminate our obligation to fund our share of further costs of the program, any future milestones and royalties payable to us under the agreement would be reduced by the amount of our unfunded share plus interest at a specified rate, subject to a maximum reduction that may be applied to any one payment. In addition, if we and AstraZeneca mutually agree to develop TC-5214 for any indication other than

major depressive disorder or in any formulation other than those contemplated by the current program, the same cost sharing arrangement would apply, except that we would have the immediate right to terminate our obligation to fund our share of development costs for the other indication or formulation. If we terminate our obligation to fund our share of these other development costs, any future milestones and royalties payable to us under the agreement would be reduced by the amount of our unfunded share plus interest at a specified rate, subject to a maximum reduction that may be applied to any one payment, but only from and after the occurrence of a specified event to be agreed upon by both parties (such as, for example, receipt of regulatory approval of the applicable indication or formulation).

AstraZeneca is responsible under the agreement for executing and funding the costs of any commercialization of TC-5214 worldwide, and we have retained an option to co-promote TC-5214 to a specified target physician audience in the United States. If we exercise our co-promotion option, AstraZeneca would compensate us on a per detail basis. AstraZeneca is also responsible under the agreement for the manufacture and supply of TC-5214.

Restrictions. For a three-year period beginning with effectiveness of the agreement in December 2009, neither we nor AstraZeneca is permitted to conduct, or to grant a license to any third party to conduct, a Phase 2 or later-stage clinical trial of a compound as an adjunct treatment (or any other term reflecting the concurrent use of two or more pharmaceutical products) for major depressive disorder, or to commercialize such a compound, subject to specified exceptions that include, among others, AstraZeneca's right to develop and commercialize quetiapine (marketed by AstraZeneca as Seroquel) and other atypical antipsychotic products that meet a specified condition.

AstraZeneca has agreed under the agreement not to take specified actions with respect to acquiring control of us without our consent for a specified period. These restrictions, which cease to apply in various circumstances, do not preclude AstraZeneca from making confidential proposals that do not require us to make a public disclosure.

Termination. AstraZeneca can terminate the agreement in its entirety: within a specified period following completion of the initial Phase 3 development program for TC-5214 as an adjunct therapy; or if AstraZeneca determines there to be a serious safety issue regarding the continued development or commercialization of TC-5214; or if, having obtained the advice of independent patent counsel, AstraZeneca believes that the commercialization of TC-5214 is more likely than not to infringe or misappropriate intellectual property rights of third parties in the United States or any two specified major pharmaceutical markets and is unable to obtain a license on commercially reasonable terms. In addition, AstraZeneca can terminate the agreement on a major pharmaceutical market by major pharmaceutical market basis at any time beginning four years after effectiveness of the agreement, except that, if AstraZeneca terminates the agreement with respect to the United States, the agreement will terminate in its entirety. We can terminate the agreement if AstraZeneca or any of its affiliates or sublicensees challenges the validity or enforceability of any of the patent rights licensed to AstraZeneca. Either party can terminate the agreement in the event of the insolvency or uncured material breach of the other party. However, if an uncured material breach by AstraZeneca is limited to a specified major pharmaceutical market, we can terminate the agreement only with respect to that market. The rights and obligations of the parties that survive termination of the agreement, including license grants and payment obligations, vary depending on the basis for the termination.

In addition, in the event of a change of control of us, AstraZeneca can terminate specified provisions of the agreement, including, among others, our right to participate on the committee overseeing development under the agreement and our co-promotion rights.

AstraZeneca AB – Cognitive Disorders

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, ADHD, cognitive dysfunction in schizophrenia, 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.

By agreement with AstraZeneca, we are currently conducting a Phase 2b clinical trial of AZD3480 as a treatment for mild to moderate Alzheimer's disease. Previously, we or AstraZeneca have conducted several clinical studies of AZD3480 in various cognitive disorders.

We and AstraZeneca also conducted a multi-year preclinical research collaboration under the agreement. The term of the research collaboration expired in January 2010. AZD1446 is the most advanced compound that arose from the research collaboration, and, in January 2012, we announced that we have been informed that AstraZeneca plans to progress the development of AZD1446 as a treatment for Alzheimer's disease.

As a result of a process that we had previously initiated under the agreement and a related election previously made by AstraZeneca, AstraZeneca had the right to license TC-5619 following completion of our prior Phase 2 clinical trial in cognitive dysfunction in schizophrenia. In 2011, AstraZeneca elected not to exercise its license right.

Payment Terms. AstraZeneca paid us an initial fee of $10 million in February 2006, an additional $20 million in January 2007 as a result of its December 2006 determination to proceed with further development of AZD3480 and an additional $10 million in July 2009 as a result of the achievement of the objective in the Phase 2 clinical trial of AZD3480 in adults with ADHD. We are eligible to receive other payments of up to $145 million, if, following completion of our ongoing clinical trial of AZD3480 in mild to moderate Alzheimer's disease, AstraZeneca advances AZD3480 into later-stage development for Alzheimer's disease and if development, regulatory and first commercial sale milestone events for AZD3480 are achieved. We would also be eligible for stepped double-digit royalties on any future AZD3480 product sales for any indication. If AZD3480 is developed further under the agreement for an indication in addition to Alzheimer's disease, we would also be eligible to receive payments of up to $52 million for each such indication, if development, regulatory, first commercial sale and first detail milestone events are achieved. Under the terms of a sponsored research agreement and a subsequent license agreement between us and University of Kentucky Research Foundation, or UKRF, if we receive any of these payments from AstraZeneca relating to AZD3480, including royalties, we are required to pay a low single digit percentage of each such payment to UKRF.

With respect to AZD1446, AstraZeneca has paid us $2.2 million upon the achievement of development and regulatory milestone events. We are also eligible to receive other payments of up to $73 million, if development, regulatory and first commercial sale milestone events for AZD1446 are achieved for Alzheimer's disease, and stepped royalties on any future AZD1446 product sales for any indication. If AZD1446 is developed under the agreement for an indication in addition to Alzheimer's disease, we would also be eligible to receive payments of up to $35 million for each such indication, if development, regulatory, first commercial sale and first detail milestone events are achieved.

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 with respect to AZD3480 expire between

2016 and 2027. The foreign patent rights with respect to AZD3480 that have issued and correspond to our issued U.S. patent rights expire between 2017 and 2027. We also have pending U.S. and foreign patent applications with respect to AZD3480 that, if issued as patents, would expire between 2017 and 2029. The U.S. patent rights with respect to AZD1446 expire in 2028. The foreign patent rights with respect to AZD1446 that have issued and correspond to our U.S. patent rights expire in 2027. We also have pending U.S. and foreign patent applications with respect to AZD1446 that, if issued as patents, would expire in 2027. None of the foregoing years of expiration reflect any patent term extension that may be available in a particular country. It is uncertain whether any of the pending U.S. and foreign patent applications, even if issued as a patent, would be sufficient to extend our royalty term under the agreement for AZD3480 or AZD1446 in any particular country. 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.

Completed Preclinical Research Collaboration. The agreement provided for a preclinical research collaboration that we and AstraZeneca conducted between January 2006 and January 2010 to discover and develop additional compounds that act on the a4ß2 NNR as treatments for conditions characterized by cognitive impairment. AstraZeneca paid us research fees based on an agreed reimbursement rate for research services rendered by us in the collaboration. AstraZeneca has exclusively licensed six of these compounds, including AZD1446, 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.

Development and Commercialization Costs. AstraZeneca is responsible for the clinical development and commercialization of AZD3480, AZD1446 and any other licensed compounds that arose from the research collaboration that it elects to advance and for funding substantially all associated costs, except as described in the next sentence. We are responsible for conducting and funding our ongoing Phase 2b clinical trial of AZD3480 as a treatment for mild to moderate Alzheimer's disease, but have received $6.2 million in payments from AstraZeneca in connection with events associated with the study. We have the option to co-promote AZD3480, AZD1446 and any other licensed compounds that arose 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.

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, ADHD, cognitive dysfunction in schizophrenia or 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 January 2010. 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 conduct 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 prior 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, 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 if development, regulatory, first commercial sale and first detail milestone events are achieved, as well as stepped royalties on any future product sales. If AstraZeneca elects not to license the compound, as in the case of TC-5619, 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 a4ß2 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, 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. 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 major pharmaceutical market, we can terminate the agreement only with respect to that compound or major pharmaceutical 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

In July 2007, we entered into a product development and commercialization agreement with SmithKlineBeecham Corporation and Glaxo Group Limited, which we refer to collectively in this annual report as GlaxoSmithKline, that set forth the terms of an alliance designed to discover, develop and market product candidates that selectively target specified NNR subtypes in specified therapeutic focus areas. In February 2010, GlaxoSmithKline announced plans to cease discovery research in selected neuroscience areas and terminated our agreement effective in May 2011.

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 29, 2012, our patent estate included 76 patents issued in the United States, 52 patent applications pending in the United States and approximately 525 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 particularly important to the protection of our most advanced product candidates.

Product Candidate	Patent Scope	Patent Expiration
TC-5214	Pharmaceutical composition of TC-5214	January 2020
	Methods of use of TC-5214 for treatment of neuropsychiatric disorders, including depression	February 2020
	Methods of use of a class of compounds that includes TC-5214 for treatment of a nicotine-responsive psychiatric disorder, including depression	September 2017
TC-5619	Composition of matter for a racemic mixture that includes TC-5619	March 2019
	Composition of matter for a family of racemic compounds that includes TC-5619	August 2019
	Methods of use of a racemic mixture that includes TC-5619 for treatment of symptoms of schizophrenia	February 2023
	Methods of use of a racemic mixture that includes TC-5619 for treatment of schizophrenia	November 2025
	Composition of matter for salt forms of TC-5619	January 2029
AZD3480 (TC-1734)	Composition of matter for a family of compounds that includes AZD3480	April 2016
	Composition of matter for AZD3480	July 2018
	Methods of use of a family of compounds that includes AZD3480 for treatment and prevention of central nervous system, or CNS, disorders	February 2017
	Methods of use for AZD3480 for treatment and prevention of CNS disorders	July 2018
	Composition of matter for preferred salt (p-hydroxybenzoate) of AZD3480	August 2026
AZD1446 (TC-6683)	Composition of matter for AZD1446	August 2028
TC-6987	Composition of matter for a family of compounds that includes TC-6987	August 2019
	Methods of use of compounds that act on a7 NNRs to treat described inflammatory conditions	February 2024

In addition to these patents, for some of these product candidates, we have later-expiring patents and patent applications that cover the product candidate, its use as part of combination therapy or otherwise or its preparation. These patents, including any patents that issue from the pending applications, could provide an additional or a longer period of protection. We also have issued patents and pending patent applications with 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 term extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of FDA approval. The patent term restoration period is generally one-half of 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 an extension, and, with limited exceptions, 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

In addition to the agreements governing our collaborations with AstraZeneca, we consider the following license agreements to be important to our business.

University of South Florida Research Foundation

Pursuant to a license agreement with 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 patent rights 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 major depressive disorder. We sublicensed rights under the licensed patents and patent applications to AstraZeneca in December 2009 pursuant to our TC-5214 agreement with AstraZeneca.

Under the license agreement with USFRF, we are obligated to pay to USFRF:

- an annual license fee of $50,000 until we or AstraZeneca or any future sublicensee files an NDA or foreign equivalent for use of a product subject to the license to treat a neuropsychiatric disease or disorder;
- an annual fee of $20,000 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 AstraZeneca or any future sublicensee;
- aggregate payments of up to $200,000 based on the achievement of specified regulatory milestones; and
- 10% of other amounts, including milestone payments, that we receive for a sublicense from AstraZeneca or any future sublicensee, subject to increase to a higher percentage in specified circumstances.

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 over each consecutive three-year period during the term of the agreement 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 if we do not cure our failure within a specified 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.

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. We sublicensed rights under the licensed patent applications to AstraZeneca in December 2009 pursuant to our TC-5214 agreement with AstraZeneca.

Under the license agreement with Yale, we are obligated to pay to Yale:

- a fee of $50,000 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 milestone events 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 specified percentage of other amounts received from any sublicensee of the licensed patent rights, if the applicable sublicense is not combined with a license to other patent rights owned or licensed by us that cover compounds or their therapeutic use in humans or with an agreement by us to collaborate to discover, research, develop or commercialize compounds or products for therapeutic use in humans. Our sublicense to AstraZeneca under our TC-5214 agreement with AstraZeneca is combined with both a license to other patent rights and an agreement by us to co-develop TC-5214 as a treatment for major depressive disorder. Accordingly, no other amounts received from AstraZeneca under our TC-5214 agreement with AstraZeneca give rise to any payment obligation to Yale.

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 research, development or marketing of, and our intent to research, develop and market, 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, UKRF agreed to assign its rights to inventions that resulted in patents related to AZD3480 to R.J. Reynolds Tobacco Company. These patents were subsequently assigned by R.J. Reynolds Tobacco Company to us in August 2000, and we licensed rights under these patents to AstraZeneca pursuant to our cognitive disorders agreement with AstraZeneca. Under the sponsored research agreement and a subsequent license agreement with UKRF, we are obligated to pay royalties to UKRF based on amounts received for a license to these patents from AstraZeneca or any future licensee.

Cornerstone Therapeutics Inc.

Pursuant to an exclusive license agreement with Cornerstone Therapeutics Inc., we hold an exclusive worldwide license and sublicense under patents and patent applications owned by Cornerstone or exclusively licensed by Cornerstone from the Feinstein Institute for Medical Research. The licensed patent rights include

issued patents and pending patent applications covering a library of preclinical compounds that act on the a7 or other nicotinic receptors, as well as the use of compounds that act on a7 NNRs to treat described inflammatory disorders. TC-6987 modulates the activity of the a7 NNR and is currently being evaluated in Phase 2 clinical trials in asthma and Type 2 diabetes.

Under the license agreement with Cornerstone, we paid Cornerstone an upfront fee of $1.5 million and are obligated to pay to Cornerstone:

- payments for each compound subject to the license for which specified clinical, regulatory and sales-related milestone events are achieved, with the aggregate amount of the potential payments for a particular compound being dependent on whether and to what extent Cornerstone had exemplified and progressed the compound as of the effective date of the agreement;
- the aggregate amount of the contingent payments described in the immediately preceding bullet ranges from up to $16.1 million to up to $74.9 million, comprised of $325,000 to $1.4 million in milestones through Phase 2 clinical proof of concept, $2.8 million to $18.5 million in later-stage pre-commercialization milestones and $13.0 million to $55.0 million in sales-based milestones; to the extent the licensed patent rights cover the use of TC-6987 or any other Targacept-discovered compound, the aggregate contingent payments would be at the low point of each of the ranges; and
- low single-digit royalties on net sales of products subject to the license (to the extent the licensed patent rights cover the use of TC-6987 or any other Targacept-discovered compound as a treatment for inflammatory disorders, the royalty rate would be less than 1%).

We are required to use commercially reasonable efforts to develop at least one compound subject to the license to regulatory approval. We are also specifically required to use commercially reasonable efforts to manufacture one of two specified in-licensed compounds, in sufficient quantities and of sufficient quality to perform specified preclinical toxicology work, and, if successful, then to perform the preclinical toxicology work within a specified timeframe, subject to extension in certain circumstances.

We may terminate the agreement upon 30 days notice to Cornerstone. Cornerstone may terminate the agreement if we successfully complete the manufacturing contemplated above but do not conduct the specified preclinical toxicology work within the requisite timeframe, or if we commit a material breach of the agreement and do not cure the breach within a specified cure period. If not earlier terminated, the agreement will expire upon expiration of the period during which royalties are payable for the last product subject to the license.

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, marketing and distribution experience with respect to pharmaceutical products and no internal sales or distribution capabilities. Our current strategy is to selectively seek alliances and collaborations, particularly for target indications for which a potential collaborator has unique 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, potentially in the future, other markets. To be successful if we exercise these rights, we would have to develop a specialized sales and marketing organization with sufficient technical expertise.

We discontinued the commercialization of Inversine, which is currently our only approved product, effective as of September 30, 2009. Inversine had been distributed by Cord Logistics, Inc., a Cardinal Health company, pursuant to an exclusive distribution agreement. We have terminated our agreement with Cord Logistics. We paid Cord Logistics $0 in 2011 and approximately $31,000 in 2010 and $140,000 in 2009.

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.

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 Roche, Abbott Laboratories, Eli Lilly, Sanofi-Aventis, Bristol-Myers Squibb, Johnson & Johnson, Novartis, NeuroSearch A/S, Solvay, Servier, CoMentis, EnVivo Pharmaceuticals, Galantos Pharma, Proximagen, Psychogenics, Suven, Asmacure and Neuroderm. 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 pursue the development and commercialization of therapeutics for nervous system diseases and disorders, whether independently or by alliance, collaboration 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:

- as an adjunct treatment for major depressive disorder, the atypical antipsychotics Seroquel XR from AstraZeneca and Abilify from Bristol-Myers Squibb/Otsuka;
- otherwise for major depressive disorder, SSRIs such as Prozac from Eli Lilly, Paxil/Seroxat 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 the SSRI and $5HT_{1A}$ receptor partial agonist Viibryd from Forest Laboratories;
- for ADHDi, 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; these products are approved for the treatment of ADHD generally and not ADHDi specifically;

- for asthma, long-acting beta agonist/inhaled corticosteroid combinations such as Advair from GlaxoSmithKline, Symbicort from AstraZeneca and Dulera from Merck, leukotriene inhibitors such as Singulair from Merck, Accolate from AstraZeneca and Zyflo from Cornerstone Therapeutics, antibodies such as Xolair from Novartis, long-acting beta agonists such as salmeterol and formoterol and short-acting beta agonists such as albutertol and levalbuterol;
- for Type 2 diabetes, glucagon-like peptide-1 analogues such as Byetta from Eli Lilly and Amylin, dipeptidyl peptidase IV inhibitors such as Januvia from Merck and Onglyza from Bristol-Myers Squibb and AstraZeneca, insulin such as Lantus from Sanofi-Aventis, sulfonylureas such as Glucotrol from Pfizer, and biguanides (metformin) such as Glucophage from Bristol-Myers Squibb; and
- 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.

There is currently no product approved in the United States, Europe or, to our knowledge, elsewhere specifically for the treatment of negative symptoms of schizophrenia or cognitive dysfunction in schizophrenia. There are however multiple third-party product candidates currently in clinical development targeting these areas, including modulators of the a7 NNR.

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, recordkeeping, promotion, advertising, distribution, marketing and export and import of drugs such as those we are developing. Our product candidates must be approved by the 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 conducted in accordance with good laboratory practices and 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 conducted in accordance with the regulations and guidelines establishing good clinical practices to establish the safety and efficacy of the drug for its intended use;
- submission to the FDA of an NDA in a form and content that the FDA deems to be acceptable for filing;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the drug is produced to assess compliance with cGMP in order 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 to assess the characteristics and potential effects of the drug. The results of preclinical testing are submitted to the FDA, along with other information about drug chemistry, manufacturing and controls and a proposed clinical trial protocol, as part of an IND. Long-term preclinical tests, such as animal tests of reproductive toxicity and the ability or tendency to produce cancer, may continue after the IND is submitted. The IND becomes effective 30 days after receipt by the FDA, unless within the 30-day time period the FDA places the clinical trial on a clinical hold. In such a case, the company responsible for the clinical trial (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 the regulations and guidelines establishing good clinical practice. These regulations include the requirement that all research subjects provide informed consent. Further, an institutional review board, or IRB, for each institution participating in a clinical trial must review and approve the plan for the clinical trial before it commences at the institution. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and 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. An IRB may impose conditions to the initiation or continued conduct of trial at the institution for which the IRB is responsible.

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.

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 volunteers 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; and
- *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 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. Any Phase 1, Phase 2 and Phase 3 trial may not be completed successfully within any specified period, or 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.

During the development of a new drug, companies have opportunities to meet with the FDA at certain times, typically prior to submission of an IND, after Phase 2 development and before an NDA is submitted. Meetings at other times may also be requested. These meetings can provide an opportunity for the company developing the drug to share information about the data gathered to date, for the FDA to provide advice, and for the company and the FDA to reach agreement on the next phase of development. Companies sometimes use the end-of-Phase 2 meeting to discuss their Phase 2 clinical trial results and present their plans for the pivotal clinical trials that they believe will support approval of the new drug.

If a Phase 2 clinical trial is the subject of discussion at an end-of-Phase 2 meeting with the FDA, a company may be able to request a Special Protocol Assessment, or SPA, the purpose of which is to reach agreement with the FDA on the protocol design and statistical analysis for the pivotal clinical trials that will form the primary basis of an efficacy claim. The FDA is supposed to evaluate the protocol within 45 days of the request to assess whether the proposed trial is adequate, and the evaluation may result in discussions and a request for additional information. An SPA request must be made before the proposed trial begins, and all open issues must be resolved before the trial begins. If an agreement is reached, it will be documented, made part of the administrative record, be binding on the FDA and not be changed unless the company fails to follow the agreed-upon protocol, data supporting the request are found to be false or incomplete or the FDA determines that a substantial scientific issue essential to determining the safety or effectiveness of the drug was identified after the testing began. Even if an SPA is agreed to, approval of the NDA is not guaranteed because a final determination that an agreed-upon protocol satisfies a specific objective, such as the demonstration of efficacy, or supports an approval decision, will be based on a complete review of all the data in the NDA.

Additionally, if a drug is intended to treat a serious or life threatening condition for which there is an unmet medical need, a company may request that the FDA consider the drug for a fast track development program at the time of submitting its IND or at any time prior to receiving marketing approval. The fast track program is designed to facilitate the development and expedite the review of a new drug for the treatment of specific conditions.

Concurrently 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. FDA approval of the NDA is required before marketing of the product may begin in the United States. The cost of preparing and submitting an NDA is substantial. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee and the manufacturer or sponsor under an approved NDA is also subject to annual establishment registration and product listing fees. These fees are typically increased annually. A waiver or reduction of the fees may be obtained under specified 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 a deferral for submission of data or a full or partial waiver. 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 filing the NDA or accepting the NDA for filing. The FDA may request additional information rather than file an NDA. 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 10 months to review and act on the NDA, depending upon whether the NDA is classified by the FDA as eligible for priority (six months) or standard (10 months) review. The review process may be extended by the FDA for an additional three-month period to consider certain information or clarification regarding information already provided in the submission. The FDA may also refer NDAs for novel drug products or for drug products that present difficult questions of safety or efficacy to an advisory committee for review, evaluation and a recommendation as to whether the NDA should be approved. Advisory committees are typically comprised of clinicians and other experts in the relevant area. The FDA is not bound by the recommendation of an advisory committee, but often follows the 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 any requested additional data or 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 or any collaborator of ours does.

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. Priority review and accelerated approval do not change the standards for approval, but may expedite the approval process.

After the FDA evaluates the NDA and the applicable manufacturing facilities, it issues an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the NDA. If and when the deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. FDA review of a resubmitted NDA can take as long as six months depending on the type of information included.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy and may impose other conditions, including labeling restrictions and risk evaluation and mitigation strategies, that can materially affect the potential market for and profitability of the drug. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

If a drug 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 product 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 product 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 generic 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 generally 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 an NDA under Section 505(b)(2) of the FDCA 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 the FDA to be essential to the approval of the application. This may include, for example, new indications for, or new 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, whether statutory or patent, may be granted based on the voluntary completion of a pediatric study in accordance with an FDA-issued "Written Request" for the 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 for seven years, except in very limited circumstances (such as a showing of clinical superiority to the product with orphan drug exclusivity). Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition or from approving the same drug for a different disease or condition.

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 proposes 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 on the market. Products may be promoted only for the approved indications and in accordance with the provisions of the approved label.

As part of the sales and marketing process, pharmaceutical companies frequently provide samples of approved drugs to physicians. The Prescription Drug Marketing Act, or the PDMA, imposes requirements and

limitations upon the provision of drug samples to physicians and prohibits states from licensing distributors of prescription drugs unless the licensing program meets federal guidelines that include minimum standards for storage, handling and record keeping. The PDMA sets forth civil and criminal penalties for violations.

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 most 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 or any collaborator of ours obtains FDA approval for a product candidate or product, we or the collaborator must obtain approval by the comparable regulatory authorities of foreign countries, or of economic areas such as the European Union, before we can commence clinical trials of the product candidate or marketing of the product in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time required may be longer or shorter than the time required for FDA approval.

Under European Union regulatory systems, we may submit marketing authorization applications either under a centralized or a decentralized procedure. The centralized procedure, which provides for the grant of a single marketing authorization that is valid for all European Union member states, is compulsory for medicines produced by biotechnology or intended to treat AIDS, cancer, neurodegenerative disorders or diabetes and optional for medicines that are highly innovative. 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, which is known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials (including a 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, any disputed issues may eventually be referred to the European Commission, the decision of which would be binding on all member states.

As in the United States, we may apply for designation of a product as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Orphan drugs in Europe enjoy economic and marketing benefits, including up to 10 years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product.

Reimbursement

Sales of pharmaceutical products depend in significant part on the availability of third-party reimbursement. Third-party payors include government health programs such as Medicare and Medicaid, 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, including prescription drugs. In addition, significant uncertainty exists as to the reimbursement status of newly approved prescription drugs and other healthcare products. We may need to conduct expensive pharmacoeconomic studies in order to demonstrate the cost-effectiveness of any of our products that is successfully developed and approved. Our product candidates may not be considered cost-effective. It is time consuming and expensive for us or any collaborator of ours to seek reimbursement from third-party payors. Reimbursement may not be available or sufficient to allow the sale of any of our products that is successfully developed and approved on a competitive and profitable basis.

The Medicare Prescription Drug, Improvement, and Modernization Act of 2003, or the MMA, established the Medicare Part D program to provide a voluntary prescription drug benefit to Medicare beneficiaries. Under Part D, Medicare beneficiaries may enroll in prescription drug plans offered by private entities to 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 Parts 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 Part D prescription 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 of the drugs within 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 that is successfully developed and approved. 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, although 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. Accordingly, 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 in the future consider legislation that would lift the ban on federal negotiations.

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research would be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes of Health, and periodic reports on the status of the research and related expenditures would be made to the U.S. Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear whether research would have any effect on the sales of any of our products that is successfully developed and approved, if the product or the condition that it is intended to treat becomes the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits of a competitor's product could adversely affect the sales of any of our products that is successfully developed and approved. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Patient Protection and Affordable Care Act, or the PPACA, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, is expected to have a significant impact on the health care industry. The PPACA is expected to expand coverage for the uninsured while at the same time containing overall healthcare costs. Among other things, the PPACA is expected to expand and increase industry rebates for drugs covered under Medicaid programs and make changes to the coverage requirements under the Medicare Part D program. We cannot predict the impact of the PPACA on pharmaceutical companies because many of the PPACA's reforms require the promulgation of detailed regulations to implement the statutory provisions, which has not yet occurred. Also, current legal challenges to the PPACA, as well as congressional efforts to repeal the PPACA, add to the uncertainty of the effects of the PPACA.

The PPACA also imposes new reporting and disclosure requirements on pharmaceutical and medical device manufacturers with regard to payments or other transfers of value made to physicians or teaching hospitals and with regard to investment interests held by physicians and their immediate family members during the preceding calendar year. The Centers for Medicare & Medicaid Services recently published a proposed rule for this requirement, and the first reports under this provision will be due by March 31, 2013. Failure to submit required information may result in civil monetary penalties of up to $150,000 per year (up to $1 million per year for "knowing failures") for all payments, transfers of value or ownership or investment interests not reported in an annual submission.

If not preempted by the PPACA, several states require pharmaceutical manufacturers to report expenses relating to the marketing and promotion of pharmaceutical products and to report gifts and payments to individual physicians in the states. Other states prohibit providing various other marketing related activities. Still other states require the posting of information relating to clinical studies and their outcomes. In addition, some states, such as California, Nevada and Massachusetts, require pharmaceutical manufacturers to implement compliance programs or marketing codes. Currently, several additional states are considering similar proposals. Compliance with these laws is difficult and time consuming, and companies that do not comply with these state laws face civil penalties.

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 respective 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 or any collaborator of ours receives marketing approval. Historically, the price structures for products launched in the European Union do not follow those of the United States and tend to be significantly lower.

Employees

As of February 29, 2012, we had 142 employees, 53 of whom are Ph.D.s, M.D.s or both. Our management believes that relations with our employees are good. None of our employees is represented under a collective bargaining agreement.

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.

Targacept®, Pentad™ and NNR Therapeutics™ are trademarks of ours. 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

We have a substantial accumulated deficit and may incur losses for future periods. We may not achieve profitability for any future period or, if we do achieve profitability for a future period, we may not sustain or grow our profitability.

We were incorporated in 1997 and operated as a wholly owned subsidiary of R.J. Reynolds Tobacco Company until August 2000. As of December 31, 2011, we had an accumulated deficit of $226.9 million. We had net loss of $8.5 million for the year ended December 31, 2011, net income of $10.9 million for the year ended December 31, 2010 and net loss of $39.4 million for the year ended December 31, 2009. Our net income for 2010 was due primarily to the recognition into revenue of a portion of the upfront payment that we received under our TC-5214 agreement with AstraZeneca that we entered into in December 2009. Our losses for other periods 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 may incur losses for future periods as our clinical-stage and preclinical product candidates advance into later-stage development and as we progress our programs, invest in additional product opportunities and grow our business. As a result, we will need to generate significant revenues to achieve profitability in the future or, if we do achieve profitability for any particular period, to sustain or grow our profitability on a quarterly or annual basis.

We derived a substantial portion of our revenue for 2011, 2010 and 2009 from our strategic alliances and collaborations. We expect that a substantial portion of our operating cash flow in the next few years will depend on the following:

- whether and to what extent milestone events are achieved for TC-5214 under our TC-5214 agreement with AstraZeneca or for either or both of AZD1446 and AZD3480 under our cognitive disorders agreement with AstraZeneca;
- the progress of, and outcomes from, Phase 3 clinical development of TC-5214 and the amount and timing of costs payable by us for ongoing or any future development of TC-5214; and
- whether we establish additional strategic alliances, collaborations or licensing or other comparable arrangements, or whether we pursue and complete any merger, acquisition or other significant corporate transactions, and, if we do, the associated terms in each case.

Sources that contributed to our revenue for any particular year may not continue. For example, we received $45 million in aggregate payments under our now terminated strategic alliance with GlaxoSmithKline. Also, the term of the preclinical research collaboration focused in cognition that we conducted previously under our cognitive disorders agreement with AstraZeneca and for which we received research fees expired in January 2010. Neither the agreement with GlaxoSmithKline nor the preclinical research collaboration with AstraZeneca is a source of future revenue. Additionally, we do not currently have any source of product revenue.

If we or a collaborator of ours is unable to develop and commercialize one or more 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 achieve profitability in the future. Even if we are profitable for any particular period, we may not be able to sustain or grow our profitability on a quarterly or annual basis.

Our failure to obtain additional capital when needed could force us to delay, reduce or eliminate our product development programs or future commercialization efforts.

Successful drug development and commercialization requires significant amounts of capital. It is foreseeable that we will in the future 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 potentially to establish sales and marketing capabilities. Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the amount of revenue that we are able to generate, which we expect will depend substantially on the outcomes of the uncertainties described in the bullets above under "*We have a substantial accumulated deficit and may incur losses for future periods. We may not achieve profitability for any future period or, if we do achieve profitability for a future period, we may not sustain or grow our profitability.*";
- the progress of, and outcomes from, Phase 3 clinical development of TC-5214 and the amount and timing of costs payable by us for ongoing or any future development of TC-5214;
- whether we elect to exercise our co-promotion rights for TC-5214 if the outcomes of the remaining Phase 3 clinical trials are favorable and AstraZeneca proceeds to file a new drug application, or NDA, for TC-5214 with the U.S. Food and Drug Administration, or FDA;
- the scope, progress, duration, results and costs of clinical trials, as well as non-clinical studies and assessments, of our product candidates and programs in addition to TC-5214;
- the extent to which we retain development and commercialization rights or responsibilities for our product candidates that are not subject to our collaborations with AstraZeneca and incur associated development costs, manufacturing costs or costs to establish sales and marketing functions;
- the number and characteristics of product candidates that we pursue and programs that we conduct;
- the costs to satisfy our obligations under existing and potential future alliances and collaborations;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending patents and other intellectual property rights;
- the costs of manufacturing-related services for our product candidates in clinical and late preclinical development;
- the costs, timing and outcomes of regulatory reviews or other regulatory actions;
- the timing, receipt and amount of sales or royalties, if any, from our potential products;
- the extent and scope of our general and administrative expenses; and
- the rate of technological advancements for the indications that we target.

In addition, we may seek additional capital, whether through offerings of securities utilizing our currently effective Registration Statement on Form S-3 or otherwise, if the conditions for raising capital are favorable or based on 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 may be diluted, and the terms of the securities may include liquidation or

other preferences that materially and 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.

We plan to continue, either alone or with AstraZeneca or one or more potential future collaborators, to advance our product candidates through the development process. We currently expect that our existing capital resources will enable us to fund our operations through at least the end of 2014. 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. Our ability to raise additional funds if and when needed on terms that are acceptable to us, or at all, may be materially and adversely affected by challenging U.S. and global financial markets and by the substantial decline in our stock price that we experienced following the announcement of top-line results from the first completed Phase 3 clinical trial of TC-5214 in November 2011. 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 establishment of any sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates; or
- scale back or eliminate research programs that are designed to identify new product candidates or to progress preclinical product candidates towards readiness for potential future clinical development.

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 or a collaborator of ours is unable to bring one or more 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.

Our ability to generate product or royalty revenue over the next few years will depend substantially on the successful development and commercialization of our clinical-stage product candidates, including in particular TC-5214 (which is currently in Phase 3 clinical development) and TC-5619, TC-6987, AZD3480 and AZD1446 (which are currently in Phase 2 clinical 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 TC-5214 to be commercially available until at least the second half of 2013, and then only if, on a timely basis, the remaining Phase 3 clinical trials of TC-5214 are completed and successful, an NDA is filed and the FDA grants approval of the NDA. We do not expect any of our other current product candidates to be commercially available for at least the next several years, if at all. If we or any applicable collaborator of ours is unable to make our product candidates commercially available, we will not generate substantial product revenue and we will not be successful.

If the favorable results of our completed Phase 2b clinical trial of TC-5214 as an adjunct therapy for major depressive disorder are not replicated in the Phase 3 clinical trials of TC-5214 that remain ongoing, or if any of the other studies included in the clinical program for TC-5214 indicates that TC-5214 is not sufficiently safe, we and AstraZeneca will not obtain the regulatory approvals required to market and sell TC-5214.

Favorable results in earlier-stage clinical trials of a product candidate may not be replicated in later clinical trials that involve different numbers of subjects, different dosing regimens and durations, different subject populations, different geographical locations, different outcome measures or other differences in design or execution. As an example, the favorable results of our completed Phase 2b clinical trial of TC-5214 as an adjunct therapy for major depressive disorder were not replicated in the first two Phase 3 clinical trials of TC-5214 that were completed in 2011, neither of which met its primary endpoint. Two additional Phase 3 clinical trials designed to evaluate the efficacy of TC-5214 remain ongoing.

There are various differences between the completed Phase 2b clinical trial and the ongoing Phase 3 clinical trials. In particular, the Phase 2b clinical trial was limited to subjects who did not respond adequately to the antidepressant citalopram and was conducted primarily in India. The two ongoing Phase 3 clinical trials include, and the two completed Phase 3 clinical trials included, subjects who did not respond adequately in the study to one of seven different antidepressant therapies. Neither of the ongoing Phase 3 clinical trials is being, and neither of the completed Phase 3 clinical trials was, conducted primarily in India, although one ongoing and one completed clinical trial utilized some investigative sites in India. Medical care in India is generally not as advanced as in the United States or Western Europe, and the treatment that subjects receive in a clinical trial in India may in some cases be their only medical treatment. Also, the Phase 2b clinical trial utilized a “flexible dose” trial design in which the dosing regimen that each subject received could be increased at various times over the course of the study at the discretion of the applicable investigator based on how the subject tolerated and responded to the then-current dosage. Although the two completed Phase 3 clinical trials also utilized a flexible dose design, the two ongoing Phase 3 clinical trials utilize a “fixed dose” design in which each subject who receives TC-5214 receives a set dosing regimen throughout the study. Prior to initiation of the Phase 3 development program, neither we nor AstraZeneca had ever conducted a fixed dose clinical trial of TC-5214 as an adjunct treatment for major depressive disorder. We and AstraZeneca were guided by data from the completed Phase 2b trial in selecting the dosages of TC-5214 to be evaluated in the fixed dose Phase 3 trials, but we cannot be certain that the optimum dosages were selected. It is possible that these differences, or any other difference in design between our completed Phase 2b clinical trial and the ongoing Phase 3 clinical trials, will impact the likelihood that the favorable results achieved in the completed Phase 2b clinical trial will be replicated in the ongoing Phase 3 clinical trials. If the favorable results achieved in our completed Phase 2b clinical trial of TC-5214 are not replicated in the ongoing or any future clinical trials of TC-5214, we and AstraZeneca will not obtain the regulatory approvals required to market and sell TC-5214.

In addition, the clinical program for TC-5214 includes a long-term study with a dosing period of one year that is designed primarily to evaluate safety, as well as multiple Phase 1 clinical trials—including a QTc study designed to confirm that various doses of TC-5214 do not disturb the electrical activity of the heart, an abuse liability study designed to assess whether TC-5214 induces craving and its excessive use in humans, and a drug-drug interaction study designed to assess the safety of TC-5214 when used together with other specified drugs. If the outcome of any of these studies indicates that TC-5214 is not sufficiently safe, we and AstraZeneca will not obtain the regulatory approvals required to market and sell TC-5214 even if the Phase 3 clinical program of TC-5214 as a whole demonstrates that TC-5214 is effective for its intended use. If the outcome of any of these studies indicates that TC-5214 is not safe for certain patients or under certain circumstances, the FDA or foreign regulatory authorities could limit the patient population for which TC-5214 is approved or require warnings or instructions to physicians, which could materially and adversely affect its commercial potential.

If we and AstraZeneca are unable to complete the Phase 3 development program for TC-5214 and submit an NDA to the FDA on or before September 30, 2012 or if other statutory conditions are not met, TC-5214 may not receive the five-year exclusivity period provided by applicable law, in which case our and AstraZeneca's ability to exclude third parties from themselves marketing TC-5214 in the United States would be substantially dependent on patents after three years.

The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a five-year period of marketing exclusivity in the United States to the first applicant to obtain approval of an NDA for a drug that qualifies as a new chemical entity. The FDA may not during this exclusivity period accept for review an abbreviated new drug application, or ANDA, or another NDA for another version of the drug in question where the applicant does not own or have a legal right of reference to all the data required for approval, except that either of these applications may be submitted after four years with a certification that applicable patents are invalid or not infringed (in which case a timely challenge to the certification would trigger a stay of the FDA's approval of the application for a defined term). The exclusivity period runs concurrently with any patents that cover the new chemical entity, but provides exclusivity independent from and irrespective of the patents. Accordingly, a new chemical entity approved in the United States has assurance of a statutory period of marketing exclusivity in the United States whether or not the patents that cover it are sufficiently strong to withstand challenge.

TC-5214 is one of two enantiomers of a racemate previously marketed in the United States. Enantiomers are mirror images of each other that have the same chemical but potentially different biological properties, and a racemate is a chemical mixture comprised of two corresponding enantiomers. Under Section 505(u) of the FDCA, as added by the FDA Amendments Act of 2007, an NDA applicant may, if certain conditions are met, elect that a single enantiomer of a previously approved racemate not be considered the same active ingredient as the racemate and thereby preserve potential eligibility for the single enantiomer as a new chemical entity. The election may only be made for an NDA submitted on or before September 30, 2012, when the statutory provision that permits the election is scheduled to expire unless it is re-authorized by the U.S. Congress. It is uncertain whether the statutory provision will be re-authorized. If for any reason we and AstraZeneca are unable to submit an NDA for TC-5214 on or before September 30, 2012, or if other statutory conditions are not met, and the statutory provision is not reauthorized, TC-5214 will not receive the five-year exclusivity period and will be limited to a three-year exclusivity period that is provided by the FDCA for certain applications. In that case, we and AstraZeneca would be substantially reliant on patent protection to provide an extended term of exclusivity in the United States. Like any patent, the patents that we own or license covering TC-5214 and those that may issue in the future are subject to being challenged, invalidated, rendered unenforceable or circumvented, any of which could limit our ability to stop third parties from marketing TC-5214 or related products themselves. If we and AstraZeneca are unable to enforce or defend patents that cover TC-5214 that we own or license and cannot stop third parties from marketing TC-5214 or related products themselves, the commercialization of TC-5214 would be materially and adversely affected and our business would suffer.

The clinical trial designs and endpoints that will be required to obtain regulatory approval of a drug to treat negative symptoms of schizophrenia, cognitive dysfunction in schizophrenia or inattentive-predominant ADHD are uncertain, and we may never receive the regulatory approvals required to market and sell TC-5619 as a treatment for any of these indications. Also, we may choose to pursue only one of negative symptoms of schizophrenia or cognitive dysfunction in schizophrenia in any future clinical trials of TC-5619, which could limit the commercial potential of TC-5619.

There is currently no product approved in the United States, Europe or, to our knowledge, elsewhere specifically for the treatment of negative symptoms of schizophrenia or cognitive dysfunction in schizophrenia. Likewise, there is currently no product approved in the United States or Europe specifically for the treatment of inattentive-predominant ADHD, or ADHDi. Accordingly, there is not a well-established development path that, with positive outcomes in clinical trials, would be reasonably assured of receiving regulatory approval for any of these indications. In particular, if either or both of our ongoing clinical trials of TC-5619 in negative symptoms and cognitive dysfunction in schizophrenia and ADHDi are successful and, in the future, we conduct later-stage

trials of TC-5619 in the applicable indication, the FDA or any foreign regulatory authority may determine that the designs or endpoints of the later-stage trials are not acceptable to support the approval required to market and sell TC-5619 as a treatment for the applicable indication, even if the outcomes from the trials are positive. Moreover, we cannot be certain that the FDA or any foreign regulatory authority will recognize ADHDi as a distinct clinical condition, or in the FDA's terminology, a clinical entity, for which approval of a drug is possible.

In addition, based on feedback from the FDA, three co-primary endpoints—one assessing negative symptoms, one assessing cognitive dysfunction and one assessing global function—in each of at least two clinical trials may be required to support approval of TC-5619 for both negative symptoms of schizophrenia and cognitive dysfunction in schizophrenia. It is difficult for any investigational drug to show statistically significant effects on three co-primary endpoints in the same clinical trial. Accordingly, it is likely that we would design any Phase 3 clinical program to support approval for either negative symptoms of schizophrenia or cognitive dysfunction in schizophrenia, depending on the particular outcomes from our ongoing Phase 2b clinical trial, but not both, which could limit the commercial potential of TC-5619.

The favorable findings in our completed Phase 2 clinical trial of TC-5619 in schizophrenia patients may not be replicated in our ongoing Phase 2b clinical trial in negative symptoms and cognitive dysfunction in schizophrenia or in any future clinical trials of TC-5619.

As noted above, favorable results in earlier-stage clinical trials of a product candidate may not be replicated in later clinical trials that involve different numbers of subjects, different dosing regimens and durations, different subject populations, different outcome measures or other differences in design or execution. There are various differences between our completed Phase 2 clinical trial of TC-5619 in cognitive dysfunction in schizophrenia and our ongoing Phase 2b clinical trial of TC-5619 in negative symptoms and cognitive dysfunction in schizophrenia. In particular, in the completed trial, the Scale for the Assessment of Negative Symptoms, or SANS, was a secondary outcome measure. Our ongoing trial utilizes SANS as the primary outcome measure and, unlike the completed trial, permits only subjects who meet specified criteria for negative symptoms of schizophrenia to be enrolled. In addition, the ongoing trial involves a larger number of subjects and a longer duration of dosing than the completed trial. Moreover, with regard to cognitive dysfunction in schizophrenia, in the completed trial, TC-5619 met the protocol criteria for a positive result on the Groton Maze Learning task, the trial's primary outcome measure and one part of the CogState Schizophrenia Battery, or CSB. However, TC-5619 did not demonstrate a drug effect on all of the completed trial's efficacy outcome measures, including the CSB composite score, or all measurement dates. The ongoing trial utilizes the CSB composite score, rather than the Groton Maze Learning task, as an identified key secondary outcome measure. It is possible that these or other differences between our completed Phase 2 clinical trial and our ongoing Phase 2b clinical trial of TC-5619 will impact the likelihood that the favorable findings in the completed trial will be replicated in the ongoing trial. If the favorable findings in the completed trial are not replicated in the ongoing trial or in any future trials of TC-5619 in schizophrenia patients that we conduct, we will not obtain the regulatory approval required to market and sell TC-5619 as a treatment for either or both of negative symptoms of schizophrenia or cognitive dysfunction in schizophrenia.

Replicating the favorable findings from our completed Phase 2 clinical trial of TC-5619 in cognitive dysfunction in schizophrenia may not be sufficient to obtain required regulatory approval of TC-5619, and any approval could be limited in a manner that adversely affects TC-5619's commercial potential.

As discussed above, in our completed Phase 2 trial in cognitive dysfunction in schizophrenia, TC-5619 met the protocol criteria for a positive result on the Groton Maze Learning task, the trial's primary outcome measure, but did not demonstrate a drug effect on the composite score on the CSB. It is unlikely that replicating a positive result on the Groton Maze Learning task in our ongoing Phase 2b clinical trial of TC-5619 and in any later-stage clinical trials that we conduct in the future would alone be acceptable to support approval from the FDA or foreign regulatory authorities to market and sell TC-5619 to treat cognitive dysfunction in schizophrenia.

In addition, the favorable findings in our completed trial of TC-5619 were driven substantially by outcomes at sites in the United States, as opposed to India, and by subjects who used tobacco, as TC-5619 did not demonstrate an effect in subjects who did not use tobacco. These differences, if replicated in any clinical trials that we conduct that are designed to support regulatory approval of TC-5619 as a treatment for either or both of negative symptoms of schizophrenia and cognitive dysfunction in schizophrenia, could have a negative impact on the likelihood of the FDA or foreign regulatory authorities granting approval to market and sell TC-5619 as a treatment for the applicable indication. Moreover, if the favorable findings in any clinical trials that we conduct that are designed to support regulatory approval are limited to subjects who use tobacco, the FDA or foreign regulatory authorities could limit the patient population for which TC-5619 is approved to tobacco users. Although it is believed that a substantial majority of schizophrenic patients use tobacco, if the patient population for which TC-5619 is approved were to be so limited, the commercial potential of TC-5619 could be materially and adversely affected.

We are developing TC-6987 in therapeutic areas in which we have limited experience, which may create additional risk that our development of this product candidate will not be successful.

We are currently conducting two Phase 2 clinical trials of TC-6987 that are designed to guide the selection of indications for which TC-6987 is best suited for later-stage development. One of the ongoing studies is in asthma and the other is in Type 2 diabetes. Asthma and Type 2 diabetes are both inflammatory disorders, and the ongoing studies are the first that we have conducted in this class of disorders. Moreover, neither asthma nor Type 2 diabetes is generally considered a disorder of the central nervous system, where substantially all of our prior clinical development has been focused. We have limited experience and expertise in inflammatory disorders and outside of the central nervous system generally. Our limited experience and expertise in this area may introduce additional uncertainty into the design and execution of our clinical trials for TC-6987 and create additional risk that we will not be successful in developing or potentially commercializing this product candidate.

If we or a collaborator of ours does 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 neither we nor any applicable collaborator of ours may ever 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;
- clinical trial results may indicate that the product candidate is not effective, whether because the product candidate does not have its intended effects in the clinical trial, because subjects given an inactive comparator (i.e., placebo) in the clinical trial experience benefits comparable to the benefits experienced by subjects given the product candidate, which obscures the effects of the product candidate, or for any other reason;
- the FDA (or any advisory committee on which the FDA relies) may interpret results of clinical trials or manufacturing or other non-clinical studies or assessments to indicate that the product candidate is not safe, effective or acceptable for commercial use, even if we or a collaborator of ours interprets the same results differently; or
- the FDA may deem the processes or 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 materially 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. This process is likely to cause delays in the marketing of any of our product candidates that receives approval and could materially and adversely impact our revenue and results of operations.

If clinical trials for our product candidates are not successful, neither we nor any applicable collaborator of ours will 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 any applicable 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. For example, TC-5214 did not achieve the primary endpoint in two Phase 3 clinical trials completed in 2011. If we or any applicable collaborator of ours experiences failures in our ongoing or future clinical trials, or if we or the collaborator 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 any applicable collaborator of ours may not be able to obtain authority or approval from the FDA, applicable foreign 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 a clinical trial is commenced, we or any applicable collaborator of ours, the FDA, applicable foreign regulatory authorities and 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 participating in the clinical trials are being exposed to unacceptable health risks or for other reasons.

If we or any applicable collaborator of ours does not prove in clinical trials that our product candidates are safe and effective, neither we nor the collaborator will obtain marketing approvals from the FDA or applicable foreign regulatory authorities. In particular, one or more of our product candidates may not exhibit the expected medical benefits in humans, may cause harmful side effects or may have other unexpected characteristics that preclude regulatory approval for any or all indications of use or limit commercial use if approved.

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 major depressive disorder, negative symptoms of schizophrenia, cognitive dysfunction in schizophrenia, ADHDi and Alzheimer’s disease. 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 clinical trials for any of our product candidates are prolonged or delayed, we and any applicable collaborator of ours would experience a delay in the commercialization of the affected product candidates, which may require us to incur additional costs and delay our receipt of any revenue from potential product sales.

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

- conditions imposed on us or any applicable collaborator of ours by the FDA or any foreign regulatory authority regarding the scope or design of the clinical trial;
- delays in recruiting and enrolling subjects into the clinical trial;
- 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 the clinical trial;
- insufficient supply or deficient quality of the product candidate or other materials necessary to conduct the clinical trial;
- lower than anticipated retention rate of subjects in the clinical trial;
- negative or inconclusive results from the clinical trial, or results that are inconsistent with earlier results, that necessitate additional study;

- serious and unexpected drug-related side effects experienced by subjects in the clinical trial; or
- failure of our or any of our collaborators' third-party contractors to comply with regulatory requirements or otherwise meet their contractual obligations to us or the collaborator 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 extent to which other clinical trials are being conducted concurrently that involve the same patient population, the number of participating clinical sites, the proximity of subjects to clinical sites, the nature of the trial protocol, the availability of effective treatments for the relevant disease, the eligibility criteria for the clinical trial and the emphasis placed on ensuring a rigorous adherence to the eligibility criteria. 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. For example, we experienced enrollment delays in our ongoing Phase 2 studies of TC-6987 in asthma and Type 2 diabetes that delayed our projected completion dates for the studies.

In addition, the FDA or foreign regulatory authorities could require us or any applicable collaborator of ours to conduct clinical trials for any of our product candidates with a larger number of subjects than we project. We or any applicable 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 analysis of those clinical trials.

We do not know whether any clinical trial of any of our product candidates will begin as planned, will need to be restructured or will be completed on schedule, if at all. Delays in clinical trials may 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 foreign regulatory authorities may require more preclinical or clinical data for any of our product candidates or more time to evaluate data than we currently anticipate because drugs that act on NNRs are not a well established class of drugs, because nicotine, which interacts with all nicotinic receptors, has addictive properties and potential for abuse, because of experiences with drugs that act on NNRs that are developed or marketed by third parties or for any other reason. In particular, the FDA has issued a public health advisory with regard to Pfizer's aid to smoking cessation product, Chantix, and requires Chantix (as well as Zyban, which is GlaxoSmithKline's aid to smoking cessation product) to include a boxed warning on its prescribing information. The warning makes prominent the risk of serious mental health events, including changes in behavior, depressed mood, hostility, agitation and suicide-related events, that have been reported in some patients attempting to quit smoking while taking these drugs. Chantix acts on several NNR subtypes, as well as other molecular targets in the body. All of our product candidates currently in development affect the activity of one or more NNR subtypes.

It is uncertain whether any adverse medical experiences associated with Chantix will impact the view of the FDA or foreign regulatory authorities regarding our product candidates. 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 or that compounds that interact with NNRs may have potential for abuse, it may require us or any applicable collaborator of ours to generate more clinical data than we currently anticipate to establish that the affected product candidate is safe or does not have abuse potential, 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 Special Protocol Assessment agreement with the FDA for our ongoing Phase 2b clinical trial of AZD3480 in mild to moderate Alzheimer's disease does not guarantee regulatory approval or any particular outcome from any future regulatory review of AZD3480.

We have obtained a Special Protocol Assessment, or SPA, agreement with the FDA for our ongoing Phase 2b clinical trial of AZD3480 in mild to moderate Alzheimer's disease. The purpose of an SPA is to reach agreement with the FDA on the protocol design and statistical analysis for clinical trials that will form the primary basis of an efficacy claim or, in other words, be pivotal. Our SPA with the FDA provides that the ongoing Alzheimer's disease trial will not alone be sufficient to support regulatory approval for AZD3480. If an NDA is submitted by us or AstraZeneca following completion of the ongoing trial and any additional clinical trials of AZD3480 that we or AstraZeneca conduct in mild to moderate Alzheimer's disease, the NDA may not be approved by the FDA notwithstanding our SPA, even if we or AstraZeneca believe that the data from the trials support approval. Approval of an NDA for AZD3480 is not guaranteed because a final determination by the FDA that an agreed-upon protocol satisfies a specific objective, such as the demonstration of efficacy, or supports an approval decision will be based on a complete review of all of the data in the NDA. The FDA retains significant latitude and discretion in interpreting the terms of an SPA, the data and results from clinical trials and all other information included in the NDA. For example, the FDA may require trial design changes or additional studies if issues arise that it believes to be relevant to determining safety or efficacy, the FDA may reconsider the agreed upon scope of review based on data that subsequently becomes available and the FDA may raise safety or efficacy concerns that arise after grant of the SPA that override it. In particular, the FDA may determine that our ongoing study of AZD3480 in mild to moderate Alzheimer's disease, which we are conducting at sites predominantly in Eastern Europe and also in the United States, did not when completed include a sufficient number of subjects at sites in the United States to support regulatory approval to market and sell AZD3480. As a result, even with an SPA, we cannot be certain that the FDA will find any particular clinical trial results acceptable to support regulatory approval to market and sell AZD3480.

Each of our product candidates will remain subject to ongoing regulatory review even if it receives 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 or any applicable collaborator could lose the approval or the sale of the affected 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 or the collaborator 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 any applicable collaborator of ours to withdraw it from the market or impede or delay the ability of us or the collaborator to obtain regulatory approvals in additional countries. If any of our product candidates that becomes an approved product either causes adverse medical experiences or becomes associated with a third-party product that is associated with adverse medical experiences such as those related to Chantix described above under "*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 overall commercial success of the affected product may be negatively impacted.

In addition, if any of our product candidates becomes an approved product, 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 recordkeeping related to the product will remain subject to extensive regulatory requirements. We or any applicable collaborator of ours may be slow to adapt, or may never adapt, to changes in existing regulatory requirements or adoption of new regulatory requirements.

The Commissioner of the FDA, who was appointed during 2009, has indicated that more enforcement actions in all areas regulated by the FDA should be expected. Although we have not received any notice that we

are the subject of any such enforcement action it is possible that we may be in the future and that could have a material adverse effect on our business. If we or any applicable collaborator of ours fails 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 or product candidates, manufacturers or manufacturing processes are discovered, we or the collaborator 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 apply our finite resources to pursue a particular product candidate or indication, fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success, or relinquish valuable rights to our disadvantage.

Because we have finite 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. Furthermore, if we do not accurately evaluate the commercial potential or target market for a particular product candidate, or if we incorrectly conclude that utilizing the expertise and resources of a collaborator in the development or potential commercialization of a particular product candidate would benefit us, we may relinquish valuable rights to that product candidate through strategic alliances, collaborations or licensing or other comparable arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights. Any of these decisions or conclusions could have a material adverse effect on our business.

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. 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 overcome attrition inherent in drug development and generate revenue in future periods, which could result in significant harm to our financial position and materially and adversely impact our stock price. Any additional product candidates that we are able to develop through our internal research programs will require the commitment of substantial time and financial resources for further preclinical research and clinical development.

Risks Related to Our Dependence on Third Parties

The successful development and commercialization of TC-5214 depends substantially on our collaboration with AstraZeneca for that product candidate.

Our TC-5214 agreement with AstraZeneca involves a complex allocation of rights and responsibilities, provides for milestone payments to us if specified development, regulatory and first commercial sale milestone events are achieved and provides us with royalty-based revenue if TC-5214 is successfully commercialized. AstraZeneca has decision-making authority for many matters under the agreement. AstraZeneca also has the right to assume control of patent matters with respect to TC-5214 and has exercised its right with respect to the prosecution of some of the applicable patents.

AstraZeneca is responsible for the conduct of substantially all development of TC-5214, except for non-clinical studies that were ongoing at the inception of our agreement, and has control or significant influence over the conduct and timing of development efforts with respect to TC-5214. AstraZeneca has engaged a global contract research organization to manage the current development program for TC-5214. We have little control over the amount and timing of resources that AstraZeneca or the contract research organization with which it has contracted devotes to the development of TC-5214. If AstraZeneca or its contract research organization fails to devote sufficient financial and other resources to its development, the development and potential commercialization of TC-5214 would be delayed. This would result in a delay in potential milestone payments and, if regulatory approval to market and sell TC-5214 is obtained, royalties that we could receive on any future TC-5214 product sales.

AstraZeneca has the right to terminate our TC-5214 agreement in its entirety:

- within a specified period following completion of the Phase 3 development program for TC-5214 as an adjunct therapy;
- if AstraZeneca determines there to be a serious safety issue regarding the continued development or commercialization of TC-5214;
- if, having obtained the advice of independent patent counsel, AstraZeneca believes that the commercialization of TC-5214 is more likely than not to infringe or misappropriate intellectual property rights of third parties in the United States or any two specified major pharmaceutical markets and is unable to obtain a license on commercially reasonable terms; or
- for an uncured material breach of the agreement by us or our insolvency.

In addition, AstraZeneca can terminate our agreement on a major pharmaceutical market by major pharmaceutical market basis at any time beginning four years after effectiveness of our agreement, except that, if AstraZeneca terminates our agreement with respect to the United States, our agreement will terminate in its entirety.

Termination of our TC-5214 agreement by AstraZeneca at any time could negatively impact our business. In particular, we would have to fund any further clinical development and potential commercialization of TC-5214 on our own, which could accelerate our need for additional capital, or alternatively seek another collaborator or licensee for clinical development and commercialization or abandon the development and commercialization of TC-5214.

If TC-5214 exhibits a similar overall therapeutic profile to AstraZeneca's product Seroquel XR, AstraZeneca may de-emphasize the development or commercialization of TC-5214, which would materially and adversely affect the revenue that we derive based on TC-5214.

AstraZeneca's product Seroquel XR is approved by the FDA for use, among other things, as an adjunct to antidepressant therapy for major depressive disorder. TC-5214 is in development as an adjunct to antidepressant therapy and as a "switch" monotherapy for major depressive disorder. Until the Phase 3 development program for TC-5214 is completed and regulatory approval is obtained, the overall therapeutic profile of TC-5214 and any patient population for which TC-5214 may be considered safe and effective are uncertain. AstraZeneca has control or significant influence over the conduct of future development and regulatory approval activities for TC-5214. If the Phase 3 clinical trials of TC-5214 indicate that its overall therapeutic profile may be similar to the overall therapeutic profile of Seroquel XR, AstraZeneca may de-emphasize or otherwise fail to devote sufficient financial and other resources to the development of TC-5214. In that event, the development and potential commercialization of TC-5214 would be delayed. This would result in a delay of milestone payments and, if regulatory approval to market and sell TC-5214 is obtained, royalties on product sales that we could receive and could result in us not receiving milestone payments or royalties at all. Even if TC-5214 is successfully developed and regulatory approvals are obtained, if AstraZeneca de-emphasizes or otherwise fails to devote sufficient financial and other resources to the commercialization of TC-5214 for any reason, the amount of royalties that we could receive on any future TC-5214 product sales would be materially and adversely affected.

The successful development and commercialization of AZD3480 and AZD1446 depends substantially on our collaboration with AstraZeneca focused in cognitive disorders. AstraZeneca may decide not to conduct any further development of either or both of AZD1446 and AZD3480, irrespective of the outcome of our ongoing Phase 2b clinical trial of AZD3480 in mild to moderate Alzheimer's disease.

Our cognitive disorders agreement with AstraZeneca involves a complex allocation of rights, provides for milestone payments to us if specified development, regulatory and first commercial sale milestone events are achieved and provides us with royalty-based revenue if AZD3480, AZD1446 or another product candidate in the collaboration is successfully commercialized. AstraZeneca has decision-making authority for most matters under the agreement, including, provided it meets its diligence obligations, whether to proceed with further development and potential commercialization of any particular product candidate in the collaboration and, if so, for what indication(s). Under the terms of the agreement, we are not permitted to conduct development of AZD3480 or AZD1446 (or any other product candidate in the collaboration) independently or with another collaborator, with the exception that we are entitled to conduct our ongoing Phase 2b clinical trial of AZD3480 in mild to moderate Alzheimer's disease. AstraZeneca had previously been considering whether to conduct further development of AZD3480 in ADHD, but determined not to do so in light of reservations about the adequacy of the therapeutic margin for that indication. Following completion of our ongoing study and irrespective of the outcome, AstraZeneca may likewise decide not to conduct any further development of AZD3480 in Alzheimer's disease. With regard to AZD1446, although we have been informed by AstraZeneca that it plans to progress the development of AZD1446 as a treatment for Alzheimer's disease, AstraZeneca may subsequently decide not to do so.

AstraZeneca has significant control and we have little control over the conduct and timing of development efforts for AZD1446 and, other than our ongoing Phase 2b clinical trial in mild to moderate Alzheimer's disease, for AZD3480. If AstraZeneca fails to devote sufficient financial and other resources to the development of either or both of AZD3480 and AZD1446, the development and potential commercialization of the affected product candidate(s) would be delayed. This would result in a delay in potential milestone payments and, if regulatory approval to market and sell AZD3480 or AZD1446 is obtained, royalties that we could receive on any future AZD3480 or AZD1446 product sales.

AstraZeneca has the right to terminate our cognitive disorders agreement in its entirety upon 90 days notice. Termination of the agreement by AstraZeneca at any time could negatively impact our business. In particular, we

would have to fund any further clinical development and commercialization of AZD3480 and AZD1446 on our own, which could accelerate our need for additional capital, or alternatively seek another collaborator or licensee for clinical development and commercialization or abandon the development and commercialization of AZD3480 and AZD1446.

AstraZeneca's plans to restructure its research and development may increase the likelihood that it will cease further development of either or both of AZD1446 and, upon completion of our ongoing Phase 2b clinical trial of AZD3480 in mild to moderate Alzheimer's disease, AZD3480.

In February 2012, AstraZeneca announced plans to restructure its research and development function, with a focus for much of the change on its neuroscience therapy area. Whether the restructuring will have any effect on AstraZeneca's plans to progress the development of AZD1446 or on the likelihood that AstraZeneca will conduct further development of AZD3480 following completion of our ongoing study is uncertain. If at any time AstraZeneca decides not to conduct further development of either or both of AZD3480 or AZD1446 and its determination does not result in a failure to meet its diligence obligations under the agreement, we would not benefit from any commercial potential of the affected product candidate(s).

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 our collaborations with AstraZeneca, we intend to selectively enter into alliances and collaborations, particularly for target indications for which a potential collaborator has unique 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 collaborations with AstraZeneca, 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 pursue further development and commercialization of our product candidates for indications that we do not believe are optimal, may not pursue further development and commercialization of our product candidates at all 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 a reallocation of internal funds or additional capital to pursue further development of the applicable product candidates. For example, our product development and commercialization agreement with GlaxoSmithKline was terminated effective in May 2011, which led us to reallocate internal resources.

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. 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 particularly for target indications for which a potential collaborator has unique expertise or that involve large primary care markets that must be served by large sales and marketing organizations.

Under the terms of our cognitive disorders agreement with AstraZeneca, 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 a4b2 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 former right to license TC-5619. However, if we do not offer a compound that meets pre-defined criteria for any NNR other than the a4b2 NNR to AstraZeneca, we are generally not permitted to develop or commercialize the compound for any of these indications. Similarly, under the terms of our TC-5214 agreement with AstraZeneca, for three years from the date the collaboration agreement became effective, we are not permitted to conduct a Phase 2 or later-stage clinical trial of a compound as an adjunct treatment (or any other term reflecting the concurrent use of two or more pharmaceutical products) for major depressive disorder, or to commercialize such a compound. As a result, our ability to seek additional alliances and collaborations for the target indications for our two collaborations with AstraZeneca is substantially limited. In addition, AstraZeneca may under certain circumstances have a right of first negotiation under our cognitive disorders agreement for the development and commercialization of compounds that act by binding to NNRs for depression, anxiety and bipolar disorder.

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 AstraZeneca's contract manufacturer for TC-5214 fails to devote sufficient resources to TC-5214, or if its performance is substandard, any future clinical trials and any product introductions of TC-5214 may be delayed or there may be a shortage of supply.

Under the terms of our TC-5214 agreement with AstraZeneca, AstraZeneca is responsible for the manufacture and supply of TC-5214 and has assumed our rights and obligations under our applicable agreements with third parties, including a supply agreement with Poli Industria Chimica, S.p.A., or Poli (acquired by Euticals S.p.A.), and Interchem Corporation, or Interchem, for the pharmaceutical development and supply of the active ingredient form of TC-5214. The agreement with Poli and Interchem assumed by AstraZeneca provides for it to purchase its requirements for the active ingredient form of TC-5214 exclusively from Poli through Interchem during the term of the agreement, subject to specified conditions. Because of the exclusive supply relationship, if Poli breaches or fails to perform as agreed under the agreement, or if the agreement terminates for any reason, there may be a delay or interruption in manufacturing of TC-5214 that leads to a shortage of supply. If AstraZeneca were to have the right to change the manufacturer for the active ingredient form of TC-5214 and were to make the change for any reason, in addition to the risks associated with changing a contract manufacturer described below under "*If the performance of our contract manufacturers or any present or future collaborator of ours with manufacturing responsibility for a particular product candidate is substandard, our clinical trials and product introductions may be delayed or there may be a shortage of commercial supply.*," it would be dependent on Poli to effect or facilitate a successful transfer of the manufacturing technology for TC-5214 to AstraZeneca or a replacement contract manufacturer. Such a technology transfer would require review and approval by the FDA or foreign regulatory authorities and would also likely require an inspection of the new manufacturer to assess compliance with current good manufacturing practices, or cGMP, mandated by the FDA or foreign regulatory authorities, both of which would be time-consuming and increase the likelihood of a delay or interruption in manufacture or a shortage of supply of TC-5214. Any delay or interruption in manufacture or shortage of supply of TC-5214 could delay or prevent the initiation or completion of clinical trials of TC-5214, the submission of applications for regulatory approvals of TC-5214 or the receipt of regulatory approvals for TC-5214, materially and adversely affect the commercialization of TC-5214 or result in higher costs or lost product revenue.

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 and applicable collaborators for our product candidates depend on independent clinical investigators and, in many 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 guidelines, commonly referred to as good clinical practice, or GCP, 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, we have conducted trials of multiple product candidates at sites in India and we and AstraZeneca are conducting the Phase 3 clinical program for TC-5214 at sites in five continents around the world. Also, we are conducting our ongoing Phase 2b

trials of TC-5619 in negative symptoms and cognitive dysfunction in schizophrenia and AZD3480 in mild to moderate Alzheimer's disease at sites in Eastern Europe, as well as in the United States.

Language barriers and the limited experience of some clinical investigators in India, Eastern Europe or other countries in conducting clinical trials in accordance with standards set forth by the FDA and applicable regulatory authorities 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 the performance of our contract manufacturers or any present or future collaborator of ours with manufacturing responsibility for a particular product candidate 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 early-stage preclinical testing and have contracted with third parties to manufacture, in collaboration with us, our product candidates for clinical trials. 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 our now discontinued product Inversine and its active ingredient.

AstraZeneca has all manufacturing responsibility for TC-5214 under our TC-5214 agreement and substantial manufacturing responsibility for AZD3480 and AZD1446 under our cognitive disorders agreement. For each of our other product candidates, we typically rely on single third-party contract manufacturers for manufacturing in drug substance form and single third-party contract manufacturers for manufacturing in a formulation for use in clinical trials. We intend to continue to rely on third-party manufacturers (or, where applicable, AstraZeneca or other current or potential future collaborators) 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 or collaborators 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 or applicable collaborator of ours could:

- encounter difficulties in achieving volume production, laboratory testing, quality control or quality assurance or suffer shortages of qualified personnel, any of which could result in its inability to manufacture sufficient quantities to meet clinical timelines for a particular product candidate, obtain approval to market and sell the product candidate or to commercialize the product candidate; or
- fail to establish and follow cGMP 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.

In addition, any contract manufacturer could:

- terminate or not renew its manufacturing agreement with us or with any applicable collaborator of ours, based on its own business priorities, at a time that is costly or inconvenient for us; or
- breach, or fail to perform as agreed under, the applicable manufacturing agreement.

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 or any applicable collaborator of ours engages for a particular product or product candidate may be difficult, as the number of potential manufacturers is limited and

we or the collaborator 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 or any applicable collaborator of ours may not be able to engage replacement manufacturers on acceptable terms quickly or at all. In addition, contract manufacturers located in foreign countries may be subject to import limitations or bans. As a result, if any contract manufacturer or applicable collaborator of ours is unable, for whatever reason, to supply the contracted amounts of any product that is successfully brought 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 or any applicable collaborator of ours is obligated to audit the performance of third-party contractors, we do not have control over third-party manufacturers' compliance with these regulations and standards. Failure by us, any applicable collaborator of ours or any third-party manufacturers 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.

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 the ability of us or any applicable collaborator of ours 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 diseases and disorders.

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 product candidates and technology will depend on the success that we or any applicable collaborator of ours has 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.* has in some cases made it more difficult to obtain a patent, or to withstand a validity challenge to an issued patent, for pharmaceutical products that have a relationship to other pharmaceutical products, such as single enantiomers of a previously known racemate, combination products or specific salt forms. TC-5214 is a single enantiomer of a previously known racemate. 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 materially and 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 patent covering one of our product candidates may expire before the product candidate can be commercialized or remain in force for only a short period following initial commercialization. In either case, any advantages of the patent would be limited. 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 and, if we have sublicensed our license rights to a third party, the loss of the license rights may breach our obligations to our sublicensee.

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 from University of South Florida Research Foundation and Yale University and have sublicensed these patent rights to AstraZeneca. In addition, we license patent rights from Cornerstone Therapeutics Inc. that cover the use of compounds that act on a7 NNRs to treat described inflammatory conditions. 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, whether as a result of actions or inactions by us, by AstraZeneca (with respect to TC-5214) or by any other present or future collaborator of ours to which we out-license patent rights that we have in-licensed from a third party, 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. In addition, the failure to comply with our obligations under our license agreement with University of South Florida Research Foundation or our license agreement with Yale University could constitute a breach of our obligations under our TC-5214 agreement with AstraZeneca. A material breach by us of our TC-5214 agreement with AstraZeneca would give rise to various remedies for AstraZeneca that could have a material adverse effect on our business.

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 or any of our applicable collaborators 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 or any of our applicable collaborators 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 materially and 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 another company, Cary Pharmaceuticals Inc., may be 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, which we are no longer commercializing. 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 materially and 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 similarly be 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, regardless of their merit, lack of merit or eventual outcome, would be costly and a significant diversion of our technical personnel's and management's attention from conducting our business, which would harm 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 material 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 allegedly 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 allegedly 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 materially and 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 material 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 foreign regulatory authorities.

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, or if we enter into such arrangements with third parties who do not perform well, we may not be successful in commercializing our products.

We currently have limited sales, marketing and distribution experience and 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, such as our collaborations with AstraZeneca. In particular, our strategy includes selectively entering into strategic alliances and collaborations with respect to product candidates for indications that require service by large sales and marketing organizations. 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 have little control over AstraZeneca’s performance under our existing collaboration agreements and would have little control over the performance of other potential future collaborators, any of which 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 any applicable collaborator of ours 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 for which regulatory approval is obtained will also depend in part on the extent to which coverage and adequate payment is available from government health programs, such as Medicare and Medicaid, private health insurers and other third-party payors. If we or any applicable collaborator of ours succeeds in bringing a product candidate to the market, it may not be considered cost-effective and reimbursement may not be available or sufficient to allow us or the collaborator 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 any applicable collaborator of ours 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 materially and adversely 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. In particular, the Patient Protection and Affordable Care Act, or the PPACA, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, is expected to substantially change the way health care is financed by both governmental and private insurers. The PPACA contains a number of provisions that could impact our business and operations, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse. We cannot predict the impact of the PPACA on us because many of the PPACA's reforms require the promulgation of detailed regulations to implement the statutory provisions, which has not yet occurred. Also, current legal challenges to the PPACA, as well as congressional efforts to repeal the PPACA, add to the uncertainty of the effects of the PPACA.

In recent years there have been other legislative and regulatory proposals to change the healthcare system in the United States and other major healthcare markets proposed and adopted in recent years and there will likely continue to be proposals by legislators at both the federal and state levels, regulators and third-party payors to keep pharmaceutical costs down while expanding individual healthcare benefits. Certain of these changes could impose additional limitations on the price that we or our applicable collaborator will be able to charge for any of our product candidates that receives regulatory approval or on the amount of reimbursement available for such approved product from governmental agencies or third-party payors. For example, The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. While the specific effects that existing or any future healthcare reform legislation or policies will have on our business is not yet known, reductions in third-party reimbursement for any of our product candidates that is successfully developed and approved or a decision by a third-party payor to not cover any of our product candidates that is successfully developed and approved could reduce prescriptions by physicians of the product candidate and have a material 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 or any applicable collaborator of ours does;
- adapt more quickly to new technologies and scientific advances than we or any applicable collaborator of ours;
- initiate or withstand substantial price competition more successfully than we or any applicable collaborator of ours does;
- have greater success in recruiting skilled scientific workers from the limited pool of available talent than we do;
- 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, Abbott Laboratories, Eli Lilly, Sanofi-Aventis, Bristol-Myers Squibb, Johnson & Johnson, Novartis, NeuroSearch A/S, Solvay, Servier, CoMentis, EnVivo Pharmaceuticals, Galantos Pharma, Proximagen, Psychogenics, Suven, Asmacure and Neuroderm. 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 pursue the development and commercialization of therapeutics for nervous system diseases and disorders, whether independently or by alliance, collaboration or acquisition.

Any products that we or any applicable collaborator of ours is 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 or any applicable collaborator of ours 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:

- as an adjunct treatment for major depressive disorder, the atypical antipsychotics Seroquel XR from AstraZeneca and Abilify from Bristol-Myers Squibb/Otsuka;
- otherwise for major depressive disorder, SSRIs such as Prozac from Eli Lilly, Paxil/Seroxat 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 the SSRI and $5HT_{1A}$ receptor partial agonist Viibryd from Forest Laboratories;
- for ADHDi, 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; these products are approved for the treatment of ADHD generally and not ADHDi specifically;
- for asthma, long-acting beta agonist/inhaled corticosteroid combinations such as Advair from GlaxoSmithKline, Symbicort from AstraZeneca and Dulera from Merck, leukotriene inhibitors such as Singulair from Merck, Accolate from AstraZeneca and Zyflo from Cornerstone Therapeutics, antibodies such as Xolair from Novartis, long-acting beta agonists such as salmeterol and formoterol and short-acting beta agonists such as albutertol and levalbuterol;
- for Type 2 diabetes, glucagon-like peptide-1 analogues such as Byetta from Eli Lilly and Amylin, dipeptidyl peptidase IV inhibitors such as Januvia from Merck and Onglyza from Bristol-Myers Squibb and AstraZeneca, insulin such as Lantus from Sanofi-Aventis, sulfonylureas such as Glucotrol from Pfizer, and biguanides (metformin) such as Glucophage from Bristol-Myers Squibb; and
- 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.

There is currently no product approved in the United States or Europe specifically for the treatment of negative symptoms of schizophrenia or cognitive dysfunction in schizophrenia. There are however multiple third-party product candidates currently in clinical development targeting these areas, including modulators of the a7 NNR.

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, lack of merit or eventual outcome, would be a significant diversion of our management’s attention from conducting our business and could be costly or materially and adversely affect our reputation or 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 successfully 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 applicable foreign 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 foreign regulatory authorities. 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. If we undertake any promotional activities in the future for any product candidate for which we receive regulatory approval 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

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. Our executive officers, including Dr. deBethizy, 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, which has been adversely impacted by the substantial decline in our stock price that we experienced in November 2011 following the announcement of top-line results from the first Phase 3 clinical trial of TC-5214. We face intense competition for skilled executives in our industry. We may not be able to continue to attract and retain personnel with the advanced qualifications necessary for the growth of our business.

Risks Related to Our Common Stock

The market price of our common stock has historically been highly volatile.

The trading price of our common stock has historically been highly volatile. For example, our stock price declined significantly following the November 2011 announcement of top-line results from the first Phase 3 clinical trial of TC-5214. In addition, 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 operating performance. 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:

- whether and to what extent milestone events are achieved for TC-5214 under our TC-5214 agreement with AstraZeneca;
- the outcomes from Phase 3 clinical development of TC-5214 and the amount and timing of costs for ongoing or any future development of TC-5214 payable by us;
- whether and to what extent milestone events are achieved for either or both of AZD3480 and AZD1446 under our cognitive disorders agreement with AstraZeneca;
- the scope, progress, duration, results and cost of clinical trials, as well as non-clinical studies and assessments, of TC-5619, TC-6987, AZD3480, AZD1446 and our other product candidates and programs;
- our inability, or the inability of AstraZeneca 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 expiration or termination of either of our agreements with AstraZeneca or with any potential future collaborator;
- whether we establish additional strategic alliances, collaborations or licensing or other comparable arrangements, or whether we pursue and complete any merger, acquisition or other significant corporate transactions, and, if we do, the associated terms in each case;
- the extent to which we retain development and commercialization rights or responsibilities for our product candidates that are not subject to either of our collaborations with AstraZeneca and incur associated development and manufacturing costs and costs to establish sales and marketing functions;
- the cost, timing and outcomes of regulatory approvals or other regulatory actions;
- the extent and scope of our general and administrative expenses;
- the number and characteristics of product candidates that we pursue and programs that we conduct;
- general and industry-specific economic conditions that may affect the research and development expenditures of AstraZeneca or any of our potential future collaborators; 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. For 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.

Our current trading volumes are modest, and 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, acquisitions or other transactions 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.

Provisions of our collaboration agreements with AstraZeneca or provisions of our charter, bylaws or Delaware law may discourage or make an acquisition of us or a change in our management more difficult.

Under each of our TC-5214 agreement with AstraZeneca and our cognitive disorders agreement with AstraZeneca, AstraZeneca may elect to terminate certain aspects of the agreement if there were to be a “change of control” of us, as that term is defined in the applicable agreement. In particular, AstraZeneca may elect to terminate our co-promotion rights under each agreement. These rights of AstraZeneca could discourage, delay or prevent a merger, acquisition or other change of control of us involving a third party that stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These rights 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.

Provisions of our certificate of incorporation and bylaws could have a similar deterrent effect on a merger, acquisition or other change of control of us and could also 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 are 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 or otherwise 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 79,000 square feet of laboratory and office space located in the Piedmont Triad Research Park in Winston-Salem, North Carolina. The term of our lease expires July 31, 2012, and we are currently in discussions with the landlord regarding terms for a potential extension. The current monthly payment under our lease is approximately $208,000. We believe our laboratory and office space is suitable for its intended purpose.

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. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

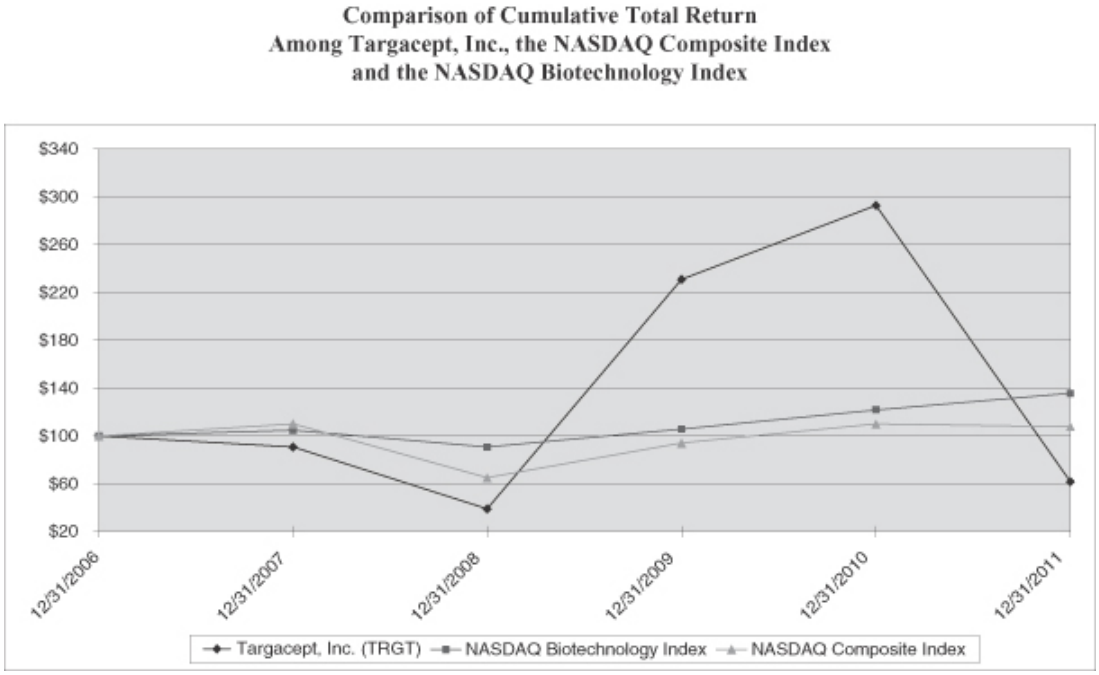
Our common stock currently trades on the NASDAQ Global Select Market under the symbol "TRGT." The following table sets forth, for the periods indicated, the high and low sales prices for our common stock:

		High	*Low*
2010:			
	First Quarter	$21.35	$18.29
	Second Quarter	$25.00	$19.25
	Third Quarter	$23.59	$17.80
	Fourth Quarter	$27.65	$20.50
2011:			
	First Quarter	$30.47	$24.45
	Second Quarter	$26.92	$20.48
	Third Quarter	$22.40	$14.42
	Fourth Quarter	$19.54	$ 4.91

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 Regulation 14A or 14C, other than as provided in Item 201 of Regulation S-K, or 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 December 31, 2006 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.



	12/31/06	12/31/07	12/31/08	12/31/09	12/31/10	12/31/11
Targacept, Inc.	100	91	39	231	293	62
NASDAQ Biotechnology Index	100	105	91	106	122	136
NASDAQ Composite Index	100	110	65	94	110	108

Stockholders

As of February 29, 2012, there were approximately 52 holders of record of our common stock. Because many of our shares are held by brokers or other nominees on behalf of beneficial owners, we are unable to determine precisely the total number of beneficial owners represented by the holders of record. As of February 29, 2012, we estimate the total number of beneficial owners of our common stock whose shares are held by brokers or other nominees on their behalf to be approximately 5,585.

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 as of the determination date were held by non-affiliates, except for shares held by our executive officers, directors and their affiliated entities. In particular, we have assumed that any stockholder that held 10% or more of our outstanding common stock as of the determination date and is not affiliated with a director was a non-affiliate and expect that we would also make that assumption in the future unless there exists facts and circumstances that indicate that the 10% or greater stockholder exercises control over us. This assumption is not intended to constitute an admission that all executive officers and directors, and any 10% or greater stockholder treated as an affiliate for this purpose, 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, 2011, 2010 and 2009 and the balance sheet data as of December 31, 2011 and 2010 from our audited financial statements included in this annual report. We derived the statements of operations data for the years ended December 31, 2008 and 2007 and the balance sheet data as of December 31, 2009, 2008 and 2007 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,				
	2011	2010	2009	2008	2007
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Net operating revenues	$ 97,637	$ 85,713	$ 25,062	$ 20,085	$ 11,576
Operating expenses:					
Research and development	95,215	64,546	40,179	40,981	34,620
General and administrative	12,167	8,052	8,167	6,499	8,013
License fees and royalties	—	—	16,350	—	—
Cost of product sales	—	—	691	749	715
Total operating expenses	107,382	72,598	65,387	48,229	43,348
(Loss) income from operations	(9,745)	13,115	(40,325)	(28,144)	(31,772)
Interest income	1,348	1,463	1,050	2,734	3,837
Interest expense	(132)	(153)	(217)	(251)	(138)
(Loss) income before income taxes	(8,529)	14,425	(39,492)	(25,661)	(28,073)
Income tax (expense) benefit	—	(3,526)	88	—	—
Net (loss) income	$ (8,529)	$ 10,899	$ (39,404)	$ (25,661)	$ (28,073)
Basic net (loss) income per share	$ (0.27)	$ 0.38	$ (1.54)	$ (1.04)	$ (1.42)
Diluted net (loss) income per share	$ (0.27)	$ 0.36	$ (1.54)	$ (1.04)	$ (1.42)
Weighted average common shares outstanding—basic	31,637,283	28,543,408	25,636,419	24,664,169	19,720,732
Weighted average common shares outstanding—diluted	31,637,283	30,150,324	25,636,419	24,664,169	19,720,732

	As of December 31,				
	2011	2010	2009	2008	2007
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and investments	$ 249,270	$ 252,509	$ 111,066	$ 88,363	$ 87,040
Working capital	120,082	119,422	213,269	78,174	77,217
Total assets	258,126	262,787	319,379	98,551	98,965
Long-term debt, net of current portion	1,986	1,349	1,966	3,408	1,686
Accumulated deficit	(226,930)	(218,401)	(229,300)	(189,896)	(164,235)
Total stockholders' equity	174,288	91,847	68,991	57,373	51,584

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 what is 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," which precedes Part I of 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 novel NNR Therapeutics for the treatment of diseases and disorders of the nervous system. Our NNR Therapeutics selectively target a class of receptors known as neuronal nicotinic receptors, which we refer to as 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, TC-5619, TC-6987, AZD3480 (TC-1734) and AZD1446 (TC-6683), and they are discussed under the caption "Business" in Item 1 of Part I of this annual report.

We have two collaboration agreements with AstraZeneca, one that we entered into in December 2009 for the global development and commercialization of TC-5214 as a treatment for major depressive disorder and refer to in this annual report as our "TC-5214 agreement with AstraZeneca" and the other focused in cognitive disorders that we entered into in December 2005 and refer to in this annual report as our "cognitive disorders agreement with AstraZeneca."

Under our TC-5214 agreement with AstraZeneca, AstraZeneca is responsible for 80% and we are responsible for 20% of the cost of the clinical program for TC-5214, except that AstraZeneca is responsible for 100% of development costs that are required only to obtain or maintain regulatory approval in countries outside the United States and the European Union. We have the right to terminate our obligation to fund our share of the costs of the program once we have funded a specified amount. In addition, for each of us and AstraZeneca, costs that were not contemplated at execution to be part of the program may in some cases be excluded from the cost-sharing arrangement. If we fund the specified amount and terminate our obligation to fund our share of further costs of the program, any future milestones and royalties payable to us under the agreement would be reduced by the amount of our unfunded share plus interest at a specified rate, subject to a maximum reduction that may be applied to any one payment. AstraZeneca is responsible for executing and funding the costs of any commercialization of TC-5214 worldwide.

Under our cognitive disorders agreement with AstraZeneca:

- AstraZeneca has an exclusive license to AZD3480, AZD1446 and earlier-stage compounds that arose from the preclinical research collaboration conducted under the agreement;
- except as discussed in the next bullet, AstraZeneca is responsible for substantially all future development costs for AZD3480, AZD1446 and each other compound arising from the preclinical research collaboration described below that it elects to advance;
- we are responsible for conducting and funding our ongoing Phase 2b clinical trial of AZD3480 as a treatment for mild to moderate Alzheimer's disease, but have received $6.2 million in payments from AstraZeneca in connection with events associated with the study; and
- from January 2006 to January 2010, we and AstraZeneca conducted a preclinical research collaboration under the agreement to discover and develop compounds that act on the a4ß2 NNR as treatments for conditions characterized by cognitive impairment; AstraZeneca paid us research fees, based on a reimbursement rate specified under the agreement, for research services rendered in the preclinical research collaboration.

In addition to our two collaboration agreements with AstraZeneca, we previously had a product development and commercialization agreement with GlaxoSmithKline. We received notice of termination of the agreement from GlaxoSmithKline in February 2011, and by the terms of the agreement, the termination became effective in May 2011.

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 R.J. Reynolds Tobacco Company. 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 public and private offerings of equity securities, payments under collaboration and alliance agreements, grants and equipment 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.

Except for the quarterly period ended March 31, 2011 and a small number of earlier periods in which we generated net income due primarily to the recognition into revenue of amounts received under collaboration agreements, we have not been profitable. As of December 31, 2011, we had an accumulated deficit of $226.9 million. We may incur losses in future periods as our clinical-stage and preclinical product candidates advance into later-stage development and as we progress our programs, invest in additional product opportunities and grow our business. Drug development, including clinical trials in particular, is time-consuming, expensive and may never yield a product that will generate revenue.

As a clinical-stage company, our revenues, expenses and results of operations are likely to fluctuate significantly from quarter to quarter and year to year. We believe that period-to-period comparisons of our results of operations should not be relied upon as indicative of our future performance.

Revenue

In January 2010, we received a $200.0 million upfront payment under our TC-5214 agreement with AstraZeneca, which we recorded as deferred revenue and are recognizing into revenue on a straight-line basis over the estimated development period for TC-5214 to a potential submission of an NDA to the FDA. As of December 31, 2011, $54.5 million of the upfront payment remained to be recognized into revenue.

Pursuant to an April 2010 amendment to our cognitive disorders agreement with AstraZeneca related to an expansion of the development program for TC-5619, we received an $11.0 million payment in May 2010, which we recorded as deferred revenue and recognized into revenue on a straight-line basis over the estimated period of our research and development obligations for TC-5619 under the agreement. We completed our research and development obligations for TC-5619 in the second quarter of 2011. Pursuant to a September 2010 amendment to our cognitive disorders agreement with AstraZeneca related to a clinical trial of AZD3480 in mild to moderate Alzheimer’s disease, we received a $500,000 payment in the fourth quarter of 2010 and cumulative payments of $5.5 million in the second half of 2011, all of which we recorded as deferred revenue and are recognizing into revenue on a straight-line basis over the estimated period of our obligations with respect to the study.

As of December 31, 2011, we had received $61.6 million in aggregate upfront fees and milestone payments under our cognitive disorders agreement with AstraZeneca and recognized an additional $26.5 million in collaboration research and development revenue for research services that we provided in the preclinical research collaboration conducted under that agreement. We immediately recognized an aggregate of $32.6 million of the amounts received under the agreement, which was for achievement of milestone events, because each event met the conditions required for immediate recognition under our revenue recognition policy. We deferred recognition of an aggregate of $29.0 million of the amounts received under the agreement and are recognizing, or in some cases have fully recognized, these deferred amounts into revenue over the periods discussed in Note 12 to our

audited financial statements for the year ended December 31, 2011 included in this annual report. As of December 31, 2011, $6.5 million of amounts received under our cognitive disorders agreement with AstraZeneca remained to be recognized into revenue for future periods.

We also received $45.0 million in aggregate payments under our now terminated product development and commercialization agreement and a related stock purchase agreement with GlaxoSmithKline. We immediately recognized an aggregate of $4.0 million of the amounts received under the agreement, which was for achievement of milestone events, because each event met the conditions required for immediate recognition under our revenue recognition policy. We deferred recognition of $29.5 million of the amounts received under the agreement and were recognizing it into revenue over the period discussed in Note 12 to our audited financial statements for the year ended December 31, 2011 included in this annual report. As a result of our receipt in February 2011 of notice of termination of the agreement, we recognized the remaining unrecognized deferred amount, $18.4 million, into revenue for the first quarter of 2011. We recorded $11.5 million of the amounts received under the agreement, which reflected the fair value of shares of our common stock sold to GlaxoSmithKline in 2007, as capital in excess of par value.

Under our TC-5214 agreement with AstraZeneca, we are eligible to receive additional payments of over $1.0 billion if development, regulatory, first commercial sale and specified sales related milestone events for TC-5214 are achieved and stepped double-digit royalties on any future TC-5214 product sales. Under our cognitive disorders agreement with AstraZeneca, we are eligible to receive additional payments of up to $145.0 million if development, regulatory and first commercial sale milestone events for AZD3480 are achieved for Alzheimer's disease. If AZD3480 is developed for a target indication under the agreement in addition to Alzheimer's disease, we would also be eligible to receive payments of up to $52.0 million for each such indication, if development, regulatory, first commercial sale and first detail milestone events are achieved. We are also eligible to receive stepped double-digit royalties on any future AZD3480 product sales for any indication.

In addition, under our cognitive disorders agreement with AstraZeneca, we are eligible to receive payments of up to $73.0 million, if development, regulatory and first commercial sale milestones are achieved for AZD1446 for Alzheimer's disease, as well as stepped royalties on any future AZD1446 product sales for any indication. If AZD1446 is developed for a target indication under the agreement in addition to Alzheimer's disease, we would also be eligible to receive payments of up to $35.0 million for each such indication, if development, regulatory, first commercial sale and first detail milestone events are achieved.

Our TC-5214 agreement with AstraZeneca can be terminated by AstraZeneca in whole or in part at various times and under various circumstances as discussed above under the caption "Business—Strategic Alliances and Collaborations—AstraZeneca AB—TC-5214—Termination" in Item 1 of Part I of this annual report. Our cognitive disorders agreement with AstraZeneca can be terminated by AstraZeneca for an uncured material breach by us or upon 90 days notice given at any time.

We acquired rights to Inversine, which is our only product to have been approved by the FDA for marketing, in August 2002. Effective September 30, 2009, we discontinued the commercialization of Inversine. Sales of Inversine generated net revenue of $473,000 for the year ended December 31, 2009.

From time to time we seek and are awarded grants or perform work under grants awarded to third-party collaborators from which we derive revenue. During the third quarter of 2011, we were awarded a third grant from the Michael J. Fox Foundation for Parkinson's Research, or MJFF, and the second to fund preclinical research involving the use of compounds that modulate NNRs to address Levodopa-induced dyskinesias. Based on the terms of the grant, we received $250,000 upon inception of the grant term and expect to receive an additional $250,000 in the first half of 2012. In addition, as of December 31, 2011, 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. Funding for awards under federal grant programs is subject to the availability of funds as determined annually in the federal appropriations process.

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 89%, 89% and 61% of our total operating expenses for the years ended December 31, 2011, 2010, and 2009, respectively. For 2009, license fees of $16.4 million, which are not included in research and development expenses, represented 25% of our total operating expenses. There was no license fees expense for the 2011 and 2010 periods.

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, equipment and supplies;
- clinical trials, including fees paid to contract research organizations to monitor and oversee some of our trials;
- the conduct of research activities under the preclinical research collaboration that we conducted with AstraZeneca from January 2006 to January 2010;
- 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 granted to personnel in research and development functions.

In particular, research and development expenses include 20% of the costs of the ongoing development program for TC-5214, as provided in our TC-5214 agreement with AstraZeneca.

We utilize our research and development personnel and infrastructure resources across several programs. We currently have clinical, preclinical and discovery-stage 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. Our current and future expenditures on preclinical and clinical development programs are subject to numerous uncertainties in timing and cost to completion. We or a collaborator of ours tests compounds in numerous preclinical studies for safety, toxicology and efficacy. We or a collaborator of ours then conducts clinical trials for those product candidates that are determined 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 or a collaborator of ours obtains results from clinical trials, we or the collaborator may elect to discontinue or delay trials for some product candidates in order to focus resources on more promising product candidates. Completion of clinical trials by us or a collaborator of ours may take several years or more, and 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 any or all of the non-clinical or clinical development of a particular product candidate, the estimated completion date may be largely under control of that third party and not under our control. We cannot forecast with any degree of certainty whether any of our product candidates will be subject to future alliances or collaborations or how any such arrangement 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.

General and Administrative Expenses

General and administrative expenses consist principally of salaries and other related costs for personnel in executive, finance, business development, legal and human resource functions. Other general and administrative expenses include expenses associated with stock options 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.

License Fees

License fees consist of amounts that we become required to pay to third parties from which we license or otherwise acquire intellectual property rights, such as University of South Florida Research Foundation, or USFRF, with respect to TC-5214 and University of Kentucky Research Foundation, or UKRF, with respect to AZD3480. Under the terms of a license agreement with USFRF, if we receive any milestone payments under our TC-5214 agreement with AstraZeneca, we would be required to pay a percentage of each such milestone payment, after deducting from the milestone payment the unexhausted portion of our projected share of the costs

of the initial development program for TC-5214, as well as royalties on any future TC-5214 product sales, to USFRF. The percentage of each milestone payment, net of any deduction, that we would be required to pay would be at least 10% and could be greater in specified circumstances. Based on the terms of the license agreement with USFRF and the terms of another license agreement with Yale University, we expect to pay royalties at an effective worldwide rate in the low single digits and that such effective royalty rate could in some circumstances reach the mid single digits. Under the terms of a sponsored research agreement and a subsequent license agreement with UKRF, if we receive any qualifying milestone or royalty payments from AstraZeneca relating to AZD3480, we are required to pay a low single digit percentage of each such payment to UKRF.

The amount and timing of our payment obligations to USFRF depend on whether and when milestone events under our TC-5214 agreement with AstraZeneca are achieved and we receive the corresponding payments from AstraZeneca and whether and when regulatory approval for TC-5214 is obtained and product sales are generated. Likewise, the amount and timing of our payment obligations to UKRF depend on whether and when milestone events for AZD3480 under our cognitive disorders agreement with AstraZeneca are achieved and we receive the corresponding payments from AstraZeneca and whether and when regulatory approval for AZD3480 is obtained and product sales are generated. Accordingly, we cannot forecast with any degree of certainty whether or to what extent we will incur license fee and royalty expense in future periods.

Income Taxes

We have incurred cumulative operating losses through December 31, 2011 and have not paid federal, state or foreign income taxes for any period. For the year ended December 31, 2010, we recorded $3.5 million of income tax expense, primarily as a result of the application of Accounting Standards Codification Topic 740, *Income Taxes*, or ASC 740, to stock-based compensation. Exercises of stock options during the year ended December 31, 2010 resulted in tax deductions for stock-based compensation in excess of expense recorded for the stock options under U.S. generally accepted accounting principles, or GAAP, resulting in an income tax benefit of $3.5 million. We recognized the income tax benefit related to the excess tax deductions as an increase to capital in excess of par value, which based on ASC 740 resulted in an offsetting charge in the same amount to income tax expense.

As of December 31, 2011, we had net operating loss carryforwards of $135.9 million for federal income tax purposes and $134.5 million for state income tax purposes. We also had research and development income tax credit carryforwards of $10.8 million for federal income tax purposes and $587,000 for state income tax purposes as of December 31, 2011. The federal net operating loss carryforwards begin to expire in 2024. The state net operating loss carryforwards begin to expire in 2019. The federal and state research and development tax credits begin to expire in 2021. As a result of various factors, including the subjectivity of measurements used in the calculation of particular tax positions taken or that may in the future be taken in our tax returns, it is uncertain whether or to what extent we will be eligible to use the tax credits.

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. A series of stock issuances occurring prior to our initial public offering gave rise to such an ownership change. As a result, an annual limitation is imposed on our use of net operating loss and credit carryforwards that are attributable to periods before the change. In addition, a portion of the net operating loss carryforwards described above may potentially not be usable by us if we experience further ownership changes in the future.

For financial reporting purposes, we have recorded a valuation allowance to fully offset the deferred tax assets related to the carryforwards and the tax credits discussed above until it is more likely than not that we will realize any benefit from them.

Fair Value

The carrying amounts of our cash and cash equivalents, investments in marketable securities, accounts receivable, accounts payable and accrued expenses are considered to be representative of their respective fair values due to their short-term natures and, in the case of short-term investments, their market interest rates. Likewise, the carrying amounts of our long-term debts are considered to be representative of their fair value due to their market interest rates. Cash that we do not expect to use to fund our short-term liquidity requirements is invested in U.S. Treasury notes and bonds, U.S. and state government agency-backed certificates, corporate debt securities that are rated at least A quality or equivalent and certificates of deposits. Our investments in marketable securities, which include marketable securities classified on our balance sheet as cash equivalents, are recorded at quoted market prices or observable market inputs and totaled $158.0 million at December 31, 2011.

Our intangible assets consist of licensed patent rights assigned to us by Layton Bioscience, Inc. in 2002.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of our financial condition and results of operations are based on our audited financial statements, which have been prepared in accordance with GAAP. 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, 2011 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 have historically derived a substantial portion of our revenues from our strategic alliances and collaborations and expect that we will continue to derive a substantial portion of our revenues from our collaborations with AstraZeneca over at least the next several years.

Our collaboration and alliance agreements contain multiple elements, including: an upfront fee, 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; research fees for ongoing research and development; payments associated with the achievement of discovery, development, regulatory and commercial milestone events; and royalties based on specified percentages of any net product sales. In determining the accounting for collaboration and alliance agreements, we first determine whether the agreement involves a single unit of accounting or separate units of accounting for revenue recognition purposes by evaluating each deliverable under the terms of the agreement. If a deliverable has value on a standalone basis, we treat the deliverable as a separate unit of accounting. We determine how to allocate amounts received under the agreement among the separate units, based on the respective selling price of each unit, and we determine the revenue

recognition applicable to each unit. If an agreement does not have multiple deliverables that have standalone value, we consider the agreement to have one unit of accounting and we determine the revenue recognition applicable to the entire agreement.

We defer recognition of non-refundable upfront fees and recognize them into revenue on a straight-line basis over the estimated period of our substantive performance obligations. If we do not have substantive performance obligations, we recognize non-refundable upfront fees into revenue through the date the deliverable is satisfied. 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, would result in decreases or increases to the recognition of deferred revenue from period to period. As of December 31, 2011, all amounts that we have received from AstraZeneca 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:

- there is substantive uncertainty regarding achievement of the milestone event at inception of the arrangement;
- the payment is commensurate with either our performance to achieve the milestone or with the enhancement of the value of the delivered item;
- the payment relates solely to past performance; and
- the payment is reasonable relative to all of the deliverables and payment terms within the arrangement.

If any of these conditions are not met, we defer recognition of the payment and recognize the payment on a straight-line basis as discussed above.

To the extent we are reimbursed under a collaboration or alliance agreement for specific research and development costs, such as third-party manufacturing costs for drug material, we reflect these reimbursable amounts as a component of collaboration research and development revenue and the costs associated with these reimbursable amounts as a component of research and development expenses.

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 among agreements and may result in uneven payment flows. Payments under these agreements depend on the performance of services or the achievement of specified events, such as the production of drug substance or drug product, the recruitment of clinical trial 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 clinical trials and non-clinical studies;
- 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
- professional service fees.

Stock-Based Compensation

We record the grant date fair value of stock options issued to employees and non-employee directors as stock-based compensation expense 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. The Black-Scholes-Merton formula requires us to make various assumptions, including among others the expected term of the award and expected volatility of our common stock. We recorded stock-based compensation expense related to stock options granted to employees and directors of $8.5 million for the year ended December 31, 2011, $4.9 million for the year ended December 31, 2010 and $2.5 million for the year ended December 31, 2009. As of December 31, 2011, we had $18.3 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 2.6 years.

Results of Operations

Years ended December 31, 2011 and December 31, 2010

Net Operating Revenues

	Year ended December 31,		
	2011	2010	Change
	(in thousands)		
Operating revenues:			
Milestones and license fees from collaborations	$96,979	$83,380	$13,599
Grant revenue	658	2,333	(1,675)
Net operating revenues	$97,637	$85,713	$11,924

Net operating revenues for the year ended December 31, 2011 increased by $11.9 million as compared to the year ended December 31, 2010. The higher net operating revenues were attributable to an increase of $13.6 million in milestones and license fees from collaborations revenue, partially offset by a decrease of $1.7 million in grant revenue. The increase in milestones and license fees from collaborations revenue was principally due to increases of $15.1 million in recognition of deferred revenue previously received from GlaxoSmithKline, as all amounts that had yet to be recognized as of the time we received notice of termination of our agreement with GlaxoSmithKline were recognized for the first quarter of 2011, and $551,000 in recognition of cumulative payments of $6.0 million received from AstraZeneca in connection with events associated with our Phase 2b clinical trial of AZD3480 as a treatment for mild to moderate Alzheimer’s disease. These increases were partially

offset by a decrease of $1.8 million in recognition of deferred revenue associated with payments previously received from AstraZeneca related to TC-5619, as all deferred revenue related to TC-5619 became fully recognized in the second quarter of 2011. The decrease in grant revenue was primarily attributable to $1.5 million received in November 2010 under the U.S. Government's Qualifying Therapeutic Discovery Project tax credit program, which did not recur in 2011.

In future periods, we are eligible to receive additional milestone payments under our agreements with AstraZeneca. The amount of milestone payments will depend on whether we achieve discovery, development, regulatory and commercial milestone events that are inherently uncertain and, if so, when. We expect that the amount of our milestone-based revenue will continue to vary from period to period.

Research and Development Expenses

	Year ended December 31,		
	2011	2010	Change
		(in thousands)	
Research and development expenses	$95,215	$64,546	$30,669

Research and development expenses for the year ended December 31, 2011 increased by $30.7 million as compared to the year ended December 31, 2010. The higher research and development expenses were principally attributable to:

- an increase of $27.3 million in costs incurred for third-party research and development services in connection with our 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 $55.0 million for 2011, from $27.6 million for 2010; this increase was principally due to our cost-sharing obligations with respect to TC-5214 as the Phase 3 development program progressed, the conduct of a Phase 2b clinical trial of AZD3480 and the conduct of two Phase 2 clinical trials of TC-6987; our costs incurred for third-party research and development services also included costs in connection with Phase 2 clinical trials of TC-5619;
- an increase of $2.5 million in costs incurred for third-party research and development services in connection with preclinical programs, to $7.1 million for 2011, from $4.6 million for 2010; and
- an increase of $2.3 million in other research and development operating costs, including stock-based compensation, salary and other compensation-related expenses for research and development activities and infrastructure costs, to $33.1 million for 2011, from $30.8 million for 2010; this increase was principally attributable to $2.1 million of additional stock-based compensation expense, which was primarily due to a significantly higher weighted average fair value for stock options that vested during the 2011 period as compared to stock options that vested during the 2010 period. Stock options granted to our employees typically vest over four years.

These increases were partially offset by the inclusion in research and development expenses for 2010 of a $1.5 million upfront payment made to Cornerstone Therapeutics Inc. in August 2010 under a license agreement.

The costs that we incurred for the years ended December 31, 2011 and 2010 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,		
	2011	2010	Change
	(in thousands)		
TC-5214	$32,046	$10,771	$21,275
TC-5619	9,847	10,483	(636)
TC-6987	8,858	5,534	3,324
AZD3480	4,110	35	4,075
TC-6499	96	798	(702)
AZD1446	—	—	—
	$54,957	$27,621	$27,336

We expect our research and development expenses for the year ending December 31, 2012 to decrease as compared to 2011, principally as a result of the anticipated completion in the first half of 2012 of the planned Phase 3 clinical development program for TC-5214.

General and Administrative Expenses

	Year ended December 31,		
	2011	2010	Change
	(in thousands)		
General and administrative expenses	$12,167	$8,052	$4,115

General and administrative expenses for the year ended December 31, 2011 increased by $4.1 million as compared to the year ended December 31, 2010. The higher general and administrative expenses were principally attributable to increases of $2.8 million in stock-based compensation, salary and other compensation-related expenses for general and administrative personnel and $1.3 million in infrastructure costs associated with support of the increased research and development activities discussed above. The largest component of the increase was stock-based compensation expense, which was primarily due to a significantly higher weighted average fair value for stock options that vested during 2011 as compared to stock options that vested during 2010.

Income Tax Expense

	Year ended December 31,		
	2011	2010	Change
	(in thousands)		
Income tax expense	$—	$3,526	$(3,526)

There was no income tax expense for the year ended December 31, 2011, as compared to income tax expense of $3.5 million for the year ended December 31, 2010. The change was primarily due to tax deductions for stock-based compensation for the 2010 period in excess of expense recorded under GAAP for the corresponding stock options. Tax deductions in excess of recorded expense are only recognized for years with net income.

Years ended December 31, 2010 and December 31, 2009

Net Operating Revenues

	Year ended December 31,		
	2010	2009	Change
	(in thousands)		
Operating revenues:			
Milestones and license fees from collaborations	$83,380	$18,934	$64,446
Collaboration research and development	—	5,246	(5,246)
Product sales, net	—	473	(473)
Grant revenue	2,333	409	1,924
Net operating revenues	$85,713	$25,062	$60,651

Net operating revenues for the year ended December 31, 2010 increased by $60.7 million as compared to the year ended December 31, 2009. The higher net operating revenues were attributable to increases of $64.4 million in milestones and license fees from collaborations revenue and $1.9 million in grant revenue, partially offset by a decrease of $5.2 million in collaboration research and development revenue. The increase in milestones and license fees from collaborations revenue was principally due to recognition of $72.6 million of the $200.0 million upfront payment received under our TC-5214 agreement with AstraZeneca and $6.3 million of the $11.0 million payment received under an April 2010 amendment to our cognitive disorders agreement with AstraZeneca related to TC-5619, partially offset by the achievement in 2009 of a milestone event under the cognitive disorders agreement for which we received $10.0 million, decreases of $2.5 million in aggregate payments received from GlaxoSmithKline upon achievement of milestone events under our product development and commercialization agreement and $1.1 million in license fees derived from the cognitive disorders agreement with AstraZeneca as a result of the expiration of the term of the preclinical research collaboration in January 2010.

The increase in grant revenue for 2010 was primarily attributable to $1.5 million received under the U.S. Government's Qualifying Therapeutic Discovery Project tax credit program. The decrease in collaboration research and development revenue for 2010 resulted from the completion of the preclinical research collaboration under our cognitive disorders agreement with AstraZeneca.

Net product sales for the year ended December 31, 2010 decreased by $473,000 as compared to the year ended December 31, 2009 as a result of our discontinuation of the commercialization of Inversine effective as of September 30, 2009.

Research and Development Expenses

	Year ended December 31,		
	2010	2009	Change
	(in thousands)		
Research and development expenses	$64,546	$40,179	$24,367

Research and development expenses for the year ended December 31, 2010 increased by $24.4 million as compared to the year ended December 31, 2009. The higher research and development expenses were principally attributable to:

- an increase of $17.3 million in costs incurred for third-party research and development services in connection with our 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 $27.6 million for 2010, from $10.3 million for 2009; this increase was principally due to our cost-sharing obligations with respect to Phase 3 clinical development of TC-5214, the conduct of Phase 2 clinical development of TC-5619 for two indications and the conduct of multiple Phase 1 clinical trials of TC-6987;

- an increase of $2.5 million in stock-based compensation, salary and other compensation-related expenses for research and development activities to $17.0 million for 2010, from $14.5 million for 2009; the largest component of this increase was stock-based compensation expense, which was primarily due to a significantly higher weighted average fair value for stock options that vested during 2010 as compared to stock options that vested during 2009;
- an increase of $3.0 million in other research and development expenses, including infrastructure costs, to $13.8 million for 2010, from $10.8 million for 2009; this increase was primarily due to increases in the number of employees and depreciable equipment utilized in our research and development functions; and
- the $1.5 million upfront payment that we made to Cornerstone Therapeutics Inc. during 2010.

Costs incurred for third-party research and development services in connection with our preclinical programs were $4.6 million for each of the years ended December 31, 2010 and 2009.

The costs that we incurred for the years ended December 31, 2010 and 2009 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,		
	2010	2009	Change
	(in thousands)		
TC-5214	$10,771	$ 5,527	$ 5,244
TC-5619	10,483	2,585	7,898
TC-6987	5,534	1,752	3,782
TC-6499	798	210	588
AZD3480	35	217	(182)
AZD1446	—	—	—
	$27,621	$10,291	$17,330

General and Administrative Expenses

	Year ended December 31,		
	2010	2009	Change
	(in thousands)		
General and administrative expenses	$8,052	$8,167	$ (115)

General and administrative expenses for the year ended December 31, 2010 decreased by $115,000 as compared to the year ended December 31, 2009. The change reflected a decrease of $839,000 in employee compensation and related expenses to $2.9 million for 2010, from $3.7 million for 2009, arising primarily from lower incentive compensation expenses, and a decrease of $344,000 in infrastructure costs to $3.0 million for 2010, from $3.3 million for 2009. These decreases were substantially offset by an increase of $1.1 million in stock-based compensation for general and administrative personnel to $2.2 million for 2010, from $1.1 million for 2009, primarily due to a significantly higher weighted average fair value for stock options that vested during 2010 as compared to stock options that vested during 2009.

License Fees

	Year ended December 31,		
	2010	2009	Change
	(in thousands)		
License fees	$—	$16,350	$(16,350)

License fees for the year ended December 31, 2010 decreased by $16.4 million as compared to the year ended December 31, 2009. License fees for 2009 reflected $16.0 million payable to USFRF based on our receipt of the $200.0 million upfront payment under our TC-5214 agreement with AstraZeneca and $350,000 paid to UKRF based on a $10.0 million milestone payment received under our cognitive disorders agreement with AstraZeneca.

Cost of Product Sales

	Year ended December 31,		
	2010	2009	Change
	(in thousands)		
Cost of product sales	$—	$691	$ (691)

Our cost of product sales were those costs related directly to the sale of Inversine. Cost of product sales for the year ended December 31, 2010 decreased by $691,000 as compared to the year ended December 31, 2009 as a result of our discontinuation of the commercialization of Inversine effective as of September 30, 2009.

Income Tax Expense

	Year ended December 31,		
	2010	2009	Change
	(in thousands)		
Income tax expense	$3,526	$—	$3,526

There was income tax expense of $3.5 million for the year ended December 31, 2010 as compared to no income tax expense for the year ended December 31, 2009. The change was primarily due to tax deductions for stock-based compensation for the 2010 period in excess of expense recorded under GAAP for the corresponding stock options.

Liquidity and Capital Resources

Sources of Liquidity

We have historically financed our operations and internal growth primarily through public and private offerings of our securities, payments received under collaboration and alliance agreements, including upfront fees, payments for research and development services and payments upon achievement of milestone events, grants and equipment financing. We discontinued the commercialization of our only approved product, Inversine, effective as of September 30, 2009. The net contribution from Inversine sales was not historically a significant source of cash.

Our cash, cash equivalents and investments in marketable securities were $249.3 million as of December 31, 2011 and $252.5 million as of December 31, 2010. As of December 31, 2011, we had $90.2 million of cash in bank depository accounts and institutional money market funds at Branch Banking and Trust Company, RBC

Bank and Wells Fargo & Company. Substantially all of our remaining cash, cash equivalents and investments were invested as of December 31, 2011 in U.S. Treasury notes and bonds, U.S. and state government agency-backed securities, corporate debt securities that are rated at least A quality or equivalent and certificates of deposit.

Stock Offerings

In May 2011, we completed an underwritten public offering of 3,658,537 shares of our common stock. In June 2011, we sold an additional 548,780 shares of our common stock upon the exercise of the overallotment option granted to the underwriters. Our net proceeds from the offering, after deducting underwriters' discounts and commissions and offering expenses paid by us, were $80.8 million. In October 2009, we completed an underwritten public offering of 2,200,000 shares of our common stock. After deducting underwriting discounts and commissions and offering expenses paid by us, our net proceeds from the offering were $44.4 million. Beginning with our initial public offering in April 2006, we have derived aggregate net proceeds of $195.1 million from public offerings of our common stock. We have also derived aggregate net proceeds of $121.8 million from private placements of convertible preferred stock, all of which occurred prior to our initial public offering.

In October 2009, we received written notice from a stockholder that the stockholder had violated Section 16(b) of the Exchange Act as a result of certain purchases and sales of shares of our common stock made by the stockholder within a period of less than six months that generated "short-swing" profits under Section 16(b). Later in October 2009, the stockholder made a $724,000 payment to us in disgorgement of the short-swing profits.

Strategic Alliances and Collaborations

As of December 31, 2011, we had received $61.6 million in aggregate upfront fees and milestone payments from AstraZeneca under our cognitive disorders agreement with AstraZeneca and an additional $26.5 million in collaboration research and development revenue for research services that we provided in the preclinical research collaboration conducted under the agreement. Most recently:

- in September and December 2011, under an amendment to the agreement, we received cumulative payments of $5.5 million in connection with events associated with our ongoing Phase 2b study of AZD3480 as a treatment for mild to moderate Alzheimer's disease;
- in May 2010, we received an $11.0 million payment in connection with a separate amendment to the agreement to modify the terms applicable to TC-5619;
- in July 2009, we received a $10.0 million payment as a result of the achievement of the objective in a completed Phase 2 trial of AZD3480 in adults with ADHD; and
- since inception, we received cumulative payments of $2.6 million upon achievement of milestone events under the agreement related to the development of AZD1446 and other product candidates arising under the preclinical research collaboration conducted under the agreement.

In December 2009, we entered into our TC-5214 agreement with AstraZeneca for the global development and commercialization of TC-5214. We received a $200.0 million upfront payment from AstraZeneca in January 2010. Under the terms of an existing license agreement, we paid $16.0 million to USFRF in January 2010 based on our receipt of the upfront payment from AstraZeneca.

In July 2007, we entered into a product development and commercialization agreement and a related stock purchase agreement with GlaxoSmithKline. The product development and commercialization agreement was terminated effective in May 2011. We received $45.0 million in aggregate payments from GlaxoSmithKline under the agreements, which are no longer a potential source of future funds.

As discussed above under the caption "—Overview—Revenue," we are eligible to receive substantial additional payments from AstraZeneca, contingent on the achievement of specified milestone events related to TC-5214, AZD3480 and AZD1446. The likelihood that we will achieve any particular milestone event in any particular period is uncertain, and we may not ever achieve future milestone events with respect to TC-5214, AZD3480 or AZD1446.

Loan Financing

In July 2010, we entered into a loan agreement with a bank that provided aggregate borrowing capacity of $4.0 million available to us at any time on or prior to June 30, 2011 to fund the purchase of equipment, furnishings, software and other fixed assets. In September 2010, we borrowed $1.2 million under the loan facility at a fixed interest rate of 3.4% per annum. We were obligated only to pay interest on the September 2010 borrowing through the remainder of 2010, and it is repayable in equal monthly installments of $28,000 that began January 1, 2011 and continue through the maturity date of December 1, 2014. In June 2011, we borrowed $2.1 million under the loan facility at a fixed interest rate of 3.471% per annum. The June 2011 borrowing is repayable in equal monthly installments of $48,000 that began July 1, 2011 and continue through the maturity date of June 1, 2015. 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. As of December 31, 2011, the outstanding principal balance under the loan facility was $2.8 million and there is no additional borrowing capacity remaining available to us.

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 a previous loan facility that we had with R.J. Reynolds Tobacco Holdings, Inc. 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 bore interest at a fixed rate of 5.231% per annum and was repayable in equal monthly installments of $112,000 beginning April 1, 2008 and continuing through the maturity date of March 1, 2012 when it was repaid in full. 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, 2011, the outstanding principal balance under the loan facility was $419,000 and there is no additional borrowing capacity remaining available to us.

In April 2002, we received a $500,000 loan from the City of Winston-Salem, North Carolina. 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 began to bear interest at an annual interest rate of 5% and became payable in 60 equal monthly installments of $9,000. In December 2010, we repaid in full the remaining outstanding balance under the loan.

Cash Flows

	Year ended December 31,		
	2011	2010	Change
	(in thousands)		
Net cash (used in) provided by operating activities	$(83,718)	$138,298	$(222,016)
Net cash used in investing activities	(57,667)	(62,799)	5,132
Net cash provided by financing activities	82,814	6,446	76,368
Net (decrease) increase in cash and cash equivalents	$(58,571)	$ 81,945	

	Year ended December 31,		
	2010	2009	Change
		(in thousands)	
Net cash provided by (used in) operating activities	$138,298	$(24,271)	$162,569
Net cash (used in) provided by investing activities	(62,799)	9,800	$ (72,599)
Net cash provided by financing activities	6,446	47,178	$ (40,732)
Net increase in cash and cash equivalents	$ 81,945	$ 32,707	

Net cash used in operating activities for the year ended December 31, 2011 was $83.7 million and net cash provided by operating activities for the year ended December 31, 2010 was $138.3 million, a difference of $222.0 million from 2011.

For 2011, net cash used in operating activities was primarily attributable to aggregate payments of $92.2 million for third-party research and development services in connection with clinical-stage product candidates and preclinical programs and personnel and infrastructure costs, partially offset by $5.5 million received from AstraZeneca in 2011 in connection with events associated with our ongoing Phase 2b clinical trial of AZD3480 as a treatment for mild to moderate Alzheimer's disease and $2.1 million of interest income and related amounts.

For 2010, net cash provided by operating activities was principally the result of our receipt of:

- the $200.0 million upfront payment under our TC-5214 agreement with AstraZeneca in January 2010;
- the $11.0 million payment under an amendment to our cognitive disorders agreement with AstraZeneca to modify the terms applicable to TC-5619 in April 2010;
- $1.5 million in payments for research services under our preclinical research collaboration with AstraZeneca, which ended in January 2010;
- the $1.5 million grant under the U.S. Government's Qualifying Therapeutic Discovery Project tax credit program; and
- $1.7 million in interest income and related amounts.

These cash inflows were partially offset by:

- our payments in January 2010 of $16.0 million to USFRF based on our receipt of the $200.0 million upfront payment under our TC-5214 agreement with AstraZeneca;
- our payment of $1.5 million to Cornerstone Therapeutics Inc. under a license agreement in August 2010; and
- aggregate payments of $58.7 million for routine operating activities, including third-party research and development services in connection with clinical-stage product candidates and preclinical programs and personnel and infrastructure costs.

We expect payments for operating activities for the year ending December 31, 2012 to decrease as compared to 2011, principally as a result of the anticipated completion in the first half of 2012 of the planned Phase 3 clinical development program for TC-5214.

Net cash used in operating activities for the year ended December 31, 2009 was $24.3 million, a difference of $162.6 million as compared to 2010. For 2009, net cash used in operating activities was principally the result of aggregate payments of $44.2 million for third-party research and development services in connection with clinical-stage product candidates and preclinical programs and personnel and infrastructure costs, partially offset by our receipt of:

- the $10.0 million milestone payment from AstraZeneca;
- $5.5 million in payments for research services under our preclinical research collaboration with AstraZeneca;

- $2.5 million in aggregate milestone payments from GlaxoSmithKline; and
- $1.0 million in interest income and related amounts.

Net cash used in investing activities for the year ended December 31, 2011 decreased by $5.1 million as compared to the year ended December 31, 2010. Cash provided by or 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 in marketable securities. A transfer of funds from an investment in marketable securities to cash generates cash provided by investing activities, while a transfer of funds from cash or a cash equivalent to investments in marketable securities generates cash used in investing activities. Our net purchases of investments in marketable securities for 2011 were $56.2 million and occurred primarily as a result of our receipt of proceeds from our common stock offering in May 2011. Our net purchases of investments in marketable securities for 2010 were $59.5 million and occurred primarily as a result of our receipt of the upfront payment under our TC-5214 agreement with AstraZeneca. Additionally, we purchased $1.4 million of property and equipment during 2011, a decrease of $1.9 million from $3.3 million during 2010.

Net cash used in investing activities for the year ended December 31, 2010 was $62.8 million and net cash provided by investing activities for the year ended December 31, 2009 was $9.8 million, a difference of $72.6 million. Our net sales of investments in marketable securities for 2009 were $10.0 million. During 2009, we re-allocated substantial funds from certificates of deposit to bank depository accounts and institutional money market funds as the certificates of deposit came due in order to yield more favorable interest rates and provide increased liquidity. Additionally, our $3.3 million of property and equipment purchases during 2010 reflected an increase of $3.1 million from $200,000 in property and equipment purchases during 2009. Purchases of property and equipment for 2011 and 2010 were primarily to expand our internal research and development capacity and capabilities.

Net cash provided by financing activities for the year ended December 31, 2011 increased by $76.4 million as compared to the year ended December 31, 2010. The increase was primarily attributable to net proceeds of $80.8 million in May and June 2011 from our common stock offering, partially offset by the income tax effect for 2010 of tax deductions for stock-based compensation in excess of expense recorded for stock options under GAAP of $3.5 million and a decrease of $1.5 million received upon the issuance of common stock related to exercises of stock options. Net cash provided by financing activities for the year ended December 31, 2010 decreased by $40.7 million as compared to the year ended December 31, 2009. The decrease was primarily attributable to net proceeds of $44.4 million in October 2009 from a common stock offering and the receipt in October 2009 of $724,000 from a stockholder for disgorgement of “short-swing” profits under Section 16(b) of the Exchange Act, partially offset by the income tax effect for 2010 of excess tax deductions of $3.5 million discussed above and a decrease in net borrowings under our loan facilities of $1.0 million.

Funding Requirements

As of December 31, 2011, we had an accumulated deficit of $226.9 million. We may incur operating losses or require additional capital in future periods as our clinical-stage and preclinical product candidates advance into later-stage development and as we progress our programs, invest in additional product opportunities and grow our business. However, we may generate operating income for any particular reporting period as a result of the recognition into revenue of amounts previously received under our agreements with AstraZeneca, including in particular our TC-5214 agreement with AstraZeneca, the timing of milestone events that may be achieved under our agreements with AstraZeneca and the timing of costs incurred related to development of our clinical-stage and preclinical product candidates. Our future capital requirements are difficult to forecast and will depend on many factors, including:

- whether and to what extent milestone events are achieved for TC-5214 under our TC-5214 agreement with AstraZeneca or for either or both of AZD3480 and AZD1446 under our cognitive disorders agreement with AstraZeneca;

- the progress of, and outcomes from, Phase 3 clinical development of TC-5214 and the amount and timing of costs payable by us for ongoing or any future development of TC-5214;
- whether we elect to exercise our co-promotion rights for TC-5214 if the outcomes of the remaining Phase 3 clinical trials are favorable and AstraZeneca proceeds to file an NDA for TC-5214 with the FDA;
- whether we establish additional strategic alliances, collaborations and licensing or other comparable arrangements, or whether we pursue and complete any merger, acquisition or other significant corporate transactions, and, if we do, the associated terms in each case;
- the scope, progress, duration, results and cost of clinical trials, as well as non-clinical studies and assessments, of our product candidates and programs in addition to TC-5214;
- the extent to which we retain development and commercialization rights or responsibilities for our product candidates that are not subject to our collaborations with AstraZeneca and incur associated development costs, manufacturing costs or costs to establish sales and marketing functions;
- the number and characteristics of product candidates that we pursue and programs that we conduct;
- the costs to satisfy our obligations under existing and potential future alliances and collaborations;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending patents and other intellectual property rights;
- the costs of manufacturing-related services for our product candidates in clinical and late preclinical development;
- the costs, timing and outcomes of regulatory reviews or other regulatory actions;
- the timing, receipt and amount of sales or royalties, if any, from our potential products;
- the extent and scope of our general and administrative expenses; and
- the rate of technological advancements for the indications that we target.

Our existing capital resources may not 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 through at least the end of 2014, without taking into account any amounts that we would be entitled to receive if milestone events are achieved under either of our collaboration agreements with AstraZeneca. 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.

To the extent our capital resources are insufficient to meet future capital requirements or to the extent the conditions for raising capital are favorable, we may finance future cash needs through public or private equity or debt offerings or other financings (whether utilizing our currently effective Registration Statement on Form S-3 or otherwise). Our access in the future to additional equity or debt financing, on acceptable terms or at all, may be impacted by challenging global credit and financial markets and by the substantial decline in our stock price that we experienced following the announcement of top-line results from the first completed Phase 3 clinical trial of TC-5214 in November 2011. We may also seek to finance future cash needs through alliances, collaborations or licensing or other comparable arrangements. Strategic alliances, collaborations or licensing or other comparable 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 significantly dilute the ownership of our stockholders.

We cannot determine precisely 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, collaborations or licensing or other arrangements for our product candidates. Our failure, or the failure of any of our present or future licensees or collaborators, to complete research and development programs for our product candidates 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, 2011:

	Payments Due by Period (in thousands)				
Contractual Obligation	Total	Less Than 1 Year	1 - 3 Years	3 - 5 Years	More Than 5 Years
Long-term debt obligations	$ 3,402	$ 1,331	$1,786	$285	$ —
Operating lease obligations	2,106	1,695	410	1	—
Purchase obligations	26,286	22,332	3,915	32	7
	$31,794	$ 25,358	$ 6,111	$318	$ 7

The amounts of license fee obligations for all periods reflected in the above table exclude contingent license and royalty payments and other contingent payments payable upon achievement of specified development, regulatory, commercial or other milestone events under our license agreements with USFRF, Yale University, UKRF or Cornerstone Therapeutics Inc. 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, but do not include our share of the anticipated development costs for TC-5214. The amounts of purchase obligations also include contractual obligations for insurance and other general and administrative expenses. The amounts of long-term debt obligations for all periods reflected in the above table include principal and interest payments on loan facilities outstanding at December 31, 2011.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Recent Accounting Pronouncements

In June 2011, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update No. 2011-05, *Presentation of Comprehensive Income*, or ASU 2011-05. ASU 2011-05 amends the current guidance on the presentation of comprehensive income to give an entity the option to present comprehensive income in either one continuous statement or two consecutive financial statements. The option under current guidance that permits the presentation of components of other comprehensive income as part of the statement of changes in stockholders' equity has been eliminated. ASU 2011-05 does not change the items that must be reported in other comprehensive income. ASU 2011-05 is effective for fiscal years beginning on or after December 15, 2011, and for interim periods within those years, applied retrospectively for all periods presented. Early adoption is permitted. We do not expect ASU 2011-05 to have a material impact on our financial position, results of operations or cash flows as it is disclosure-only in nature.

In May 2011, the FASB issued Accounting Standards Update No. 2011-04, *Amendments to Achieve Common Fair Value Measurement and Disclosure Requirements in U.S. GAAP and IFRSs*, or ASU 2011-04. ASU 2011-04 amends the current guidance to expand existing disclosure requirements and to change the

description of many of the GAAP requirements for measuring fair value. ASU 2011-04 is effective for fiscal years beginning after December 15, 2011, and for interim periods within those years. We do not expect ASU 2011-04 to have a material impact on our financial position, results of operations or cash flows.

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

The primary objectives of our investment activities are to preserve our capital and meet our liquidity needs to fund operations. We also seek to generate competitive rates of return 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 of high credit quality based on ratings from commonly relied upon rating agencies. As of December 31, 2011, we had cash, cash equivalents and investments in marketable securities of $249.3 million. Our cash equivalents and investments in marketable securities may be subject to interest rate risk and could fall in value if market interest rates increase. However, because our cash equivalents are invested in accounts with market interest rates and are short term in nature and because our investments in marketable securities are traded in active markets, 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, 2011 would not have a material impact on the total fair value of our portfolio.

We sometimes contract for the conduct of clinical trials or other research and development and manufacturing activities with contract research organizations, clinical trial sites and contract manufacturers in Europe or elsewhere outside of the United States. We may be subject to exposure to fluctuations in foreign currency exchange rates in connection with these agreements. If the average exchange rate between the currency of our payment obligations under any of these agreements and the U.S. dollar were to strengthen or weaken by 10% against the corresponding exchange rate as of December 31, 2011, 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, 2011 and 2010, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2011. 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, 2011 and 2010, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2011, 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, 2011, 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 6, 2012 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Raleigh, North Carolina
March 6, 2012

TARGACEPT, INC.

BALANCE SHEETS
(in thousands, except share and par value amounts)

	December 31, 2011	December 31, 2010
ASSETS		
Current assets:		
Cash and cash equivalents	$ 107,283	$ 165,854
Investments in marketable securities—short term	87,721	48,168
Receivables from collaborations	218	838
Prepaid expenses	3,471	3,219
Total current assets	198,693	218,079
Investments in marketable securities—long term	54,266	38,487
Property and equipment, net	5,035	6,072
Intangible assets	132	149
Total assets	$ 258,126	$ 262,787
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 3,489	$ 4,721
Accrued expenses	16,167	10,516
Current portion of long-term debt	1,241	1,710
Current portion of deferred revenue	57,714	81,710
Total current liabilities	78,611	98,657
Long-term debt, net of current portion	1,986	1,349
Deferred revenue, net of current portion	3,241	70,934
Total liabilities	83,838	170,940
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.001 par value, 100,000,000 shares authorized; 33,383,403 and 28,870,691 shares issued and outstanding at December 31, 2011 and December 31 2010, respectively	33	29
Preferred stock, $0.001 par value, 5,000,000 shares authorized; 0 shares issued and outstanding at December 31, 2011 and 2010	—	—
Capital in excess of par value	401,149	309,994
Accumulated other comprehensive income	36	225
Accumulated deficit	(226,930)	(218,401)
Total stockholders' equity	174,288	91,847
Total liabilities and stockholders' equity	$ 258,126	$ 262,787

See accompanying notes.

TARGACEPT, INC.

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

	Year ended December 31,		
	2011	2010	2009
Operating revenues:			
License fees and milestones from collaborations	$ 96,979	$ 83,380	$ 18,934
Collaboration research and development	—	—	5,246
Product sales, net	—	—	473
Grant revenue	658	2,333	409
Net operating revenues	97,637	85,713	25,062
Operating expenses:			
Research and development (including stock-based compensation of $4,885, $2,768 and $1,353 in 2011, 2010 and 2009, respectively)	95,215	64,546	40,179
General and administrative (including stock-based compensation of $3,628, $2,169 and $1,101 in 2011, 2010 and 2009, respectively)	12,167	8,052	8,167
License fees	—	—	16,350
Cost of product sales	—	—	691
Total operating expenses	107,382	72,598	65,387
(Loss) income from operations	(9,745)	13,115	(40,325)
Other income (expense):			
Interest income	1,348	1,463	1,050
Interest expense	(132)	(153)	(217)
Total other income (expense)	1,216	1,310	833
(Loss) income before income taxes	(8,529)	14,425	(39,492)
Income tax (expense) benefit	—	(3,526)	88
Net (loss) income	$ (8,529)	$ 10,899	$ (39,404)
Basic net (loss) income per share	$ (0.27)	$ 0.38	$ (1.54)
Diluted net (loss) income per share	$ (0.27)	$ 0.36	$ (1.54)
Weighted average common shares outstanding—basic	31,637,283	28,543,408	25,636,419
Weighted average common shares outstanding—diluted	31,637,283	30,150,324	25,636,419

See accompanying notes.

TARGACEPT, INC.

STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands, except share amounts)

	Common Stock		Capital in Excess of Par Value	Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balances at December 31, 2008	24,964,373	$ 25	$247,244	$ —	$ (189,896)	$ 57,373
Issuance of common stock related to exercise of stock options	1,062,456	1	3,353	—	—	3,354
Stock-based compensation	—	—	2,454	—	—	2,454
Net proceeds from public stock offering	2,200,000	2	44,447	—	—	44,449
Stockholder short swing profit payment	—	—	724	—	—	724
Excess tax deductions from stock-based compensation	—	—	41	—	—	41
Net loss and comprehensive loss	—	—	—	—	(39,404)	(39,404)
Balances at December 31, 2009	28,226,829	28	298,263	—	(229,300)	68,991
Issuance of common stock related to exercise of stock options	643,862	1	3,291	—	—	3,292
Stock-based compensation	—	—	4,937	—	—	4,937
Excess tax deductions from stock-based compensation	—	—	3,503	—	—	3,503
Net change in unrealized holding gain on available for sale marketable securities	—	—	—	225	—	225
Net income	—	—	—	—	10,899	10,899
Comprehensive income	—	—	—	—	—	11,124
Balances at December 31, 2010	28,870,691	29	309,994	225	(218,401)	91,847
Issuance of common stock related to exercise of stock options	305,395	—	1,802	—	—	1,802
Stock-based compensation	—	—	8,513	—	—	8,513
Net proceeds from public stock offering	4,207,317	4	80,840	—	—	80,844
Net change in unrealized holding gain on available for sale marketable securities	—	—	—	(189)	—	(189)
Net loss	—	—	—	—	(8,529)	(8,529)
Comprehensive loss	—	—	—	—	—	(8,718)
Balances at December 31, 2011	33,383,403	$ 33	$401,149	$ 36	$ (226,930)	$ 174,288

See accompanying notes.

TARGACEPT, INC.

STATEMENTS OF CASH FLOWS
(in thousands)

	Year ended December 31,		
	2011	2010	2009
Operating activities			
Net (loss) income	$ (8,529)	$ 10,899	$ (39,404)
Adjustments to reconcile net (loss) income to net cash (used in) provided by operating activities:			
Recognition of deferred revenue	(97,439)	(83,767)	(6,383)
Amortization of premium on marketable securities, net	911	416	—
Depreciation and amortization	2,480	1,997	1,835
Stock-based compensation expense	8,513	4,937	2,454
Excess tax benefits from stock-based compensation	—	(3,503)	(41)
Changes in operating assets and liabilities:			
Receivables from collaborations	620	200,963	272
Other current assets	(443)	(1,815)	(28)
Accounts payable, license fees payable and accrued expenses	4,419	(3,802)	16,551
Deferred license fee revenue	5,750	11,973	473
Net cash (used in) provided by operating activities	(83,718)	138,298	(24,271)
Investing activities			
Purchase of investments in marketable securities	(156,253)	(144,012)	(31,000)
Proceeds from sale of investments in marketable securities	100,012	84,481	41,000
Purchase of property and equipment	(1,431)	(3,311)	(200)
Proceeds from sale of property and equipment	5	43	—
Net cash (used in) provided by investing activities	(57,667)	(62,799)	9,800
Financing activities			
Proceeds from issuance of long-term debt	2,132	1,228	—
Principal payments on long-term debt	(1,964)	(1,577)	(1,390)
Proceeds from issuance of common stock, net	82,646	3,292	48,527
Excess tax benefits from stock-based compensation	—	3,503	41
Net cash provided by financing activities	82,814	6,446	47,178
Net (decrease) increase in cash and cash equivalents	(58,571)	81,945	32,707
Cash and cash equivalents at beginning of year	165,854	83,909	51,202
Cash and cash equivalents at end of year	$ 107,283	$ 165,854	$ 83,909

See accompanying notes.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS
DECEMBER 31, 2011

1. The Company and Nature of Operations

Targacept, Inc., or the Company, is a Delaware corporation formed on March 7, 1997. The Company is a biopharmaceutical company engaged in the design, discovery and development of novel NNR Therapeutics™ for the treatment of diseases and disorders of the nervous system. The Company's NNR Therapeutics selectively target neuronal nicotinic receptors, which it refers to as NNRs. Its facilities are located in Winston-Salem, North Carolina.

2. Summary of Significant Accounting Policies

Use of Estimates, Reclassifications and Revisions

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 years ended December 31, 2010 and 2009 to conform to the presentation in the financial statements for the year ended December 31, 2011. These reclassifications had no impact on previously reported net loss or stockholders' equity. Also, certain revisions have been made to the notes to the financial statements. In particular, the fair value hierarchy inputs used to determine the fair value of corporate debt securities were reflected as Level 1 inputs in the 2010 audited financial statements. The Company has revised the applicable footnote as of December 31, 2010 to reflect the inputs as Level 2 inputs. This revision had no impact on the recorded value of the securities.

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.

Investments in Marketable Securities

Consistent with its investment policy, the Company invests its cash allocated to fund its short-term liquidity requirements with prominent financial institutions in bank depository accounts and institutional money market funds and the Company invests the remainder of its cash in U.S. Treasury notes and bonds, U.S. and state government agency-backed certificates, corporate debt securities that are rated at least A quality or equivalent and certificates of deposit.

The Company determines the appropriate classification of marketable securities at the time of purchase and reevaluates its classification as of each balance sheet date. All marketable securities owned during 2011 and 2010 were classified as available for sale. The cost of securities sold is based on the specific identification method. Investments in marketable securities are recorded as of each balance sheet date at fair value, with unrealized gains and, to the extent deemed temporary, unrealized losses included in stockholders' equity. Interest and dividend income on investments in marketable securities, accretion of discounts and amortization of premiums and realized gains and losses are included in interest income in the statement of operations.

An investment in marketable securities is considered to be impaired when a decline in fair value below its cost basis is determined to be other than temporary. The Company evaluates whether a decline in fair value of an investment in marketable securities below its cost basis is other than temporary using available evidence. In the

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

2. Summary of Significant Accounting Policies (continued)

event that the cost basis of the investment exceeds its fair value, the Company evaluates, among other factors, the amount and duration of the period that the fair value is less than the cost basis, the financial health of and business outlook for the issuer, including industry and sector performance and operational and financing cash flow factors, overall market conditions and trends, the Company's intent to sell the investment and whether it is more likely than not the Company would be required to sell the investment before its anticipated recovery. If a decline in fair value is determined to be other than temporary, the Company records an impairment charge in the statement of operations and establishes a new cost basis in the investment.

Receivables from Collaborations

Substantially all of the Company's collaboration revenue is related to the collaboration and alliance agreements discussed in Note 12. A substantial majority of the Company's receivables from collaborations at December 31, 2011 and 2010 are related to the Company's collaboration agreements with AstraZeneca AB.

During 2011, 2010, and 2009, the Company recognized revenue of $96,979,000, $83,380,000, and $24,180,000, respectively, or 99%, 97% and 96% of net operating revenues, respectively, from the collaboration and alliance agreements discussed in Note 12.

Product Sales

Effective as of September 30, 2009, the Company discontinued commercialization of its only marketed product, Inversine. Cost of product sales for the year ended December 31, 2009 includes materials and manufacturing costs, applied by the weighted average method, FDA fees and other fees associated with the manufacture and sale of Inversine. As a result of the discontinuation of the commercialization of Inversine, the Company recorded aggregate charges of $77,000 related to the impairment of its remaining raw materials and finished goods inventory to cost of product sales for the year ended December 31, 2009. The discontinuation of the commercialization of Inversine did not have a material impact on the Company's cash flows or results of operations for any of the periods presented.

During 2009, cost of product sales included shipping and handling costs of $183,000.

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

The Company capitalizes the costs of intellectual property acquired or licensed from external sources as intangible assets if, at the time of acquisition, the intellectual property has reached technological feasibility. Intellectual property acquired or licensed from external sources that has not reached technological feasibility at the time of acquisition or that has no expected future use is charged to research and development expense as incurred. The Company records all other charges related to the filing, prosecution and maintenance of patents to expense as incurred.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

2. Summary of Significant Accounting Policies (continued)

The Company assesses the net realizable value of its long-lived assets and evaluates these assets for impairment whenever events or changes in business circumstances indicate that the carrying amount of an asset may not be recoverable. An impairment charge 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 charge, if recognized, would be based on the excess of the carrying value of the impaired asset over its estimated fair value.

Research and Development Expense

Research and development costs are expensed as incurred and include direct costs incurred to third parties related to the Company's clinical and preclinical product candidates, 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 12.

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 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, vary from contract to contract and may result in uneven payment flows. Payments under these agreements depend on the performance of services or the achievement of specified events, such as the production of drug substance or drug product, the recruitment of clinical trial 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 a particular contract as giving rise to a payment.

Credit Risk

Financial instruments that potentially subject the Company to credit risk consist principally of cash, investments in marketable securities and receivables from collaborations. The Company has established guidelines for investment of its cash that are designed to emphasize safety, liquidity and preservation of capital. The Company places its cash and cash equivalents with prominent financial institutions. At December 31, 2011 and 2010, the Company had deposits in excess of federally insured limits of $102,412,000 and $160,932,000, respectively.

Revenue Recognition

The Company uses the revenue recognition guidance established by Financial Accounting Standards Board, or FASB, Accounting Standards Codification, or ASC, Topic 605, *Revenue Recognition*, or ASC 605. In determining the accounting for collaboration and alliance agreements, the Company follows the provisions of

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

2. Summary of Significant Accounting Policies (continued)

ASC 605, Subtopic 25, *Multiple Element Arrangements*, or ASC 605-25. ASC 605-25 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 division is required, how the arrangement consideration should be allocated among the separate units of accounting. If the arrangement constitutes separate units of accounting according to the separation criteria of ASC 605-25, the consideration received is allocated among the separate units of accounting and the applicable revenue recognition criteria must be applied to each unit. If the arrangement constitutes a single unit of accounting, the revenue recognition policy must be determined for the entire arrangement and the consideration received is recognized over the period of inception through the date the last deliverable within the single unit of accounting is expected to be delivered. Revisions to the estimated period of recognition are reflected in revenue prospectively.

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, for example, an initial payment upon effectiveness 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 revenue and recognized into revenue as license fees and milestones from collaborations on a straight-line basis over the estimated period of the Company's substantive performance obligations. If the Company does not have substantive performance obligations, it recognizes non-refundable upfront fees into revenue through the date the deliverable is satisfied.

Revenue for non-refundable payments based on the achievement of milestone events under collaboration agreements is recognized in accordance with ASC 605, Subtopic 28, *Milestone Method*, or ASC 605-28, which the Company adopted as of January 1, 2011. Milestone events under the Company's collaboration agreements may include research, development, regulatory, commercialization or sales events. Under ASC 605-28, a milestone payment is recognized as revenue when the applicable event is achieved if the event meets the definition of a milestone and the milestone is determined to be substantive. ASC 605-28 defines a milestone event as an event having all of the following characteristics: (1) there is substantive uncertainty regarding achievement of the milestone event at the inception of the arrangement; (2) the event can only be achieved based, in whole or in part, on either the company's performance or a specific outcome resulting from the company's performance; and (3) if achieved, the event would result in additional payment due to the company. The Company also treats events that can only be achieved based, in whole or in part, on either a third party's performance or a specific outcome resulting from a third party's performance as milestone events if the criteria of ASC 605-28 are otherwise satisfied.

A milestone is considered substantive if it meets all of the following criteria: (A) the payment is commensurate with either the Company's performance to achieve the milestone or with the enhancement of the value of the delivered item; (B) the payment relates solely to past performance; and (C) the payment is reasonable relative to all of the deliverables and payment terms within the arrangement. If any of these conditions is not met, the milestone payment is deferred and recognized on a straight-line basis over a period determined as discussed above.

Research and development costs that are reimbursable under collaboration agreements are recorded in accordance with ASC 605, Subtopic 45, *Principal Agent Considerations*. Amounts reimbursed under a cost sharing arrangement are reflected as a reduction of research and development expense.

Product sales revenue, net of allowances for returns and discounts, is recognized when goods are shipped, at which point title has passed. Grant payments received prior to the Company's performance of work required by

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

2. Summary of Significant Accounting Policies (continued)

the terms of the award are recorded as deferred revenue and recognized as grant revenue as the Company performs the work and incurs qualifying costs.

Income Taxes

The Company uses the liability method in accounting for income taxes as required by ASC Topic 740, *Income Taxes*, or ASC 740. Under ASC 740, deferred tax assets and liabilities are recorded for operating loss and tax credit carryforwards and for the future tax consequences attributable to the differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect of a change in tax rates on deferred tax assets and liabilities 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 the assets will be realized. ASC 740 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. ASC 740 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 ASC 740 as interest expense and to classify any penalties recognized in accordance with ASC 740 as an expense other than income tax expense.

Net Income or Loss Per Share

The Company computes net income or loss per share in accordance with ASC Topic 260, *Earnings Per Share*, or ASC 260. Under the provisions of ASC 260, basic net income or loss per share, or Basic EPS, is computed by dividing net income or loss by the weighted average number of common shares outstanding. Diluted net income or loss per share, or Diluted EPS, is computed by dividing net income or loss by the weighted average number of common shares outstanding plus, in the case of diluted net income per share, dilutive common share equivalents outstanding. The calculations of Basic EPS and Diluted EPS are set forth in the table below (in thousands, except share and per share amounts):

	Year Ended December 31,		
	2011	2010	2009
Basic:			
Net (loss) income	$ (8,529)	$ 10,899	$ (39,404)
Weighted average common shares—basic	31,637,283	28,543,408	25,636,419
Basic EPS	$ (0.27)	$ 0.38	$ (1.54)
Diluted:			
Net (loss) income	$ (8,529)	$ 10,899	$ (39,404)
Weighted average common shares—basic	31,637,283	28,543,408	25,636,419
Common share equivalents	—	1,606,916	—
Weighted average common shares—diluted	31,637,283	30,150,324	25,636,419
Diluted EPS	$ (0.27)	$ 0.36	$ (1.54)

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

2. Summary of Significant Accounting Policies (continued)

Common share equivalents consist of the incremental common shares that would be outstanding upon the exercise of stock options, calculated using the treasury stock method. For each of the years ended December 31, 2011 and 2009, the Company excluded all common share equivalents from the calculation of Diluted EPS because the Company had a net loss. As a result, Diluted EPS is identical to Basic EPS for those years. If the Company had been in a net income position for the years ended December 31, 2011 and 2009, 3,597,530 and 3,648,268 shares, respectively, subject to outstanding stock options may have been included in the calculation of common share equivalents using the treasury stock method. For the year ended December 31, 2010, a period in which the Company had net income, shares subject to outstanding stock options that were antidilutive and consequently not included in the calculation of common share equivalents totaled 850,683, calculated on a weighted-average basis.

Public Offerings of Common Stock

In May 2011, the Company completed an underwritten public offering of 3,658,537 shares of its common stock. In June 2011, the Company sold an additional 548,780 shares of its common stock upon the exercise of the over-allotment option granted to the underwriters. The Company's net proceeds from the offering, after deducting underwriters' discounts and commissions and offering expenses paid by the Company, were $80,840,000.

On October 13, 2009, the Company completed a public offering of 2,200,000 shares of its common stock. The Company's net proceeds from the offering, after deducting underwriters' discounts and commissions and offering expenses paid by the Company, were $44,449,000.

In October 2009, the Company was notified by one of its stockholders that the stockholder had generated short swing profits under the provisions of Section 16(b) of the Exchange Act on its purchases and sales of shares of the Company's common stock. The amount of realized profit under Section 16(b) was calculated to be $724,000, and the stockholder made a payment to the Company in that amount later in October 2009.

Stock-Based Compensation

The Company has two stock-based incentive plans, the 2000 Equity Incentive Plan of Targacept, Inc., as amended and restated through March 15, 2006, or the 2000 Plan, and the Targacept, Inc. 2006 Stock Incentive Plan, as amended and restated through March 9, 2011, or the 2006 Plan. The 2000 Plan and the 2006 Plan, or the Plans, are described more fully in Note 9.

The Company records stock-based compensation under the fair value recognition provisions of ASC Topic 718, *Compensation—Stock Compensation*, or ASC 718. Under ASC 718, the Company calculates the fair value of each option grant using the Black-Scholes-Merton valuation formula. The fair value of each grant is recorded as expense on a straight-line basis over the option's vesting period.

ASC 718 also requires the benefits of tax deductions in excess of recognized compensation expense to be reported as a financing cash flow, rather than as an operating cash flow. This requirement reduces net operating cash flows and increases net financing cash flows for periods after adoption. The Company cannot estimate the future effect of excess tax deductions or shortfalls on cash flows because they depend on, among other things, when employees exercise stock options and the tax deductions available to the Company at those times. No

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

2. Summary of Significant Accounting Policies (continued)

financing or operating cash flows have been recognized in periods prior to 2009 for excess tax deductions because of cumulative net operating losses generated since inception and because the related deferred tax assets are offset by a valuation allowance.

Prepaid Expenses

The Company defers and capitalizes non-refundable advance payments for goods or services to be received in the future. The Company then charges the advance payments to expense ratably as the goods are delivered or the services are rendered. The Company may make adjustments to the amount charged to expense each period if expectations change regarding the timing of delivery of goods or rendering of services.

Fair Value

The carrying amounts of cash and cash equivalents, investments in marketable securities, receivables from collaborations, accounts payable and accrued expenses are considered to be representative of their respective fair values due to their short-term natures and, in the case of investments in marketable securities, their market interest rates. Likewise, the carrying amounts of the Company's long-term debts are considered to be representative of their fair value due to their respective market interest rates.

The Company follows ASC Topic 820, *Fair Value Measurements and Disclosures*, or ASC 820, for application to financial assets. ASC 820 defines fair value, provides a consistent framework for measuring fair value under GAAP and requires fair value financial statement disclosures. ASC 820 applies only to the measurement and disclosure of financial assets that are required or permitted to be measured and reported at fair value under other ASC topics (except for standards that relate to share-based payments such as ASC Topic 718, *Compensation—Stock Compensation*).

The valuation techniques required by ASC 820 may be based on either observable or unobservable inputs. Observable inputs reflect readily obtainable data from independent sources, and unobservable inputs reflect the Company's market assumptions. These inputs are classified into the following hierarchy:

Level 1 Inputs—quoted prices (unadjusted) in active markets for identical assets that the reporting entity has the ability to access at the measurement date;

Level 2 Inputs—inputs other than quoted prices included within Level 1 that are observable for the asset, either directly or indirectly; and

Level 3 Inputs—unobservable inputs for the assets.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

2. Summary of Significant Accounting Policies (continued)

The following tables present the Company's investments in marketable securities (including those classified on the Company's balance sheet as cash equivalents) that are measured at fair value on a recurring basis as of December 31, 2011 and 2010, respectively:

December 31, 2011	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
		(in thousands)	
U.S. Treasury and U.S. or state government agency-backed securities	$69,474	$ —	$ —
Corporate debt securities	—	75,007	—
Certificates of deposit	13,000	—	—
Accrued interest	506	—	—
Total cash equivalents and marketable securities	$82,980	$ 75,007	$ —

December 31, 2010	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
		(in thousands)	
U.S. Treasury and U.S. or state government agency-backed securities	$47,463	$ —	$ —
Corporate debt securities	—	41,874	—
Certificates of deposit	13,000	—	—
Accrued interest	314	—	—
Total cash equivalents and marketable securities	$60,777	$ 41,874	$ —

Corporate debt securities are valued based on various observable inputs such as benchmark yields, reported trades, broker/dealer quotes, benchmark securities and bids.

Comprehensive Loss or Income

Comprehensive loss or income is comprised of net loss or income and net other comprehensive loss or income. Net other comprehensive loss or income includes unrealized gains and losses on the Company's available-for-sale securities, which are excluded from net loss or income. The following is a reconciliation of net loss or income to comprehensive loss or income for the years presented.

	Year Ended December 31,		
	2011	2010	2009
		(in thousands)	
Net (loss) income	$(8,529)	$10,899	$(39,404)
Unrealized (loss) gain on marketable securities, net	(189)	225	—
Comprehensive (loss) income	$(8,718)	$11,124	$(39,404)

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

2. Summary of Significant Accounting Policies (continued)

Recent Accounting Pronouncements

In June 2011, the FASB issued Accounting Standards Update No. 2011-05, *Presentation of Comprehensive Income*, or ASU 2011-05. ASU 2011-05 amends the current guidance on the presentation of comprehensive income to give an entity the option to present comprehensive income in either one continuous statement or two consecutive financial statements. The option under current guidance that permits the presentation of components of other comprehensive income as part of the statement of changes in stockholders' equity has been eliminated. ASU 2011-05 does not change the items that must be reported in other comprehensive income. ASU 2011-05 is effective for fiscal years beginning on or after December 15, 2011, and for interim periods within those years, applied retrospectively for all periods presented. Early adoption is permitted. The Company does not expect ASU 2011-05 to have a material impact on its financial position, results of operations or cash flows.

In May 2011, the FASB issued Accounting Standards Update No. 2011-04, *Amendments to Achieve Common Fair Value Measurement and Disclosure Requirements in U.S. GAAP and IFRSs*, or ASU 2011-04. ASU 2011-04 amends the current guidance to expand existing disclosure requirements and to change the description of many of the GAAP requirements for measuring fair value. ASU 2011-04 is effective for fiscal years beginning after December 15, 2011, and for interim periods within those years. The Company does not expect ASU 2011-04 to have a material impact on its financial position, results of operations or cash flows.

3. Investments in Marketable Securities

The following is a reconciliation of amortized cost to fair value of available-for-sale marketable securities (including those classified on the Company's balance sheet as cash equivalents) held at December 31, 2011 and 2010:

December 31, 2011	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
		(in thousands)		
Security type				
Cash Equivalents				
Corporate debt securities	$ 16,000	$ —	$ —	$ 16,000
Marketable Securities—Short term				
U.S. Treasury and U.S. or state government agency-backed securities	35,908	32	—	35,940
Corporate debt securities	38,531	37	(34)	38,534
Certificates of deposit	13,000	—	—	13,000
Accrued interest	247	—	—	247
Marketable Securities—Long term				
U.S. Treasury and U.S. or state government agency-backed securities	33,466	75	(7)	33,534
Corporate debt securities—long term	20,540	39	(106)	20,473
Accrued interest	259	—	—	259
Total available-for-sale marketable securities	157,951	$ 183	$ (147)	157,987

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

3. Investments in Marketable Securities (continued)

December 31, 2010	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
		(in thousands)		
Security type				
Cash Equivalents				
U.S. Treasury and U.S. or state government agency-backed securities	$ 11,998	$ 1	$ —	$ 11,999
Corporate debt securities	3,999	—	(2)	3,997
Marketable Securities—Short term				
U.S. Treasury and U.S. or state government agency-backed securities	14,698	2	—	14,700
Corporate debt securities	20,391	18	—	20,409
Certificates of deposit	13,000	—	—	13,000
Accrued interest	59	—	—	59
Marketable Securities—Long term				
U.S. Treasury and U.S. or state government agency-backed securities	20,689	84	(9)	20,764
Corporate debt securities—long term	17,337	149	(18)	17,468
Accrued interest	255	—	—	255
Total available-for-sale marketable securities	$102,426	$ 254	$ (29)	$102,651

As of December 31, 2011, the Company held investments in marketable securities with unrealized gains of $183,000 and unrealized losses of $147,000. For investments in an unrealized loss position, the duration of the loss was less than 12 months. None of these investments is considered to be other-than-temporarily impaired.

As of December 31, 2011, the Company's investments in marketable securities including those classified on its balance sheet as cash equivalents, reach maturity between January 6, 2012 and November 25, 2014, with a weighted average maturity date of approximately November 24, 2012.

4. Property and Equipment

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

	December 31,	
	2011	2010
	(in thousands)	
Laboratory equipment	$ 12,218	$ 12,133
Office furniture and fixtures	4,254	4,640
Leasehold improvements	1,395	1,175
	17,867	17,948
Less: accumulated depreciation	(12,832)	(11,876)
Property and equipment, net	$ 5,035	$ 6,072

The Company recorded $2,463,000, $1,979,000, and $1,818,000 of depreciation expense for the years ended December 31, 2011, 2010 and 2009, respectively.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

5. Intangible Assets

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

	December 31,	
	2011	2010
	(in thousands)	
Patents	$ 296	$ 296
Less: accumulated amortization	(164)	(147)
Total	$ 132	$ 149

Intangible assets consist of licensed patent rights assigned to the Company by Layton Bioscience, Inc. in 2002, which had an original value to the Company of $296,000.

The Company's prospective amortization of its intangible assets is $17,000 per year to research and development expense on a straight-line basis over the remaining useful life of the patents, a period of 17 years from the date of acquisition.

6. Accrued Expenses

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

	December 31,	
	2011	2010
	(in thousands)	
Clinical trial and preclinical study costs	$14,859	$ 8,326
Employee compensation	1,178	2,032
Other	130	158
Total	$16,167	$10,516

7. Long-term Debt

In July 2010, the Company entered into a loan agreement with a bank that provides aggregate borrowing capacity of $4,000,000 to be provided in up to three individual term loans on or prior to June 30, 2011 to fund the purchase of equipment, furnishings, software and other fixed assets. The Company borrowed $1,228,000 under the loan agreement in September 2010 and borrowed an additional $2,132,000 in June 2011. The Company's September 2010 borrowing bears interest at a fixed rate of 3.40% per annum and is repayable in equal monthly installments of $28,000 beginning January 1, 2011 through the maturity date of December 1, 2014. The Company's June 2011 borrowing bears interest at a fixed rate of 3.471% per annum and is repayable in equal monthly installments of $48,000 beginning July 1, 2011 through the maturity date of June 1, 2015. Pursuant to the loan agreement, the Company granted a first priority security interest in favor of the bank in the assets acquired with the proceeds of the loan.

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 an existing loan facility with another lender. 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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

7. Long-term Debt (continued)

borrowing bore interest at a fixed rate of 5.231% per annum and was repayable in equal monthly installments of $112,000 beginning April 1, 2008 through the maturity date of March 1, 2012. The March 2008 borrowing was paid and satisfied in full on March 1, 2012. The Company used $1,679,000 of the proceeds from the March 2008 borrowing to pay and satisfy in full the principal and interest outstanding on two tranches of the existing loan facility with another lender 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 borrowing 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.

During 2002, the Company borrowed $500,000 from the City of Winston-Salem. No payments were due on the City of Winston-Salem note until April 2007, when the Company began making monthly payments of $9,000 on the loan based on an interest rate of 5%. The note payable to the City of Winston-Salem was scheduled to mature on April 19, 2012. In December 2010, the Company repaid the remaining $135,000 balance of the note payable.

The Company paid $134,000, $156,000 and $223,000 in interest under notes payable during the years ended December 31, 2011, 2010 and 2009, respectively. Maturities of long-term debt were as follows at December 31, 2011 (in thousands):

2012	$1,240
2013	851
2014	853
2015	283
	$3,227

8. Income Taxes

For the year ended December 31, 2011, the Company did not recognize any income tax expense. For the year ended December 31, 2010, the Company recognized $3,526,000 of income tax expense primarily as a result of the application of ASC 740 to stock-based compensation. Exercises of stock options during year ended December 31, 2010 resulted in tax deductions for stock-based compensation in excess of expense recorded for the stock options under GAAP, resulting in an income tax benefit of $3,503,000. The Company recognized the income tax benefit related to the excess tax deductions as an increase to capital in excess of par value, which based on ASC 740 resulted in an offsetting charge in the same amount to income tax expense.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

8. Income Taxes (continued)

For the year ended December 31, 2009, the Company recognized an $88,000 income tax benefit primarily as a result of elections to forgo certain "bonus depreciation" deductions for federal income tax purposes in exchange for $131,000 of refundable research and development tax credits under the Housing Assistance Tax Act of 2008, as extended by the American Recovery and Reinvestment Act of 2009. These tax credits were partially offset by income tax expense of $41,000 related to tax deductions for stock-based compensation in excess of expense recorded for the stock options under GAAP. The Company has incurred cumulative net operating losses since inception. For the years shown, components of the Company's income tax expense (benefit) were as follows:

	Year Ended December 31,		
	2011	2010	2009
		(in thousands)	
Current:			
Federal	$ —	$ 3,086	$ (96)
State	—	440	8
Net current income tax expense (benefit)	—	3,526	(88)
Deferred:			
Federal	(6,147)	1,519	(13,230)
State	(1,095)	(1,321)	(2,951)
Valuation allowance	7,242	(198)	16,181
Net deferred income tax expense (benefit)	—	—	—
Net income tax expense (benefit)	$ —	$ 3,526	$ (88)

The following is a reconciliation from the federal income tax rate to the Company's effective tax rate:

	Year Ended December 31,		
	2011	2010	2009
Expected federal income tax benefit/expense at statutory rate	35%	35%	35%
Increase (decrease) resulting from:			
Research and development credits	19	(12)	5
Stock-based compensation	(13)	4	(1)
State income tax expense, net of federal benefit	3	3	4
Qualifying Therapeutic Drug Project grant	—	(3)	—
Change in unrecognized tax benefit reserves	—	(3)	—
Change in valuation allowance	(85)	(1)	(41)
Other	41	1	(2)
	— %	24%	— %

At December 31, 2011, 2010 and 2009, the Company had net operating loss carryforwards for federal income tax purposes of $135,860,000, $39,011,000, and $152,839,000, respectively, and for state income tax purposes of $134,470,000, $76,178,000 and $135,789,000, respectively. At December 31, 2011, 2010 and 2009, the Company had research and development income tax credit carryforwards for federal income tax purposes of $10,778,000, $9,556,000 and $7,340,000, respectively. The Company had research and development income tax credit carryforwards for state income tax purposes of $587,000 at December 31, 2011, 2010 and 2009. The

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

8. Income Taxes (continued)

federal net operating loss carryforwards begin to expire in 2024. The state net operating loss carryforwards begin to expire in 2019. The federal and state 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. A series of stock issuances occurring prior to the Company's initial public offering gave rise to such an ownership change. As a result, 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 recognition of deferred license fees from collaborations, research and development tax credits and net operating loss carryforwards. 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 the period in which the benefit is recorded as a reduction of income tax expense. However, in the event the Company has excess tax deductions related to the exercise of stock options, the tax benefit will be reflected as an increase to capital in excess of par value. 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 year ended December 31, 2011, the valuation allowance increased by $7,242,000. For the year ended December 31, 2010, the valuation allowance decreased by $198,000. For the year ended December 31, 2009, the valuation allowance increased by $16,181,000.

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

	December 31,	
	2011	2010
	(in thousands)	
Deferred tax assets:		
Collaboration revenue	$ 21,193	$ 55,857
Research and development tax credit	10,049	8,443
Net operating loss carryforward	45,901	7,463
Patents	1,968	2,125
Stock-based compensation	3,509	1,903
Accrued royalties	—	—
Other	48	35
Total gross deferred tax assets	82,668	75,826
Valuation allowance	(82,356)	(75,114)
Net deferred tax asset	312	712
Deferred tax liabilities		
Equipment and other	(312)	(712)
Net deferred tax asset	$ —	$ —

As of December 31, 2011, the Company had cumulative tax deductions from exercises of stock options in excess of expense recorded for the stock options under GAAP. The $7,534,000 benefit of these excess tax deductions had not begun to be realized as of December 31, 2011 because the Company incurred operating losses

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

8. Income Taxes (continued)

in the years the respective stock options were exercised and has incurred cumulative net operating losses since inception. Accordingly, the tax benefit will not be recognized as an increase to capital in excess of par value unless and until the excess deductions reduce income taxes payable.

The Company follows the provisions of ASC 740, which prescribes a 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 and also provides guidance on de-recognition, classification, interest and penalties, accounting in interim periods and disclosures. There was no cumulative effect adjustment upon adoption.

A reconciliation of beginning and ending unrecognized tax benefits is as follows (in thousands):

Balance at January 1, 2009	$1,220
Additions based on tax positions related to the current year	532
Additions based on tax positions related to prior years	134
Balance at December 31, 2009	1,886
Decreases based on tax positions related to prior years	(412)
Balance at December 31, 2010	1,474
Additions (decreases) based on tax positions related to current and prior years	—
Balance at December 31, 2011	$1,474

None of the unrecognized tax benefits would, if recognized, affect the effective tax rate because the Company has recorded a valuation allowance to fully offset federal and state deferred tax assets. The Company has no tax positions for which it is reasonably possible that the total amount of unrecognized tax benefits will significantly increase or decrease during 2012. 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, 2011, 2010 or 2009.

Because the Company has incurred cumulative net operating losses since inception, all tax years remain open to examination by U.S. federal, North Carolina and Massachusetts tax authorities. An examination of the Company's 2006 federal income tax return was completed in 2009 with no adjustments. An examination of the Company's 2009, 2008, 2007, and 2006 North Carolina income tax returns was recently completed with no material adjustments.

In November 2010, the Internal Revenue Service notified the Company that it had approved cumulative grants of $1,467,000 to the Company under the Qualifying Therapeutic Discovery Project tax credit program enacted as part of the Patient Protection and Affordable Care Act of 2010. In the fourth quarter of 2010, the Company recorded the cumulative grants as grant revenue in its financial statements.

9. Stock-Based Incentive Plans

The 2000 Plan became effective in August 2000. 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, 2011, the number of shares authorized for issuance under the Plans was 7,282,078, of which 1,276,173 shares remained available for grant.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

9. Stock-Based Incentive Plans (continued)

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 ASC 718, the Company recognizes the grant date fair value of stock options 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 primarily based on the Company's implied volatility, the calculated historical volatility of twelve to sixteen benchmark companies in the Company's industry that have been identified as comparable public entities, the Company's historical volatility and the implied volatility of the same benchmark companies. The expected term for stock options granted during 2011, 2010 and 2009 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 stock options granted as of the respective dates shown:

	Year ended December 31,		
	2011	2010	2009
Dividend yield	—	—	—
Risk-free interest rate	2.5%	2.9%	2.0%
Volatility	0.7	0.7	0.7
Expected term	6.00 years	6.27 years	6.72 years

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

9. Stock-Based Incentive Plans (continued)

A summary of option activity and changes during each of the years ended December 31, 2011, 2010 and 2009 appears below:

	Shares Subject to Options	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value (in thousands)
Outstanding at December 31, 2008	3,119,097	$ 5.21		
Granted	779,400	3.06		
Forfeited	(12,229)	4.30		
Exercised	(1,062,456)	3.16		
Outstanding at December 31, 2009	2,823,812	5.40		
Granted	941,532	20.88		
Forfeited	(21,867)	17.63		
Exercised	(643,862)	5.12		
Outstanding at December 31, 2010	3,099,615	10.07		
Granted	1,014,561	25.63		
Forfeited	(28,915)	20.03		
Exercised	(305,395)	5.89		
Outstanding at December 31, 2011	3,779,866	$ 14.51	7.01 years	$ 1,921
Vested and exercisable at December 31, 2011	2,403,785	$ 10.71	6.09 years	$ 1,468

The weighted average grant date fair value of options granted during the years ended December 31, 2011, 2010, and 2009 was $15.87, $13.46 and $2.03, respectively. The total intrinsic value of options exercised during the years ended December 31, 2011, 2010, and 2009 was $6,082,000, $11,527,000, and $16,833,000, respectively.

A summary of the status of non-vested stock options granted under the 2006 Plan as of December 31, 2011 and changes during the year ended December 31, 2011 appears below:

	Shares Subject to Options	Weighted Average Grant-Date Fair Value Per Share
Non-vested at January 1, 2010	1,166,371	$ 9.41
Granted	1,014,561	15.87
Vested	(780,114)	10.87
Forfeited	(24,737)	12.90
Non-vested at December 31, 2011	1,376,081	$ 13.28

As of December 31, 2011, there was $18,275,000 of total unrecognized compensation expense related to non-vested stock-based compensation arrangements granted under the Plans, before considering forfeitures. That cost is expected to be recorded over a weighted average period of 2.61 years. The total fair value of shares subject to stock-based compensation arrangements granted under the Plans that vested during the years ended December 31, 2011, 2010, and 2009 was $8,481,000, $4,396,000 and $2,338,000, respectively.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

9. Stock-Based Incentive Plans (continued)

The Company had 3,779,866 and 3,099,615 shares of common stock reserved for future issuance upon the exercise of outstanding stock options at December 31, 2011 and 2010, respectively.

10. Commitments and Contingencies

Leases

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 rental rate for the renewal term similar to the initial term. From 2005 to 2010, the terms of the lease were amended to, among other things, increase the rental space and include a second renewal term, exercisable at the Company's option, at the then-existing market rate for similar space in the Piedmont Triad in North Carolina. The Company exercised its first renewal option in January 2007 and, as a result, the lease extends until July 31, 2012.

The Company has entered into various other lease agreements, primarily for equipment. Rent expense incurred by the Company under the office lease and other operating leases was $2,575,000, $2,003,000 and $2,148,000 for the years ended December 31, 2011, 2010 and 2009, respectively.

The following table illustrates expected future lease payments under all operating leases (in thousands):

2012	$1,695
2013	234
2014	176
2015	1
2016 and thereafter	—
	$2,106

Employment Arrangements

The Company has entered into employment agreements with some of its executive officers. Under the agreements, if the Company terminates the employment of the executive officer other than for just cause or if the executive officer terminates his employment for good reason, in each case as that term is defined in the agreement, the executive officer is entitled, among other things, to receive severance equal to his current base salary for nine to twelve months following termination or, if shorter, until he secures other employment. The executive officer would also be entitled to continuation of the health and life insurance benefits coverage provided to him as of the date of termination for the period during which he receives severance.

11. Retirement Savings Plan

The Company has a 401(k) retirement plan in which all of its employees are eligible to participate. The Company contributed $535,000, $487,000, and $666,000 to the plan for the years ended December 31, 2011, 2010 and 2009, respectively. The Company matched employee contributions to the plan, on a per employee basis, up to 4% of each employee's wages for the years ended December 31, 2011 and 2010. During 2009 the Company matched employee contributions to the plan, on a per employee basis, up to 6% of each employee's wages.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

12. Strategic Alliance and Collaboration Agreements

AstraZeneca AB

Cognitive Disorders

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 AZD3480 (TC-1734) as a treatment for specified conditions characterized by cognitive impairment, including Alzheimer's disease and attention deficit/hyperactivity disorder, or ADHD. The Company is eligible to receive license fees and milestone payments under the agreement. The amount of license fees and milestone payments depends on the timing and achievement of specified milestone events.

AstraZeneca paid the Company an initial fee of $10,000,000 in February 2006. Based on the agreement terms, the Company allocated $5,000,000 of the initial fee to the research collaboration, which the Company recognized as revenue on a straight-line basis over the 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. 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 development period for AZD3480. In July 2009, based on feedback received from AstraZeneca regarding its development plans for AZD3480 as a treatment for ADHD, the Company extended its estimate of the development period for AZD3480 to continue through 2013 and began recognizing the part of the $5,000,000 portion of the initial fee not yet recognized as of April 1, 2009 into revenue on a straight-line basis over the remaining estimated development period. In September 2010, the Company and AstraZeneca amended the agreement to enable the Company to conduct a clinical trial of AZD3480 in mild to moderate Alzheimer's disease and to provide for respective roles and responsibilities and associated financial terms for such a study. Under the amendment, the Company received from AstraZeneca $500,000 in October 2010, $2,000,000 in September 2011 and $3,500,000 in December 2011. The Company is recognizing both the portion of the $5,000,000 of the initial fee attributable to AZD3480 license grants not yet recognized and the payments received under the amendment into revenue on a straight-line basis through 2013, which is the estimated period of the Company's performance obligations under the agreement as amended. The Company recognized $579,000, $683,000, and $1,934,000 of the initial fee as revenue for the years ended December 31, 2011, 2010, and 2009, respectively. The Company recognized $613,000 of the payments received under the amendment for the year ended December 31, 2011.

Under the agreement, the Company is also eligible to receive additional payments from AstraZeneca if specified milestone events for AZD3480 are achieved for Alzheimer's disease, including up to an additional $35,000,000 if development milestone events are achieved, an additional $20,000,000 if a regulatory milestone event is achieved, and up to an additional $90,000,000 if first commercial sale milestone events are achieved, plus, if regulatory approval is achieved for AZD3480 for any indication, stepped double-digit royalties on any sales of AZD3480 for that indication or any other indication. The Company is also eligible to receive other payments under the agreement if development, regulatory, first commercial sale and first detail milestone events for AZD3480 are achieved for any other target indication under the agreement. AZD3480 is not currently in development for any indication other than Alzheimer's disease. Under the terms of a sponsored research agreement and a subsequent license agreement between the Company and University of Kentucky Research Foundation, or UKRF, if the Company receives any of these payments from AstraZeneca related to AZD3480, including royalties, the Company is required to pay a low-single digit percentage of each such payment to UKRF.

12. Strategic Alliance and Collaboration Agreements (continued)

Based solely on projected activities and timelines, the Company does not expect it to be possible for it to achieve any contingent milestone event for AZD3480 during 2012. The likelihood that the Company will achieve any particular milestone event with respect to AZD3480 in any future period is uncertain, and the Company may not ever achieve any of the milestone events with respect to AZD3480.

With respect to AZD1446, the most advanced product candidate that arose out of the parties' preclinical research collaboration described below, the Company is eligible to receive additional payments from AstraZeneca if specified milestone events for AZD1446 under the agreement are achieved for Alzheimer's disease, including up to an additional $14,000,000 if development milestone events are achieved, an additional $10,000,000 if a regulatory milestone event is achieved and up to an additional $49,000,000 if first commercial sale milestone events are achieved, plus, if regulatory approval is achieved for AZD1446 for any indication, stepped royalties on any sales of AZD1446 for that indication or any other indication. The Company is also eligible to receive other payments under the agreement if development, regulatory, first commercial sale and first detail milestone events for AZD1446 are achieved for any other target indication under the agreement. AZD1446 is not currently in development for any indication other than Alzheimer's disease. Based solely on projected activities and timelines, the Company does not expect it to be possible for it to achieve any contingent milestone event for AZD1446 during 2012. The likelihood that the Company will achieve any particular milestone event with respect to AZD1446 in any future period is uncertain, and the Company may not ever achieve any of the milestone events with respect to AZD1446.

The Company considers that each of the potential milestone events under the agreement with respect to AZD3480 or AZD1446 would be substantive because the applicable criteria of its revenue recognition policy (see Note 2) would be satisfied.

The Company and AstraZeneca conducted a multi-year preclinical research collaboration under the agreement. The term of the research collaboration expired in January 2010 and, as a result, the Company did not recognize any collaboration research and development revenue for the years ended December 31, 2011 and 2010. While the research collaboration was ongoing, the Company was eligible to receive payments from AstraZeneca for research services performed. The Company recognized collaboration research and development revenue as the research was performed and related expenses were incurred. The Company recognized collaboration research and development revenue of $5,246,000 for the year ended December 31, 2009.

In October 2007, the Company provided notice under the agreement 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 clinical proof of concept clinical trial in accordance with a mutually acceptable development plan, following which AstraZeneca would have the right to license TC-5619 on terms specified in the agreement (as it was amended in April 2010 as described below). The Company recognized the $2,000,000 payment as revenue on a straight-line basis over the period estimated from time to time for the Company's research and development obligations for TC-5619. The Company completed its research and development obligations for TC-5619 under the agreement in the second quarter of 2011. Accordingly, as of June 30, 2011, all of the $2,000,000 payment related to TC-5619 received from AstraZeneca was recognized into revenue. The Company recognized $87,000, $278,000 and $596,000 of the payment as revenue for the years ended December 31, 2011, 2010 and 2009, respectively.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

12. Strategic Alliance and Collaboration Agreements (continued)

In April 2010, the Company and AstraZeneca amended the agreement to modify the terms applicable to TC-5619. In conjunction with the amendment, the Company and AstraZeneca agreed to an expanded development program for TC-5619 and the Company received a payment of $11,000,000 to maintain AstraZeneca's option to license TC-5619. The Company recorded the $11,000,000 payment as deferred revenue and recognized it as revenue on a straight-line basis over the period estimated from time to time for the Company's research and development obligations for TC-5619 under the agreement, which, as noted above, were completed in the second quarter of 2011. Accordingly, as of June 30, 2011, all of the $11,000,000 payment related to TC-5619 received from AstraZeneca was recognized into revenue. The Company recognized $4,714,000 and $6,286,000 of the payment as revenue for the years ended December 31, 2011 and 2010, respectively. In late April 2011, the Company received notice from AstraZeneca that it had determined not to exercise its license option.

The Company has received payments upon achievement of milestone events under the agreement that it recognized in full as revenue upon achievement because the event met each of the conditions required for immediate recognition under its revenue recognition policy (see Note 2). In particular, the Company received a $10,000,000 payment from AstraZeneca in July 2009 based on achievement of the objective in a completed Phase 2 clinical trial of AZD3480 in adults with ADHD, a milestone event under an amendment to the agreement. The Company made a payment of $350,000 to UKRF in January 2010 as a result of the $10,000,000 payment received from AstraZeneca. The Company has also received cumulative payments from AstraZeneca of $2,600,000 based on the achievement of milestone events related to the development of product candidates arising under the parties' completed preclinical research collaboration, including AZD1446.

AstraZeneca has paid the Company an aggregate of $88,120,000 under the agreement since its inception.

TC-5214

In December 2009, the Company entered into a collaboration and license agreement with AstraZeneca AB for the global development and commercialization of TC-5214. Under the agreement, AstraZeneca made an upfront payment to the Company of $200,000,000 and the Company is eligible to receive additional payments if specified milestone events for TC-5214 are achieved, plus significant stepped double-digit royalties on net sales of TC-5214 worldwide. The Company recorded the upfront payment made by AstraZeneca as deferred revenue and is recognizing the payment as revenue on a straight-line basis over the estimated period of the Company's substantive performance obligations under the agreement, or approximately 33 months. The Company recognized $72,565,000 of the upfront payment as revenue for each of the years ended December 31, 2011 and 2010 and $398,000 of the upfront payment as revenue for the year ended December 31, 2009.

The Company is eligible to receive additional payments from AstraZeneca if specified milestone events for TC-5214 are achieved, including up to an additional $10,000,000 if a development milestone event is achieved, up to an additional $275,000,000 if regulatory milestone events are achieved, up to an additional $105,000,000 if first commercial sale milestone events for TC-5214 are achieved, up to an additional $150,000,000 if development, labeling and marketing criteria are achieved and up to an additional $500,000,000 if sales milestone events for TC-5214 are achieved. Based solely on projected activities and timelines, the Company expects that the only milestone payment for which it is eligible and that could possibly be earned during 2012 would be $50,000,000 upon acceptance by the FDA of an NDA for TC-5214 as adjunct therapy for major depressive disorder. If an NDA for TC-5214 is submitted and then accepted for filing by the FDA, the next

12. Strategic Alliance and Collaboration Agreements (continued)

regulatory milestone for which the Company is eligible would be $150,000,000 upon approval of the NDA. The likelihood that the Company will achieve any particular milestone event with respect to TC-5214 in 2012 or in any future period is uncertain, and the Company may not ever achieve any of the milestone events with respect to TC-5214.

The Company considers that each of the potential milestone events under the agreement would be substantive because the applicable criteria of its revenue recognition policy (see Note 2) would be satisfied.

The Company and AstraZeneca jointly designed a program for the global development of TC-5214 as an adjunct therapy and as a “switch” monotherapy, in each case in patients with major depressive disorder who do not respond adequately to initial antidepressant treatment. AstraZeneca is responsible for 80% and the Company is responsible for 20% of the costs of this program, except that AstraZeneca is responsible for 100% of development costs that are required only to obtain or maintain regulatory approval in countries outside the United States and the European Union. The Company has the right to terminate its obligation to fund its share of the costs of the program once it has funded a specified amount. In addition, for each of the Company and AstraZeneca, costs that were not contemplated at execution to be part of the program may in some cases be excluded from the cost-sharing arrangement. If the Company funds the specified amount and terminates its obligation to fund its share of further costs of the program, any future milestones and royalties payable to the Company under this agreement would be reduced by the amount of the Company’s unfunded share plus interest at a specified rate, subject to a maximum reduction that may be applied to any one payment. In addition, if the Company and AstraZeneca mutually agree to develop TC-5214 for any indication other than major depressive disorder or in any formulation other than those contemplated by the current program, the same cost-sharing arrangement would apply, except that the Company would have the immediate right to terminate its obligation to fund its share of development costs for the other indication or formulation. If the Company terminates its obligation to fund its share of these other development costs, any future milestones and royalties payable to the Company under this agreement would be reduced by the amount of the Company’s unfunded share plus interest at a specified rate, subject to a maximum reduction that may be applied to any one payment, but only from and after the occurrence of a specified event to be agreed upon by the parties.

The Company’s portion of the costs of the TC-5214 development program was $32,046,000 and $10,771,000 for the years ended December 31, 2011 and 2010, respectively. AstraZeneca’s allocable portion of the program costs paid by the Company was $336,000 and $2,023,000 for the years ended December 31, 2011 and 2010, respectively. AstraZeneca’s allocable portion of the program costs paid by the Company is reflected in the Company’s financial statements as a reduction to research and development expense.

AstraZeneca is responsible under the agreement for executing and funding the costs of any commercialization of TC-5214 worldwide. The Company has retained an option to co-promote TC-5214 to a specified target physician audience in the United States. If the Company exercises its co-promotion option, AstraZeneca would compensate the Company on a per detail basis. AstraZeneca is also responsible under the agreement for the manufacture and supply of TC-5214.

Under the terms of an existing license agreement, the Company paid $16,000,000 to University of South Florida Research Foundation, or USFRF, in February 2010 based on the Company’s receipt of the upfront payment from AstraZeneca and would be required to pay to USFRF a percentage of each milestone payment that may be received from AstraZeneca, after deducting from the milestone payment the unexhausted portion of the

12. Strategic Alliance and Collaboration Agreements (continued)

Company's projected share of the costs of the initial development program for TC-5214, as well as royalties on any future TC-5214 product sales. The percentage of each milestone payment, net of any deduction, that the Company would be required to pay would be at least 10% and could be greater in specified circumstances. Based on the terms of the license agreement with USFRF and the terms of another existing license agreement with Yale University, the Company expects to pay royalties at an effective worldwide rate in the low single digits and that the effective royalty rate could in some circumstances reach the mid single digits.

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 set forth the terms of an alliance designed to discover, develop and market product candidates that selectively target specified NNR subtypes for specified therapeutic focus areas. In February 2011, the Company received notice of termination of the agreement. By the terms of the agreement, the termination became effective in May 2011.

Under the 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 on July 27, 2007. 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 recognition of both the initial payment made by GlaxoSmithKline and the deemed premium paid for the shares of the Company's common stock purchased by GlaxoSmithKline and was recognizing both amounts into revenue on a straight-line basis over the nine-year period of the Company's research and early development obligations estimated at inception of the agreement. The Company recognized $2,613,000 of the initial payment and deemed premium as revenue for each of the years ended December 31, 2010 and 2009.

In December 2007, the Company received a $6,000,000 payment from GlaxoSmithKline upon the achievement of a specified 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, there was not substantive uncertainty regarding achievement of the milestone event within the meaning of the Company's revenue recognition policy. Accordingly, the Company recorded the payment as deferred revenue and was recognizing it into revenue on a straight-line basis over the remaining portion of the nine-year period of the Company's research and early development obligations estimated at inception of the agreement. The Company recognized $692,000 of the payment as revenue for each of the years ended December 31, 2010 and 2009.

The Company received an aggregate of $2,500,000 in payments from GlaxoSmithKline for achievement of specified milestone events under the agreement for the year ended December 31, 2009. The Company immediately recognized the full amount of each payment as revenue upon achievement of the corresponding milestone event because each event met each of the conditions required for immediate recognition under its revenue recognition policy (see Note 2).

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2011

12. Strategic Alliance and Collaboration Agreements (continued)

As a result of its receipt in February 2011 of notice of termination of the agreement, the Company recognized the remaining $18,421,000 of the payments discussed above not previously recognized into revenue for the first quarter of 2011 in accordance with its revenue recognition policy (see Note 2).

13. Selected Quarterly Financial Data (unaudited)

	2011 Quarter			
	First	Second	Third	Fourth
	(in thousands, except share and per share amounts)			
Net operating revenues	$ 38,994	$ 20,743	$ 18,955	$ 18,945
Income (loss) from operations	12,302	(2,571)	(9,331)	(10,145)
Net income (loss)	12,587	(2,257)	(9,054)	(9,805)
Basic net income (loss) per share(1)	$ 0.43	$ (0.07)	$ (0.27)	$ (0.29)
Diluted net income (loss) per share(1)	$ 0.41	$ (0.07)	$ (0.27)	$ (0.29)
Weighted average common shares outstanding—basic	28,996,060	30,725,227	33,377,874	33,382,640
Weighted average common shares outstanding—diluted	30,399,750	30,725,227	33,377,874	33,382,640

	2010 Quarter			
	First	Second	Third	Fourth
	(in thousands, except share and per share amounts)			
Net operating revenues	$ 19,518	$ 20,902	$ 21,798	$ 23,495
Income (loss) from operations	7,089	4,966	2,417	(1,357)
Income tax expense	(626)	(1,512)	(257)	(1,131)
Net income (loss)	6,795	3,782	2,486	(2,164)
Basic net income (loss) per share(1)	$ 0.24	$ 0.13	$ 0.09	$ (0.08)
Diluted net income (loss) per share(1)	$ 0.23	$ 0.13	$ 0.08	$ (0.08)
Weighted average common shares outstanding—basic	28,311,452	28,509,619	28,622,187	28,724,965
Weighted average common shares outstanding—diluted	29,172,218	30,152,309	30,173,406	28,724,965

(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 for the second, third and fourth quarters of 2011 and for the fourth quarter of 2010 because common share equivalents are excluded from the calculations of diluted weighted average common shares outstanding for those quarters, as their effect is antidilutive.

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

None.

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(b) 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 Rule 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, 2011 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, 2011, 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, 2011. 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, 2011, 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, 2011, 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, 2011 and 2010, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2011 and our report dated March 6, 2012 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Raleigh, North Carolina
March 6, 2012

(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, 2011 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 2012 Annual Meeting of Stockholders to be filed with the SEC under the captions “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 and 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 2012 Annual Meeting of Stockholders to be filed with the SEC under the captions “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 2012 Annual Meeting of Stockholders to be filed with the SEC under the captions “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 2012 Annual Meeting of Stockholders to be filed with the SEC under the captions “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 2012 Annual Meeting of Stockholders to be filed with the SEC under the caption “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 91.

(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 6, 2012

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.

Signature	Title	Date
/s/ J. DONALD DEBETHIZY **J. Donald deBethizy**	Chief Executive Officer, President and Director (principal executive officer)	March 6, 2012
/s/ ALAN A. MUSSO **Alan A. Musso**	Senior Vice President, Finance and Administration, Chief Financial Officer and Treasurer (principal financial officer and principal accounting officer)	March 6, 2012
/s/ MARK SKALETSKY **Mark Skaletsky**	Chairman of the Board of Directors	March 6, 2012
/s/ M. JAMES BARRETT **M. James Barrett**	Director	March 6, 2012
/s/ CHARLES A. BLIXT **Charles A. Blixt**	Director	March 6, 2012
/s/ JULIA R. BROWN **Julia R. Brown**	Director	March 6, 2012
/s/ G. STEVEN BURRILL **G. Steven Burrill**	Director	March 6, 2012
/s/ ERROL B. DE SOUZA **Errol B. De Souza**	Director	March 6, 2012
/s/ ALAN W. DUNTON **Alan W. Dunton**	Director	March 6, 2012
/s/ JOHN P. RICHARD **John P. Richard**	Director	March 6, 2012
/s/ RALPH SNYDERMAN **Ralph Snyderman**	Director	March 6, 2012

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 and further amended effective as of August 6, 2009 (incorporated by reference to Exhibit 3.1 to the Company's Current Report on Form 8-K, as filed with the SEC on August 11, 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, 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, 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, as filed with the SEC on March 16, 2006 (Registration No. 333-131050))
10.2(a)	Lease, 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 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 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, effective August 1, 2002, by and between the Company and Wake Forest University Health Sciences
10.2(e)	Fourth Lease Amendment, dated September 18, 2007 effective August 1, 2007, to Lease, effective August 1, 2002, by and between the Company and Wake Forest University Health Sciences (incorporated by reference to Exhibit 10.2(e) to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2009)

Exhibit Number	Description
10.2(f)	Fifth Lease Amendment, executed January 20, 2010 effective October 1, 2009, to Lease, effective August 1, 2002, by and between the Company and Wake Forest University Health Sciences (incorporated by reference to Exhibit 10.2(f) to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2009)
10.2(g)	Sixth Lease Amendment, effective June 30, 2010, to Lease, 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, 2010)
10.3(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))
10.3(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))
10.3(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))
10.3(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))
10.4(a)*	Targacept, Inc. 2006 Stock Incentive Plan, as amended and restated through March 9, 2011 (incorporated by reference to Exhibit 10.4(a) to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2010)
10.4(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, as filed with the SEC on March 16, 2006 (Registration No. 333-131050))
10.4(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, as filed with the SEC on March 16, 2006 (Registration No. 333-131050))
10.4(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, as filed with the SEC on March 16, 2006 (Registration No. 333-131050))
10.4(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, as filed with the SEC on March 16, 2006 (Registration No. 333-131050))
10.5(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))
10.5(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)
10.6(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))

Exhibit Number	Description
10.6(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)
10.7(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))
10.7(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)
10.8(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))
10.8(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)
10.9(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))
10.9(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)
10.10(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))
10.10(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)
10.10(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)
10.11*	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)
10.12(a)+	Amended and Restated License Agreement, dated as of March 9, 2004, by and between the Company and 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))
10.12(b)+	Amendment No. 1, effective September 21, 2009, to Amended and Restated License Agreement dated March 9, 2004, by and between the Company and University of South Florida Research Foundation, Inc. (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2009)
10.13(a)+	License Agreement, dated May 26, 1999, by and between the Company and 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))

Exhibit Number	Description
10.13(b)+	Amendment No. 1, dated August 16, 2005, to License Agreement, dated May 26, 1999, by and between the Company and 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, as filed with the SEC on April 6, 2006 (Registration No. 333-131050))
10.14(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)
10.14(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)
10.14(c)+	Amendment No. 2 dated July 8, 2009 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, 2009)
10.14(d)+	Amendment No. 3, effective as of April 30, 2010, 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 June 30, 2010)
10.14(e)+	Amendment No. 4, effective as of September 28, 2010, 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, 2010)
10.15+	Exclusive License Agreement, dated January 22, 2007, by and between the Company and Yale University
10.16+	Collaboration and License Agreement, dated as of December 3, 2009, by and between the Company and AstraZeneca AB (incorporated by reference to Exhibit 10.20 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2009)
10.17+	Exclusive License Agreement, effective August 3, 2010, between the Company and Cornerstone Therapeutics Inc. (incorporated by reference to Exhibit 10.18 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2010)
10.18*	Description of Annual Cash Incentive Program (incorporated by reference to Exhibit 10.19 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2010)
10.19*	Description of Non-Employee Director Compensation Program (incorporated by reference to Exhibit 10.22 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2009)
23.1	Consent of Ernst & Young LLP
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

Exhibit Number	Description
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
101**	The following materials from the Company's Annual Report on Form 10-K for the year ended December 31, 2011, formatted in XBRL (eXtensible Business Reporting Language): (i) the Balance Sheets, (ii) the Statements of Operations, (iii) the Statements of Stockholders' Equity, (iv) the Statements of Cash Flows, and (v) Notes to Financial Statements, tagged as blocks of text.

+ 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 contract, compensatory plan or arrangement.

** Pursuant to Rule 406T of Regulation S-T, the Interactive Data Files in Exhibit 101 hereto are deemed not filed or part of a registration statement or prospectus for purposes of Sections 11 or 12 of the Securities Act of 1933, as amended, are deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and otherwise are not subject to liability under those sections.

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

Exhibit 10.2(d)

NORTH CAROLINA)
) THIRD LEASE AMENDMENT
FORSYTH COUNTY)

This Third Lease Amendment ("**Amendment**") is made effective as of the 1st day of January, 2007 (the "**Amendment Date**"), by and between Wake Forest University Health Sciences, a North Carolina non-profit corporation having its principal office in Winston-Salem, North Carolina ("**Landlord**"), and Targacept, Inc., a Delaware corporation having its principal office in Winston-Salem, North Carolina ("**Tenant**"). Unless otherwise defined herein, all of the capitalized terms of this Amendment shall have the same meanings ascribed to them in the Lease effective August 1, 2002, as amended by the First Lease Amendment effective January 1, 2005 (the "**First Lease Amendment**") and the Second Lease Amendment effective March 31, 2006 (the "**Second Lease Amendment**"), which is hereinafter referred to as the "**Lease**."

WITNESSETH:

WHEREAS, pursuant to the Lease, Tenant has an option to lease up to 12,338 additional rentable square feet of space on the first floor of the Building (the "**First Floor Option Space**"); and

WHEREAS, pursuant to the Lease, Tenant also has an option to lease up to 4,387 additional rentable square feet of space on the first floor of the Building (the "**PTRP Option Space**"); and

WHEREAS, Tenant provided Landlord notice on July 3, 2006, of its exercise of its Option to Lease as to all of the First Floor Option Space and of its exercise of its Option to Lease as to a portion of the PTRP Option Space, all such space (together with some additional space determined in connection with the BOMA Plan referenced below) as further described in this Amendment (the "**January 2007 Expansion Space**"), Tenant's lease of the January 2007 Expansion Space to become effective on January 1, 2007 and through the Renewal Term; and

WHEREAS, Tenant in such written notice also exercised its Option to Lease as to the remaining PTRP Option Space, as further described in this Amendment (the "**August 2007 Expansion Space**" and, together with the January 2007 Expansion Space, the "**Expansion Space**"), Tenant's lease of the August 2007 Expansion Space to be effective August 1, 2007 and through the Renewal Term; and

WHEREAS, Landlord is willing to provide an amount to Tenant for certain Tenant improvements to the Expansion Space in consideration of the rents agreed to be paid for such Expansion Space by Tenant as further provided herein; and

WHEREAS, per a BOMA Plan of the first floor prepared in August 2006 by Specialty Operations Solutions (which BOMA Plan is attached hereto as part of Exhibit A-2), the Expansion Space totals 16,924 square feet (which number does not include approximately 6,564 of square feet comprised of building and floor common area and vertical penetrations); and

WHEREAS, Tenant desires to Lease from Landlord and Landlord desires to lease to Tenant the Expansion Space, upon the terms and for the rents as further set forth herein; and

WHEREAS, Tenant has agreed that its execution of this Lease Amendment constitutes written notice of the exercise of its Renewal Option, resulting in a Renewal Term ending July 31, 2012; and

WHEREAS, in connection with Tenant's exercises of the Options to Lease described herein and Tenant's exercise of the Renewal Option, Landlord is willing to provide Tenant with the right, but not the obligation, to extend the term of the Lease for a second additional five (5) year term (the "**Second Renewal Term**");

NOW, THEREFORE, for and in consideration of the premises, of the rents reserved and to be paid by Tenant to Landlord, and of the additional mutual covenants of the parties, the parties hereby agree to amend the Lease as follows:

1. The Lease is amended by:

   A. Deleting Exhibit A of the Lease, as amended, and substituting in lieu thereof the attached Exhibit A, describing the Demised Premises.

   B. Deleting Exhibit A-2 ("One Technology Place First Level Floor Plan") and substituting in lieu thereof the attached Exhibit A-2, which reflects modifications to the first and second pages only. In particular, the new first page of such Exhibit shows the allocation of additional pro rata parking spaces based upon the additional occupancy by Tenant upon execution of this Amendment.

   C. Revising the caption of paragraph 2 of the Lease to read: "INITIAL TERM, OPTIONS TO RENEW, RIGHT OF FIRST REFUSAL ON ADDITIONAL SPACE."

   D. Deleting paragraph 2.2 of the Lease and substituting in lieu thereof the following paragraph 2.2:

      "2.2 Renewal Rights. So long as Tenant is not in default under this Lease, Tenant has the right, but not the obligation, to extend the term of this Lease (a "Renewal Option") under the same terms and conditions for an additional five (5) year term (the "Renewal Term") and, if the Renewal Option for the Renewal Term is exercised, for a second additional five (5) year term (the "Second Renewal Term"). Tenant must exercise its right for (i) the Renewal Term by written notice to Landlord given on or before the date that is one hundred eighty (180) days prior to the expiration of the Initial Term and (ii) the Second Renewal Term by written notice to Landlord given on or before the date that is one hundred eighty (180) days prior to the expiration of the Renewal Term. If Tenant does not exercise its right to extend in a timely manner, Tenant will have irretrievably lost its right to extend the term of this Lease. Rental payments applicable for the Renewal Term or the Second Renewal Term, in each case if exercised, shall be as set forth in paragraphs 3.1 and 3.2. Any extension of this Lease beyond the Second Renewal Term (if exercised) shall be upon the terms and conditions mutually agreed upon by Landlord and Tenant, and unless such agreement is reached, this Lease shall expire."

E. Deleting paragraph 2.4 of the Lease and its subparagraphs and Exhibit C, and substituting in lieu thereof the following.

"2.4 Except as otherwise provided in this subparagraph, Tenant shall have the unilateral right to terminate this Lease ("Termination Right") at any time after July 31, 2010 and upon payment as required by paragraph 6.2.2 of the Lease. In order to exercise the Termination Right, Tenant shall provide Landlord with not less than one hundred eighty (180) days prior written notice. Provided, however, Tenant shall have waived its Termination Right in each of the following circumstance and for the period stated upon Tenant's request pursuant to paragraph 6.1 to require Landlord to provide Tenant an allowance for redecorating or for upfitting of the Demised Premises, and continuing for the remainder of the Renewal Term."

F. Deleting the table appearing in paragraph 3.1 of the Lease and substituting in lieu thereof the following table and accompanying notes:

"3.1 Tenant will pay annual rental pursuant to the following schedule ("rsf" indicates "rentable square foot"):

Initial Term

	Demised Premises		
Effective Date	3rd & 4th Floors (40,432 rsf)	1,000 rsf 1st Floor	13,955 rsf 1st Floor (includes 1,000 rsf)
Commencement Date 8/1/02	$36.00/rsf	--	--
Amendment Date 1/1/05-12/31/06	$36.00/rsf	$15.00/rsf	--
1/1/07-7/31/07	$36.00/rsf	--	$18.80/rsf Base ($21,862.83/month)
1/1/07-7/31/07	$36.00/rsf	--	$34.59/rsf Upfit Amortized (a total of $281,577.01 for the 7-month period)

Renewal Term

ONE TECH SPACE TERM	SF	RENT	COMMENTS	TOTAL ANNUAL (per month)
1st Floor:				
8/1/07-7/31/12	13,955	$18.80/rsf Base		$262,354.00 ($21,862.83/mo)
8/1/07-7/31/12	13,955	$34.59/rsf Upfit Amortized	Upfit costs of $2.5 million @ 9%/7 years	$482,672.40

SUBTOTAL				**$745,026.40**
3rd and 4th Floor: 8/1/07-7/31/12	40,432	$33.60/rsf	Current rate is $36.00/sf to 7/31/07	$1,358,515.20 ($113,209.60)
1st Floor: 8/1/07-7/31/12	2,969	$18.80/rsf		$55,817.20 ($4,651.43)
SUBTOTAL				**$1,414,332.40**
TOTAL:				**$2,159,358.80**
Second Floor*	20,669	20.00/rsf		$413,380.00 ($34,448.33)

* if corresponding Option to Lease is exercised by Tenant

Second Renewal Term

The annual rent per rentable square foot for all of the space leased during the Second Renewal Term, if any, shall be equal to the then-existing market rate for similar space in the Piedmont Triad in North Carolina, as mutually determined in good faith by Landlord and Tenant. Unless Tenant does not have an interest in extending the term of the Lease for the Second Renewal Term, Landlord and Tenant shall exercise the requisite diligence to ensure that they mutually determine the annual rent per rentable square foot applicable to the Second Renewal Term, in writing, on or before July 31, 2011.

The annual rent payable during the Initial Term, the Renewal Term, and, if applicable, the Second Renewal Term (herein collectively "Rent") is payable in equal monthly installments in advance on the first day of each calendar month of each calendar year during the Initial Term, the Renewal Term, and, if applicable, the Second Renewal Term, prorated for any partial month. Any increases or decreases in the amount of square footage leased during a month will be adjusted in the subsequent monthly payment. Rent payments shall be payable to "Wake Forest University Health Sciences" and sent to Landlord in care of Controller's Office, Attention: Doug Edgeton, Medical Center Boulevard, Winston-Salem, NC 27157.

G.

- deleting each reference to "Renewal Term" in paragraph 2.3.3 and replacing it with a reference to "Renewal Term and, if applicable, Second Renewal Term";
- deleting "During the Initial Term and the Renewal Term" from paragraph 3.2.1 and replacing it with "During the Initial Term and, if any, the Renewal Term and the Second Renewal Term";
- deleting "During the Initial Term and the Renewal Term" from paragraph 3.2.2.1 and replacing it with "During the Initial Term and, if any, the Renewal Term and the Second Renewal Term";
- deleting "any Renewal Term" from paragraph 18.1 and replacing it with ", if any, the Renewal Term and the Second Renewal Term";
- deleting "Renewal Term (as applicable)" from paragraph 19 and replacing it with "Renewal Term or Second Renewal Term (as applicable)";

- deleting “a Renewal Term” from paragraph 33 and replacing it with “the Renewal Term or Second Renewal Term”; and
- deleting “any Renewal Term” from paragraph 38 and replacing it with “, if any, Renewal Term or Second Renewal Term.”

H. Adding the following sentence to the end of paragraph 6.1: “In addition to, and not in substitution for, the allowance provided pursuant to the preceding sentence, at any time during 2014, Landlord shall provide Tenant, upon Tenant’s request, an allowance of Five Dollars ($5.00) per rentable square foot of the Demised Premises located on the first floor of the Building for use by Tenant in the redecoration of such first floor Demised Premises.”

I. Deleting “the Amendment Date” from paragraph 6.2 of the Lease and replacing it with “January 1, 2005” and then adding the following subparagraphs 6.2.1 and 6.2.2:

6.2.1 Landlord has agreed to pay directly to third parties designated by Tenant, or alternatively at Tenant’s discretion to reimburse Tenant, amounts incurred in connection with the upfitting and improvement of the Expansion Space (the “**2007 Upfitting Funding**”); provided that the 2007 Upfitting Funding shall be equal to two million, five hundred thousand dollars ($2,500,000) in the aggregate.

6.2.2 Landlord’s recovery of the 2007 Upfitting Funding is reflected in the rental rate for the January 2007 Expansion Space over a period of eighty-four (84) months. The parties acknowledge that the remaining Lease Term (inclusive of the Renewal Term) extends for sixty-seven (67) months; therefore, if the lease is terminated prior to the expiration of the Renewal Term, Tenant agrees to pay to Landlord, in addition to any other amounts which may be due Landlord, that portion of the 2007 Upfitting Funding which is unpaid as of the date of such termination. If the Lease terminates upon expiration of the Renewal Term, the amount payable to Landlord will be $674,903.49, provided that all installments of Rent have been timely paid. Landlord has previously provided to Tenant a schedule depicting the amortization of the 2007 Upfitting Funding.

3. The sum of $7,402.80 (three (3) months times $2,467.60, the monthly amount (when amortized over twelve (12) months) of the $29,611.20 additional space hold fee) shall be applied as a credit against the first Rent due for the First Floor Option Space.

4. Landlord affirms and acknowledges its obligations pursuant to paragraphs 6.3 and 6.4 of the Lease.

5. Landlord shall pay directly to third parties designated by Tenant, or alternatively at Tenant’s discretion shall reimburse Tenant, within fifteen (15) days following the date of each invoice provided by Tenant to Landlord therefor from time to time after the date hereof, the 2007 Upfitting Funding (as defined in the Lease); provided that Landlord’s obligation under this paragraph 5 shall be equal to two million, five hundred thousand dollars ($2,500,000) in the aggregate.

6. Except as amended herein, all of the terms and conditions of the Lease remain in full force and effect.

[signature page follows]

IN WITNESS WHEREOF, Landlord and Tenant have caused this Amendment to be executed, pursuant to authority duly granted, effective as of the Amendment Date set forth above.

LANDLORD:

Wake Forest University Health Sciences

By: /s/ Richard H. Dean
Richard H. Dean, M.D.
President

Date: 1-18-07

TENANT:

Targacept, Inc.

By: /s/ J. Donald deBethizy
J. Donald deBethizy
President

Date: January 22, 2007

Exhibit A

Demised Premises

The Demised Premises consist of the following:

- As of the Commencement Date, all of the third and fourth floors, consisting of 40,432 rentable square feet, including within the meaning of "Premises" or "Demised Premises" the entire fourth floor of the Building, to be utilized as Tenant's laboratory facilities, encompassing 20,216 rentable square feet, and 20,216 rentable square feet of general office space on the third floor;
- As of January 1, 2005, an additional 1,000 rentable square feet on the first floor of the Building, to be utilized as "Tenant's Storage Space";
- As of January 1, 2007, additional space located on the first floor of the Building, consisting of 13,955 rentable square feet (inclusive of the 1,000 rentable square feet described above), as depicted on the attached First Level Floor Plan attached hereto as a part of Exhibit A-2:

Rentable square footage*	Designation on Exhibit A-2 First Floor Plan	Color of Designated Space on Plan
6,555	Lab-1	blue
2,293	Office-1	purple
3,171	Office-2	olive
1,936	Office-5	yellow

; and

- As of August 1, 2007, further additional space located on the first floor of the Building, consisting of 2,969 rentable square feet, as depicted on the attached First Level Floor Plan attached hereto as a part of Exhibit A-2:

Rentable square footage	Designation on Exhibit A-2 First Floor Plan	Color of Designated Space on Plan
741	Office-3	beige
2,228	Office-4	salmon

; in each case together with rights of use of and subject to the rights of others in and to the Common Areas of the Building. Diagrams of the Demised Premises and Common Areas are as shown on the attached Exhibit A-2 (5 pages).

Exhibit A-2

(5 pages)

[GRAPHIC OF FLOOR PLANS]

Exhibit 10.15

[********] Certain confidential information contained in this document, marked by brackets, has been omitted and filed separately with the Securities and Exchange Commission pursuant to Rule 24b-2 of the Securities Exchange Act of 1934, as amended.

EXCLUSIVE LICENSE AGREEMENT

THIS AGREEMENT (the "Agreement") by and between YALE UNIVERSITY, a corporation organized and existing under and by virtue of a charter granted by the general assembly of the Colony and State of Connecticut and located in New Haven, Connecticut ("YALE"), and Targacept, Inc., a corporation organized and existing under the laws of the State of Delaware with principal offices located in Winston-Salem, North Carolina ("LICENSEE"), is effective as of the date of final signature below ("EFFECTIVE DATE").

ARTICLE 1 BACKGROUND

1.1. In the course of research conducted under YALE auspices, Drs. Tony George, Kristi Sacco, and Jennifer Vessicchio, in the Department of Psychiatry at YALE (the "INVENTORS"), have produced an invention entitled "Mecamylamine and Other Nicotinic Antagonists for Augmentation of SSRI, MAOIs, TCA and Other Antidepressants (OCR 1625)" (the "INVENTION").

1.2. The INVENTORS have assigned to YALE all of all INVENTORS' right, title and interest in and to the INVENTION and any resulting patents.

1.3. YALE wishes to have the INVENTION and any resulting patents commercialized to benefit the public good.

1.4. LICENSEE has agreed with YALE to induce YALE to enter into this Agreement that it shall, solely to the extent expressly provided in Article 7, act diligently to develop and commercialize the LICENSED PRODUCTS for public use.

1.5. YALE is willing to grant a license to LICENSEE, subject to the terms and conditions of this Agreement.

1.6. In consideration of these statements and mutual promises, YALE and LICENSEE agree to the terms of this Agreement.

ARTICLE 2 DEFINITIONS

The following terms used in this Agreement shall be defined as set forth below:

2.1. "AFFILIATE" shall mean, with respect to any entity (including, without limitation, either party hereto), any entity or person that directly or indirectly controls, is controlled by or is under common control with such entity. For purposes of this definition, "control" means possession of the power to direct the management of an entity, whether through ownership of more than fifty percent (50%) of voting securities, by contract or otherwise.

2.2. "CONFIDENTIAL INFORMATION" shall mean all information disclosed by one party to the other during the negotiation of, or under, this Agreement in any manner, whether orally,

visually or in tangible form, that directly relates to LICENSED PATENTS, LICENSED PRODUCTS or LICENSED METHODS or the Agreement itself, unless such information is subject to an exception described in Article 8.2; provided, however, that CONFIDENTIAL INFORMATION that is disclosed in tangible form shall be marked "Confidential" at the time of disclosure and CONFIDENTIAL INFORMATION that is disclosed orally or visually shall be identified as confidential at the time of disclosure and subsequently reduced to writing (including, for this purpose, email), marked confidential and delivered to the other party within thirty (30) days after such disclosure. Subject to Article 8.2, CONFIDENTIAL INFORMATION shall include, without limitation, materials, know-how and data, technical or non-technical, trade secrets, inventions, methods and processes, whether or not patentable.

2.3. "EARNED ROYALTY" is defined in Article 6.1.

2.4. "EFFECTIVE DATE" is defined in the introductory paragraph of this Agreement.

2.5. "FIELD" shall mean all therapeutic uses in humans.

2.6. "FIRST SALE" shall mean, with respect to a LICENSED PRODUCT or LICENSED METHOD, the first sale, that results in NET SALES, to a third party of such LICENSED PRODUCT or LICENSED METHOD after all regulatory approvals necessary for the commercialization of such LICENSED PRODUCT or LICENSED METHOD in the country in which such sale is made have been obtained. For purposes of clarity, for each LICENSED PRODUCT developed by LICENSEE, there can only be one FIRST SALE under this Agreement.

2.7. "INSOLVENT" shall mean that LICENSEE is insolvent as defined by the United States Bankruptcy Code, as amended from time to time

2.8. "INVENTION" and "INVENTOR" are defined in Article 1.1.

2.9. "LICENSE" refers to the license granted under Article 3.1.

2.10. "LICENSED INFORMATION" shall mean all preclinical and clinical data controlled by Yale as of the EFFECTIVE DATE and directly relating to the INVENTION.

2.11. "LICENSED METHODS" shall mean any method, procedure, service or process the practice of which, in the absence of a license from YALE, would infringe a VALID CLAIM of a LICENSED PATENT.

2.12. "LICENSED PATENTS" shall mean: (i) the patent applications listed in Appendix A, together with all continuations, divisionals and continuations-in-part that include any claim that is directed to subject matter described in the patent applications listed on Appendix A (collectively, the "Applications"); (ii) all patents issuing from or claiming priority to any of the Applications during the TERM, together with all reissues, re-examinations or extensions thereof or substitutes therefor (the "Patents") and (iii) the relevant international counterparts of each of the Applications and Patents. Appendix A is incorporated into this Agreement herein by reference.

2.13. "LICENSED PRODUCT" shall mean any product (including any apparatus or kit), or component part thereof, the manufacture, use or sale of which, in the absence of a license from YALE, would infringe a VALID CLAIM of a LICENSED PATENT.

2.14. “LICENSED TERRITORY” shall mean the entire world.

2.15. “NDA” shall mean a new drug application filed with the United States Food and Drug Administration to obtain marketing approval for a LICENSED PRODUCT in the United States.

2.16. “NET SALES” shall mean:

(a) gross invoice price from the sale or other transfer or disposition of the LICENSED PRODUCTS or LICENSED METHODS, or from services performed using LICENSED PRODUCTS or LICENSED METHODS, by LICENSEE, SUBLICENSEES or its AFFILIATES to third parties, except as set forth in Article 2.16(b), less the following deductions, provided they actually pertain to the disposition of the LICENSED PRODUCTS or LICENSED METHODS:

(i) all discounts (including chargebacks), credits and allowances on account of returns;

(ii) all amounts repaid or credited by reason of rejection, returns or recalls of goods, rebates or bona fide price reductions determined by LICENSEE or a SUBLICENSEE or an AFFILIATE in good faith;

(iii) all rebates and similar payments made with respect to sales paid for by any governmental or regulatory authority such as, by way of illustration and without limitation, Federal or state Medicaid, Medicare or similar state program in the United States or equivalent governmental program in any other country;

(iv) all invoiced amounts that are not collected by LICENSEE or a SUBLICENSEE or an AFFILIATE, including bad debts (provided that deductions for bad debt in any calendar quarter shall not exceed [********]of aggregate gross sales for such quarter pursuant to clause (a) (i.e., before application of sub clauses (i-v)));

(v) all duties, taxes and other governmental levies, fees or charges levied on the sale, transportation or delivery of LICENSED PRODUCTS or practice of the LICENSED METHODS (to the extent included separately on the applicable invoice), but not including income taxes; and

(vi) [********]of the amount arrived at after application of the provisions of items (i) through (v) above as an allowance for transportation costs, distribution expenses, special packaging and related insurance charges; provided that, if such costs, expenses and charges are itemized separately on the applicable invoice, such deduction shall instead be equal to the aggregate amount therefor shown on such invoice.

No deductions shall be made for any other costs or expenses, including but not limited to commissions to independents, agents or those on LICENSEE’s, SUBLICENSEE’s or an AFFILIATE’s payroll or for the cost of collection.

NET SALES shall be calculated using the selling party’s (LICENSEE’s or a SUBLICENSEE’s or an AFFILIATE’s) internal audited systems used to report such sales, as adjusted for any of items (i) to (vi) (inclusive) above not taken into account in such systems. Deductions pursuant to clause (iv) above shall be taken in the quarter in which such sales are no longer recorded as a receivable.

For purposes of clarity, sales of a LICENSED PRODUCT or LICENSED METHOD in any country in the LICENSED TERRITORY in which the sale of such LICENSED PRODUCT or LICENSED METHOD would not infringe a VALID CLAIM of a LICENSED PATENT shall not be taken into account in determining NET SALES.

(b) "NET SALES" shall not include the gross invoice price for LICENSED PRODUCTS or LICENSED METHODS sold to, or services performed using LICENSED PRODUCTS or LICENSED METHODS for, any SUBLICENSEE or AFFILIATE unless such SUBLICENSEE or AFFILIATE is the end user of any LICENSED PRODUCT or LICENSED METHOD, in which case such consideration shall be included in NET SALES at the average selling price charged to a third party during the same quarter. Also, none of (i) the use of any LICENSED PRODUCT in a clinical trial, preclinical study or other research or development activity, (ii) the disposal or transfer of a LICENSED PRODUCT for purposes of a sampling program or for charitable, manufacturing, testing or qualification, regulatory or governmental purposes, or (iii) the sale, disposal or transfer of a LICENSED PRODUCT on a treatment investigational new drug application, named patient or compassionate use or other similar basis, shall give rise to any NET SALES.

2.17. "QUALIFIED SUBLICENSEE" shall mean any entity that is, or is an Affiliate of, either (i) one of the [********] largest biotechnology or pharmaceutical companies in the world, as measured by annual sales, or (ii) any other entity that has assets of at least $[********].

2.18. "REASONABLE COMMERCIAL EFFORTS" shall mean documented efforts that are consistent with those typically utilized by companies of similar size and with similar resources and expertise in the development of products and services with market potential similar to LICENSED PRODUCTS and LICENSED METHODS, taking into account all relevant scientific, clinical, regulatory, financial, competitive and commercial factors.

2.19. "ROYALTY TERM" is defined in Article 3.4.

2.20. "SUBLICENSE INCOME" shall mean all amounts (excluding Excluded Amounts, as described below) received by LICENSEE from a SUBLICENSEE, but only if the sublicense to LICENSED PATENTS or LICENSED METHODS is not combined, whether or not in the same agreement, with (i) a license to issued patents or pending patent applications owned or licensed by LICENSEE or its AFFILIATES (other than LICENSED PATENTS) that claim or cover compounds or their use in the FIELD or (ii) an agreement by LICENSEE or its AFFILIATES to collaborate with such SUBLICENSEE to discover, research, develop or commercialize compounds or products for use in the FIELD.

"Excluded Amounts" means all payments made to LICENSEE or its AFFILIATES: (i) as royalties on the sale of products; (ii) upon the achievement of, or based on, clinical, regulatory, commercialization or sales milestones; (iii) under a credit facility; (iv) in consideration of (A) any issuance of equity or debt securities by LICENSEE or its AFFILIATES, (B) any supply of compounds or related materials by or on behalf of LICENSEE or its AFFILIATES, or (C) any research, development or other activities that LICENSEE or its AFFILIATES may perform on behalf of a SUBLICENSEE, provided that such payments do not exceed the fair market value of such securities, supply or activities, as applicable; (v) that LICENSEE or its AFFILIATES may be required to repay (e.g., a loan); (vi) as reimbursement of actual patent prosecution and maintenance costs and expenses; or (vii) in connection with awards or judgments in patent or other intellectual property right enforcement.

2.21. “SUBLICENSEE” shall mean any third party sublicensed by LICENSEE to make, have made, use, sell, have sold, import or export any LICENSED PRODUCT or to practice any LICENSED METHOD; provided that a contract research organization or contract manufacturer contracted by LICENSEE or a SUBLICENSEE or an AFFILIATE to perform services on a fee-for-service basis related to the manufacturing and/or research or development of LICENSED PRODUCTS only, and not sales of LICENSED PRODUCTS, shall not be a SUBLICENSEE.

2.22. “TARGACEPT PATENT” shall mean all issued and unexpired patents or pending patent applications owned or licensed by LICENSEE or any of its AFFILIATES during the TERM that contain a VALID CLAIM that would be infringed by the manufacture, use, sale or other exploitation of a LICENSED PRODUCT by a third party in the absence of a license from LICENSEE (or such AFFILIATE); provided that (i) LICENSED PATENTS are not TARGACEPT PATENTS, (ii) no pending patent application that solely covers a method of manufacture or delivery shall be a TARGACEPT PATENT and (iii) no issued patent that solely covers a method of manufacture or delivery shall be a TARGACEPT PATENT unless, with respect to a particular LICENSED PRODUCT, no third party could reasonably be expected to manufacture and market such LICENSED PRODUCT to treat the indication for which LICENSEE or any of its AFFILIATES or SUBLICENSEES is commercializing such LICENSED PRODUCT without infringing such patent in the absence of a license from LICENSEE or any of its AFFILIATES.

2.23. “TERM” is defined in Article 3.4.

2.24. “VALID CLAIM” shall mean a claim of a pending or issued and unexpired LICENSED PATENT so long as such LICENSED PATENT (i) if a pending patent application, is being prosecuted in good faith and shall not have been irrevocably abandoned or finally disallowed without the possibility of appeal or re-filing or (ii) if an issued and unexpired patent, shall not have been finally canceled, withdrawn, abandoned or rejected by any administrative agency or other authority of competent jurisdiction, shall not have been permanently revoked, declared to be invalid, unpatentable or unenforceable in an unappealable (or unappealed within the time allowed for appeal) decision of a court or other authority or competent jurisdiction through no challenge by LICENSEE.

ARTICLE 3 LICENSE GRANT AND TERM

3.1. Subject to the terms and conditions of this Agreement, YALE hereby grants to LICENSEE an exclusive license, with the right to sublicense, under the LICENSED PATENTS and a non-exclusive license, with the right to sublicense, under the LICENSED INFORMATION, in each case to make, have made, use, sell, have sold, import, export and otherwise exploit LICENSED PRODUCTS, and to practice any LICENSED METHOD, within the FIELD in the LICENSED TERRITORY (the “LICENSE”). YALE (i) represents to LICENSEE that The Donaghue Foundation (“TDF”) provided funding (but not any inventive contribution) to YALE in support of the research activities giving rise to the INVENTION and (ii) covenants to LICENSEE that TDF has irrevocably waived and disclaimed all of TDF’s right, title and interest in and to the INVENTION and the LICENSED PATENTS in a valid, binding and enforceable written agreement between TDF and YALE so as to enable LICENSEE to enjoy the exclusivity intended by the LICENSE with no obligation, financial or otherwise, of LICENSEE to TDF.

3.2. To the extent that any invention included within the LICENSED PATENTS has been funded in whole or in part by the United States government, the United States government retains certain rights in such invention as set forth in 35 U.S.C. §200-212 and all regulations promulgated thereunder, as amended, and any successor statutes and regulations (the "Federal Patent Policy"). As a condition of the LICENSE granted hereby, LICENSEE acknowledges and shall comply with all aspects of the Federal Patent Policy applicable to the LICENSED PATENTS, including, solely if and to the extent applicable, the obligation that LICENSED PRODUCTS used or sold in the United States be manufactured substantially in the United States. Nothing contained in this Agreement obligates or shall obligate YALE to take any action that would conflict in any respect with its past, current or future obligations to the United States Government under the Federal Patent Policy with respect to the LICENSED PATENTS.

3.3. The LICENSE is expressly made subject to YALE's reservation of the right, on behalf of itself and all other non-profit academic research institutions, to make, use and practice the LICENSED PATENTS and LICENSED METHODS for research, clinical, teaching or other non-commercial purposes, and not for purposes, whether itself or through any licensee or other third party, of commercial development, use, manufacture or distribution. Nothing in this Agreement shall be construed to grant by implication, estoppel or otherwise any licenses under patents of YALE other than the LICENSED PATENTS.

3.4. Unless terminated earlier as provided in Article 13, the royalty term of this Agreement (the "ROYALTY TERM") shall commence on the EFFECTIVE DATE and shall automatically expire, for purposes of any country, on the date on which the last of the LICENSED PATENTS in such country that include at least one VALID CLAIM expires. The term of this Agreement (the "TERM") shall expire upon expiration of the last-to-expire ROYALTY TERM or, if earlier, upon the effective date of termination in accordance with Article 13.

3.5. Except as expressly provided in this Agreement, under no circumstances will LICENSEE, as a result of this Agreement, obtain any interest in or any other right to any technology, know-how, patents, patent applications, materials or other intellectual or proprietary property of YALE.

ARTICLE 4 SUBLICENSES

4.1. LICENSEE may sublicense the rights granted to it under this Agreement without the consent of YALE.

4.2. Any sublicense granted by LICENSEE shall include provisions designed to protect CONFIDENTIAL INFORMATION and substantially the same provisions on Patent Notices and Use of YALE's Name as are agreed to in this Agreement and such other provisions as are needed to enable LICENSEE to comply with this Agreement. LICENSEE will provide YALE with a copy of each sublicense agreement (and all amendments thereof) promptly after execution. LICENSEE shall remain responsible for the performance of all SUBLICENSEES under any such sublicense as if such performance were carried out by LICENSEE itself, including, without limitation, the payment of any royalties or other payments provided for hereunder, regardless of whether the terms of any sublicense provide for such amounts to be paid by the SUBLICENSEE directly to YALE.

4.3. LICENSEE shall pay royalties to YALE on NET SALES of SUBLICENSEES based on the same royalty rate as apply to NET SALES by LICENSEE and its AFFILIATES, regardless of the royalty rates payable by SUBLICENSEES to LICENSEE under a sublicense agreement. In addition, LICENSEE shall pay to YALE [*********] ([*********]) of any SUBLICENSE INCOME.

4.4. LICENSEE agrees that it has sole responsibility to promptly notify YALE of termination of any sublicense.

ARTICLE 5 LICENSE INITIATION FEE; MILESTONE; ROYALTIES

5.1. LICENSEE shall pay to YALE, (i) a non-refundable license initiation fee of Twenty-Five Thousand Dollars ($25,000.00) and (ii) the amount of Twenty-Two Thousand, Four Hundred Nineteen Dollars and 30/100 ($22,419.30) to reimburse YALE for all expenses incurred as of the EFFECTIVE DATE in the filing, prosecution, and maintenance of the LICENSED PATENTS.

5.2. LICENSEE shall make the following non-refundable milestone payments to YALE within thirty (30) days after the applicable milestone event(s) set forth below:

(a) Fifty Thousand Dollars ($50,000.00) (i) upon the issuance of the first U.S. patent included in the LICENSED PATENTS that would be infringed, in the absence of a license from YALE, by the commercial sale by LICENSEE of mecamylamine hydrochloride together with citalopram hydrobromide or (ii) if the first to issue U.S. patent included in the LICENSED PATENTS would not be infringed, in the absence of a license from YALE, by the commercial sale by LICENSEE of mecamylamine hydrochloride together with citalopram hydrobromide, upon the sixtieth (60^{th}) day after the date on which LICENSEE pays the issuance fee (following receipt of the notice of allowance) for such U.S. patent.

(b) [********] ($[********]) when LICENSEE or any of its SUBLICENSEES or AFFILIATES files an NDA for each LICENSED PRODUCT developed by LICENSEE.

(c) [********] ($[********]) upon the FIRST SALE of each LICENSED PRODUCT developed by LICENSEE.

For purposes of clarity, the racemate and enantiomers of any compound shall be considered to be the same compound such that, to the extent that any of the racemate or either of the enantiomers is contained in or comprises a LICENSED PRODUCT, such racemate and enantiomers shall be considered together to be the same LICENSED PRODUCT and therefore subject to a single milestone stream hereunder.

For purposes of further clarity, with respect to each of the foregoing milestone payments, such milestone payment shall not be due or payable by LICENSEE if this Agreement is terminated pursuant to Article 13 and such termination becomes effective prior to the date on which the event (or, in the case of Article 5.2(a)(ii), the date) giving rise to such milestone payment occurs.

5.3. Neither the license initiation fee set forth in Article 5.1 nor the milestone payments set forth in Article 5.2 shall be credited against EARNED ROYALTIES payable under Article 6.

ARTICLE 6 EARNED ROYALTIES; MINIMUM ROYALTY PAYMENTS

6.1. During the TERM, as partial consideration for the LICENSE, LICENSEE shall pay to YALE an earned royalty on cumulative NET SALES of LICENSED PRODUCTS or LICENSED METHODS by LICENSEE or its SUBLICENSEES or AFFILIATES in each calendar (January 1 through December 31) year (“EARNED ROYALTIES”) according to the following schedule:

Annual NET SALES	Prior to Expiration of the Last TARGACEPT PATENT	After Expiration of the last TARGACEPT PATENT
$[********]	[********]%	[********]%
>$[********]	[********]%	[********]%
>$[********]	[********]%	[********]%
> $[********]	[********]%	[********]%

By way of example, if cumulative NET SALES of LICENSED PRODUCTS in a particular calendar year are $[********]and there is at least one unexpired TARGACEPT PATENT, EARNED ROYALTIES payable hereunder would be determined as follows:

[********]

For purposes of clarity, LICENSEE's obligation to pay EARNED ROYALTIES shall be imposed only once with respect to the same unit of a LICENSED PRODUCT or LICENSED METHOD regardless of how many LICENSED PATENTS or VALID CLAIMS pertain thereto.

6.2. Notwithstanding Article 6.1, if (i) the practice of any portion of the LICENSE (including, without limitation, the sale of LICENSED PRODUCTS or LICENSED METHODS), or the manufacture, use, sale or other exploitation of a LICENSED PRODUCT or LICENSED METHOD, by LICENSEE or any of its AFFILIATES or SUBLICENSEES in a particular country would or would reasonably be expected to infringe upon an issued patent of a third party in the absence of a license (whether or not any other LICENSED PRODUCT or LICENSED METHOD could be manufactured, used, sold or otherwise exploited without a license to such third party patent) and (ii) LICENSEE or any of its AFFILIATES or SUBLICENSEES obtains a license to such third party patent, the amount of EARNED ROYALTIES payable by LICENSEE shall be reduced by an amount equal to the lesser of (A) [********] ([********]) of the amounts paid to secure such third party license or (B) the amount that results in aggregate EARNED ROYALTIES of at least [********]of NET SALES for such calendar quarter.

6.3. LICENSEE shall pay all EARNED ROYALTIES accruing to YALE within ninety (90) days from the end of each calendar quarter (i.e., March 31, June 30, September 30 and December 31), beginning in the first calendar quarter in which NET SALES occur.

6.4. During the TERM, LICENSEE agrees to pay YALE annual Minimum Royalty Payments ("MRP"), commencing after the first anniversary of the date of the FIRST SALE of the first LICENSED PRODUCT or LICENSED METHOD. The MRP shall be in the following amounts:

1st anniversary of FIRST SALE	$[********]
2nd anniversary of FIRST SALE	$[********]
3rd anniversary of FIRST SALE and every anniversary of FIRST SALE thereafter	$[********]

Each MRP shall be payable by LICENSEE on the anniversary of the EFFECTIVE DATE that first occurs after the applicable anniversary of FIRST SALE.

6.5. LICENSEE shall continue to pay the MRP until the end of the TERM. YALE shall fully credit each MRP made against any EARNED ROYALTIES payable by LICENSEE in the same year and thereafter until exhausted.

6.6. All EARNED ROYALTIES and other payments due under this Agreement shall be paid to YALE in United States Dollars. In the event that conversion from foreign currency is required in calculating a payment under this Agreement, the exchange rate used shall be the Interbank rate quoted by Citibank at the end of the last business day of the quarter in which the royalty was earned. If overdue, the royalties and any other payments due under this Agreement shall bear interest until payment at a per annum rate two percent (2%) above the prime rate in effect at Citibank on the due date and YALE shall be entitled to recover reasonable attorneys' fees and costs related to the enforcement of this Agreement to collect such payment. The payment of such interest shall not foreclose YALE from exercising any other right it may have as a consequence of the failure of LICENSEE to make any payment when due.

ARTICLE 7 DUE DILIGENCE

7.1. LICENSEE shall use all REASONABLE COMMERCIAL EFFORTS to develop at least one LICENSED PRODUCT or LICENSED METHOD for commercialization in the United States. Failure to do so shall, if determined to be a material breach and subject to the applicable cure period, be subject to termination under Article 13.

7.2. Within sixty (60) days after each anniversary of the EFFECTIVE DATE, LICENSEE shall provide a written report to YALE summarizing LICENSEE's progress in its development or commercialization of at least one LICENSED PRODUCT or LICENSED METHOD; provided that such reporting obligation shall expire upon the FIRST SALE of at least one LICENSED PRODUCT.

7.3. LICENSEE shall immediately notify YALE if at any time LICENSEE finally abandons both its research, development or marketing of LICENSED PRODUCTS and LICENSED METHODS and its intent to research, develop and market such products or methods.

7.4. Without prejudice to YALE's rights under Article 13, LICENSEE agrees that YALE shall be entitled to terminate this Agreement if LICENSEE provides YALE with the notice set forth in Article 7.3.

ARTICLE 8 CONFIDENTIALITY AND PUBLICITY

8.1. Subject to the parties' rights and obligations pursuant to this Agreement, YALE and LICENSEE agree that during the TERM and for five (5) years thereafter, each of them:

(a) will keep confidential and will cause their AFFILIATES and, in the case of LICENSEE, its SUBLICENSEES, to keep confidential, CONFIDENTIAL INFORMATION disclosed to it by the other party, by taking whatever action the party receiving the CONFIDENTIAL INFORMATION would take to preserve the confidentiality of its own CONFIDENTIAL INFORMATION, which in no event shall be less than reasonable care; and

(b) will only disclose that part of the other party's CONFIDENTIAL INFORMATION to its officers, employees or agents that is necessary for those officers, employees or agents to carry out its responsibilities under this Agreement; and

(c) will not use the other party's CONFIDENTIAL INFORMATION other than as expressly set forth in this Agreement (including, in the case of LICENSEE, in the development or commercialization of LICENSED PRODUCTS OR LICENSED METHODS) or disclose the other party's CONFIDENTIAL INFORMATION to any third parties under any circumstance without advance written permission from the other party; provided that LICENSEE shall be permitted to disclose YALE's CONFIDENTIAL INFORMATION (including, solely for this purpose, the terms of this Agreement) (i) to its legal and financial advisors, (ii) to its auditor, (iii) in connection with any actual or potential debt or equity financing, (iv) to any actual or potential SUBLICENSEE or (v) in connection with any acquisition or business combination; provided that, in case of clauses (iv) or (v), any such disclosure is made subject to an obligation of confidentiality at least substantially similar to those contained herein; and

(d) will, within sixty (60) days of receipt of written request from a party following termination of this Agreement, return all the CONFIDENTIAL INFORMATION disclosed to it by the other party pursuant to this Agreement, except for one copy which may be retained by the recipient for monitoring compliance with this Article 8.

8.2. The obligations of non-use and confidentiality described above shall not pertain to that part of the CONFIDENTIAL INFORMATION that:

(a) was known to the recipient prior to the disclosure by the disclosing party; or

(b) is at the time of disclosure or has become thereafter publicly known through no fault or omission attributable to the recipient; or

(c) is rightfully given to the recipient from sources independent of the disclosing party; or

(d) is established by written evidence to have been independently developed by the receiving party without use of or reference to the CONFIDENTIAL INFORMATION of the other party; or

(e) is required to be disclosed by law, rule or regulation (including, in the case of LICENSEE or AFFILIATES, stock exchange or listing organization requirements) in the opinion of recipient's attorney, but only after the disclosing party is given prompt written notice and an opportunity to seek a protective order (in each case to the extent practicable under the circumstances).

8.3. Except as required by law, rule or regulation (including, in the case of LICENSEE or its AFFILIATES, stock exchange or listing organization requirements) or permitted by Article 8.1(c), neither party may disclose the financial terms of this Agreement without the prior written consent of the other party.

ARTICLE 9 REPORTS, RECORDS AND INSPECTIONS

9.1. LICENSEE shall, within ninety (90) days after the calendar year in which NET SALES first occur, and within ninety (90) days after each calendar quarter (i.e., March 31, June 30, September 30 and December 31) thereafter, provide YALE with a written report detailing the NET SALES and uses, if any, made by LICENSEE, its SUBLICENSEES and AFFILIATES of LICENSED PRODUCTS and LICENSED METHODS during the preceding calendar quarter and calculating the payments due pursuant to Article 6. NET SALES of LICENSED PRODUCTS or LICENSED METHODS shall be deemed to have occurred on the date of invoice for such LICENSED PRODUCTS or LICENSED METHODS. Each such report shall be signed by an officer of LICENSEE (or the officer's designee), and must include:

(a) the number of LICENSED PRODUCTS sold or otherwise transferred or disposed of, and the amount of LICENSED METHODS sold, by LICENSEE, SUBLICENSEES and AFFILIATES;

(b) a calculation of NET SALES for the applicable reporting period, including the gross invoice prices charged for the LICENSED PRODUCTS and LICENSED METHODS and detailing any permitted deductions made pursuant to Article 2.16;

(c) a calculation of total royalties or other payment due, including any exchange rates used for conversion; and

(d) names and addresses of all SUBLICENSEES and the type and amount of SUBLICENSE INCOME, if any, received from each SUBLICENSEE.

9.2. LICENSEE and its SUBLICENSEES shall keep and maintain complete and accurate records and books containing an accurate accounting of all data in sufficient detail to enable verification of EARNED ROYALTIES and other payments under this Agreement. LICENSEE shall preserve such books and records for three (3) years after the calendar year to which they pertain. Such books and records shall be open to inspection by YALE or an independent certified public accountant selected by YALE, at YALE's expense, during normal business hours upon thirty (30) days prior written notice, for the purpose of verifying the accuracy of the reports and computations rendered by LICENSEE. In the event LICENSEE underpaid the amounts due to YALE with respect to the audited period by more than five percent (5%), LICENSEE shall pay the reasonable cost of such examination, together with the deficiency not previously paid, within thirty (30) days of receiving notice thereof from YALE.

9.3. On or before the ninetieth (90^{th}) day following the close of LICENSEE's fiscal year, LICENSEE shall provide YALE with LICENSEE's certified financial statements for the preceding fiscal year including, at a minimum, a balance sheet and an income statement. This Article 9.3 shall not apply if and for so long as LICENSEE has a class of securities registered under Section 12 of the Securities Exchange Act of 1934.

ARTICLE 10 PATENT PROTECTION

10.1. From and after the EFFECTIVE DATE, LICENSEE shall be responsible for all actually incurred, reasonable costs of filing, prosecution and maintenance of all United States patent applications contained in the LICENSED PATENTS. Any and all such United States patent applications, and resulting issued patents, shall remain the property of YALE.

10.2. From and after the EFFECTIVE DATE, LICENSEE shall be responsible for all actually incurred, reasonable costs of filing, prosecution and maintenance of all foreign patent applications, and patents contained in the LICENSED PATENTS in countries outside the United States in the LICENSED TERRITORY selected by LICENSEE with the consent of YALE, not to be unreasonably withheld, conditioned or delayed. All such applications or patents shall remain the property of YALE.

10.3. If LICENSEE fails to pay the expenses of filing, prosecuting or maintaining a LICENSED PATENT in the United States, then LICENSEE's rights under this Agreement shall terminate automatically with respect to such LICENSED PATENT in the United States.

10.4. The costs mentioned in Articles 10.1 and 10.2 shall include, but are not limited to, taxes, annuities, working fees, maintenance fees and renewal and extension charges. Payment of such costs shall be made, at YALE's option, either directly to patent counsel or by reimbursement to YALE. In either case, LICENSEE shall make payment directly to the appropriate party within thirty (30) days after receiving its invoice.

10.5. (a) Subject to this Article 10.5, all pending patent applications and issued patents included in the LICENSED PATENTS shall be prepared, prosecuted, filed and maintained by outside patent counsel chosen by YALE subject to the approval of LICENSEE, not to be unreasonably withheld. YALE shall instruct patent counsel to (i) keep both YALE and LICENSEE regularly informed of the progress of the prosecution, issuance and maintenance of all such patent applications and patents, (ii) make itself available with reasonable notice, at reasonable times and with reasonable frequency for consultation with LICENSEE and its outside patent counsel, (iii) give both YALE and LICENSEE reasonable opportunity to review and comment on the type and scope of useful claims and the nature of supporting disclosures, (iv) give due consideration in good faith to comments received from LICENSEE or its outside patent counsel and (v) give LICENSEE at least thirty (30) days prior written notice of all meetings and material communications with any patent authorities concerning the LICENSED PATENTS and to permit LICENSEE to participate in such meetings or communications. YALE will not finally abandon any patent application included in the LICENSED PATENTS without LICENSEE's prior written consent. LICENSEE shall have the sole right, in good faith, to determine whether to seek or obtain any patent term extension(s), restoration(s) or the like that may be available in the future with respect to the LICENSED PATENTS in any part of the LICENSED TERRITORY. Neither party shall have any liability to the other party for damages, whether direct, indirect or incidental, consequential or otherwise, arising from its good faith decisions, actions and omissions in connection with patent prosecution hereunder if such party shall have complied with its obligations under this Article 10.5(a).

(b) Notwithstanding Article 10.5(a), upon thirty (30) days written notice to YALE, LICENSEE (or its AFFILIATES or SUBLICENSEES) shall have the right to assume the sole responsibility for the preparation, prosecution, filing and maintenance, by outside patent counsel chosen thereby and reasonably acceptable to YALE, of all pending patent applications and issued

patents included in the LICENSED PATENTS; provided that such rights shall be expressly subject to the obligations of LICENSEE (or, as applicable, its AFFILIATES or SUBLICENSEES) to instruct patent counsel to (i) [*********], (ii) keep YALE regularly informed of the progress, issuance and maintenance of all such patent applications and patents, (iii) give YALE reasonable opportunity to comment on the type and scope of useful claims and the nature of supporting disclosures, (iv) give due consideration in good faith to comments received from YALE or its outside patent counsel, (v) not make any changes that would materially limit either the scope or number of claims without YALE's prior written consent and (vi) not to finally abandon any patent application included in the LICENSED PATENTS without YALE's prior written consent.

10.6. LICENSEE shall mark, and shall contract with its SUBLICENSEES to mark, all LICENSED PRODUCTS with the numbers of all patents included in LICENSED PATENTS that cover the LICENSED PRODUCTS. Without limiting the foregoing, all LICENSED PRODUCTS shall be marked in such a manner as to conform with the patent marking notices required by the law of any country where such LICENSED PRODUCTS are made, sold, used or shipped, including, but not limited to, the applicable patent laws of that country.

ARTICLE 11 INFRINGEMENT AND LITIGATION

11.1. Each party shall promptly notify the other in writing in the event that it obtains knowledge of infringing activity by third parties, or is sued or threatened with an infringement suit, in any country in the LICENSED TERRITORY as a result of activities that concern the LICENSED PATENTS and shall supply the other party with documentation of the infringing activities that it possesses, if any.

11.2. During the TERM:

(a) LICENSEE shall have the first right, but shall not be obligated, to defend the LICENSED PATENTS against infringement or interference in the FIELD and in the LICENSED TERRITORY by third parties. This right includes bringing any legal action for infringement and defending any counterclaim of invalidity or action of a third party for declaratory judgment for non-infringement or non-interference. If, in the reasonable opinion of LICENSEE's and YALE's respective counsels, YALE is required to be a named party to any such suit for standing purposes, LICENSEE may join YALE as a party; provided, however, that (i) YALE shall not be the first named party in any such action, (ii) the pleadings and any public statements about the action shall state that the action is being pursued by LICENSEE and that LICENSEE has joined YALE as a party; and (iii) LICENSEE shall keep YALE reasonably apprised of all material developments in any such action. LICENSEE may settle such suits, whether by agreement, consent, judgment, voluntary dismissal or otherwise, solely in its own name and solely at its own expense and through counsel of its own selection; provided, however, that any such settlement that imposes any restrictions or obligations on YALE shall be entered into only with YALE's prior written consent. LICENSEE shall bear the expense of such legal actions. Except for providing reasonable assistance, at the request and reasonable expense of LICENSEE, YALE shall have no obligation regarding the legal actions described in Article 11.2 unless required to participate by law. However, YALE shall have the right to participate in any such action through its own counsel and at its own expense. Any recovery shall first be applied to LICENSEE's out of pocket expenses and second to YALE's out of pocket expenses, in each case including legal fees. If there is any excess recovery following payment of such expenses: (A) any amount recovered specifically for lost profits or sales shall be treated as NET SALES in the calendar quarter in which such recovery is paid and shall be subject to EARNED

ROYALTIES payable to YALE in respect of such NET SALES; (B) any amount recovered specifically as punitive or treble damages shall be treated as SUBLICENSE INCOME; and (C) if both clause (A) and clause (B) apply, the amount of such excess recovery shall apply to clause (A) and clause (B) in the same proportion as (1) the amount recovered specifically for lost profits or sales bears to (2) the amount recovered specifically as punitive or treble damages.

(b) In the event LICENSEE fails to initiate and pursue commercially reasonable steps within one hundred twenty (120) days of (i) notification of infringement from YALE to eliminate the infringement or interference or (ii) the date LICENSEE otherwise first becomes aware of an infringement, whichever is earlier, YALE shall have the right to initiate such legal action at its own expense. If, in the reasonable opinion of YALE's and LICENSEE's respective counsel, LICENSEE is required to be a named party in any such suit for standing purposes, YALE may join LICENSEE as a party, subject to the same conditions to the joining of YALE set forth in Article 11.2(a). In such case, LICENSEE shall provide reasonable assistance to YALE if requested to do so. YALE may settle, whether by agreement, consent, judgment, voluntary dismissal or otherwise, such actions solely through its own counsel; provided, however, that any such settlement that imposes any restrictions or obligations on LICENSEE shall be entered into only with LICENSEE's prior written consent. Any recovery shall be retained by YALE.

11.3. In the event LICENSEE is permanently enjoined from exercising its LICENSE under this Agreement pursuant to an infringement action brought by a third party, or if both LICENSEE and YALE elect not to undertake the defense or settlement of a suit alleging infringement for a period of six (6) months from notice of such suit, then either party shall have the right to remove the country where the suit was filed from the LICENSED TERRITORY upon thirty (30) days written notice to the other party in accordance with the terms of Article 15.

ARTICLE 12 USE OF YALE'S NAME

LICENSEE shall not use the name "Yale" or "Yale University," or any variation or adaptation thereof, or any trademark, tradename or other designation owned by YALE, or the names of any of its trustees, officers, faculty, students, employees or agents, for any purpose without the prior written consent of YALE in each instance, except that LICENSEE may state that it has licensed from YALE one or more of the patents and applications comprising the LICENSED PATENTS. YALE shall not use the name "Targacept" or any variation or adaptation thereof, or any trademark, tradename or other designation owned by LICENSEE, or the names of any of its directors, officers, employees or agents, for any purpose without the prior written consent of LICENSEE in each instance, except that YALE may state that LICENSEE has licensed from it one or more of the patents and applications comprising the LICENSED PATENTS.

ARTICLE 13 TERMINATION

13.1. YALE shall have the right to terminate this Agreement upon written notice to LICENSEE in the event LICENSEE:

(a) fails to make any payment whatsoever due and payable pursuant to this Agreement unless LICENSEE shall make all such payments (and all interest due on such payments under Article 6.4) within the thirty (30) day period after receipt of written notice from YALE; or

(b) subject to Article 16.3, commits a material breach of any other provision of this Agreement which is not cured (if capable of being cured) within the one hundred twenty (120) day period after receipt of written notice thereof from YALE (or upon receipt of such notice if such breach is not capable of being cured);

(c) fails to obtain or maintain adequate insurance as described in Article 14 and does not cure such breach within the ten (10) day period after receipt of written notice thereof from YALE;

(d) as provided in Article 7.4.

13.2. This Agreement shall terminate automatically without any notice to LICENSEE in the event LICENSEE shall cease to carry on its business or becomes INSOLVENT, or a petition in bankruptcy is filed against LICENSEE and is consented to, acquiesced in or remains undismissed for sixty (60) days, or LICENSEE makes a general assignment for the benefit of creditors, or a receiver is appointed for LICENSEE.

13.3. LICENSEE shall have the right to terminate this Agreement upon thirty (30) days prior written notice to YALE.

13.4. Upon termination of this Agreement for any reason (but, for purposes of clarity, not expiration of the TERM), all rights and licenses granted to LICENSEE under the terms of this Agreement are terminated and YALE has the option, in its discretion, to terminate any sublicense granted by LICENSEE. Upon such termination (but not expiration of the TERM), LICENSEE shall cease to manufacture or sell LICENSED PRODUCTS and cease to practice LICENSED METHODS; provided that, as applied to the terms “LICENSED PRODUCTS” and “LICENSED METHODS” as used in this Article 13.4 and notwithstanding Article 2.24, “VALID CLAIM” shall, mean (i) a valid and enforceable claim of an issued and unexpired LICENSED PATENT or (ii) a claim of a pending application included in LICENSED PATENTS that is being prosecuted in good faith and that has not been irrevocably abandoned or finally disallowed without the possibility of appeal or re-filing where such claim, if such patent application were to issue as a patent, would be valid and enforceable. Within sixty (60) days after the effective date of termination LICENSEE shall deliver to YALE:

(a) the last report required under Article 7 or 9; and

(b) all payments incurred up to the effective date of termination.

13.5. Termination of this Agreement shall not affect any rights or obligations accrued prior to the effective date of such termination and specifically LICENSEE’s obligation to pay all such accrued royalties and other payments specified by Article 5 and 6. The following provisions shall survive any termination: Articles 2 and 8, Article 9.2, Article 10.5 (last sentence only), Article 12, this Article 13.5, Article 14, Article 15, Article 16.1, Article 16.3 and Article 17. The parties agree that claims giving rise to indemnification may arise after the TERM or termination of the LICENSE granted herein.

13.6. The rights provided in this Article 13 shall be in addition and without prejudice to any other rights which the parties may have with respect to any default or breach of the provisions of this Agreement.

13.7. Waiver by either party of one or more defaults or breaches shall not deprive such party of the right to terminate because of any subsequent default or breach.

ARTICLE 14 INDEMNIFICATION; INSURANCE; WARRANTIES AND DISCLAIMERS

14.1. LICENSEE shall defend, indemnify and hold harmless YALE, its trustees, directors, officers, employees, and agents and their respective successors, heirs and assigns ("Indemnified Parties") against any and all liabilities, claims, demands, damages, judgments and expenses of any nature, including without limitation legal expenses and reasonable attorneys' fees, under any theory of liability (including, without limitation, tort, warranty, or strict liability), arising out of the death, personal injury or illness of any person, or damage to any property, resulting from the production, manufacture, sale, use, lease or other disposition or consumption, promotion or advertisement of the LICENSED PRODUCTS or LICENSED METHODS by LICENSEE, its AFFILIATES, SUBLICENSEES; provided that LICENSEE shall have no obligation hereunder to Indemnified Parties with respect to liabilities, claims or demands ("Claims"), damages, judgments, losses and expenses to the extent that they arise out of the gross negligence or willful misconduct of any Indemnified Party.

14.2. YALE shall give LICENSEE prompt (and, in any event, within thirty (30) days after YALE's receipt of written notice of a Claim) written notice of any Claim asserted for which any Indemnified Party seeks to enforce Article 14.1, specifying in an amount of detail reasonable under the circumstances the nature of the Claim; provided that the failure to provide such notice on a timely basis shall not relieve LICENSEE of any obligation that it may have under Article 14.1, except to the extent that the defense of such Claim is materially prejudiced by such failure. LICENSEE shall have the opportunity to defend, negotiate and settle such claims using counsel of its choice; provided, however, that (i) any Indemnified Party shall be entitled to participate in the defense of such matter and to employ, at its expense, counsel to assist therein and (ii) LICENSEE shall not be responsible or bound by any settlement of any Claim without its prior written consent. YALE shall ensure that all Indemnified Parties seeking to enforce Article 14.1 provide LICENSEE with such information and assistance as LICENSEE may reasonably request, at the reasonable expense of LICENSEE.

14.3. LICENSEE shall purchase and maintain in effect during the TERM, and shall require its SUBLICENSEES (other than QUALIFIED SUBLICENSEES which may elect to self-insure and other than SUBLICENSEES with rights limited to *in vitro* and animal research) to purchase and maintain in effect during the TERM, a policy of general liability insurance. Such insurance shall:

(a) list "YALE, its trustees, directors, officers, employees and agents" as additional insureds under the policy and provide for thirty (30) days written notice prior to any cancellation or material change to the policy(ies); and

(b) be endorsed such that it provides contractual liability coverage for LICENSEE's indemnification under Article 14.1.

In addition, LICENSEE shall purchase and maintain in effect during the TERM a policy covering product liability in amounts no less than $[********]Dollars per incident and $[********]Dollars annual aggregate; provided that, by virtue of such minimum amount of coverage required, such insurance not be construed to create a limit of LICENSEE's liability with respect to its indemnification under Article 14.1.

14.4. By signing this Agreement, LICENSEE certifies that the requirements of Article 14.3 will be met on or before the earlier of (a) the date of FIRST SALE of any LICENSED PRODUCT or LICENSED METHOD or (b) the first date, after the EFFECTIVE DATE, any LICENSED PRODUCT or LICENSED METHOD is tested or used by LICENSEE, a SUBLICENSEE or an AFFILIATE on humans, and will continue to be met thereafter. Upon YALE's request during the TERM, LICENSEE shall furnish a Certificate of Insurance and a copy of the current insurance policy(ies) to YALE.

14.5. YALE represents and warrants to LICENSEE that (i) to YALE's knowledge, the INVENTORS are the only persons who contributed to either the conception or first reduction to practice of the INVENTION, (ii) each INVENTOR was an employee of YALE at the time the INVENTION was first disclosed to YALE's Office of Cooperative Research, (iii) YALE has secured a valid and binding written assignment to the INVENTION (including, without limitation, the LICENSED PATENTS) from each INVENTOR, (iv) YALE has made due inquiry of each INVENTOR and has no reason to believe that any such INVENTOR has granted, purported to grant or agreed to grant any right or license to the INVENTION or any of the LICENSED PATENTS to any third party, (v) to YALE's knowledge, YALE owns all right, title and interest in and to the LICENSED PATENTS, (vi)YALE has the lawful right to grant the LICENSE, (vii)YALE has not granted rights or licenses in derogation of this Agreement other than those rights granted or reserved to the U.S. Government, (viii) to YALE's knowledge, the LICENSED PATENTS are not invalid or unenforceable and (ix) in respect of the pending U.S. patent application included in the LICENSED PATENTS, YALE has presented all relevant prior art of which YALE and, to YALE's knowledge, the INVENTORS have knowledge to the relevant Patent Examiner at the United States Patent and Trademark Office. YALE agrees that, during the TERM, YALE shall not enter into any other agreements that conflict with the rights or obligations provided hereunder, including any rights and obligations that survive termination of this Agreement.

14.6. (a) EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN ARTICLE 14.5, YALE MAKES NO, AND EXPRESSLY DISCLAIMS ALL, REPRESENTATIONS OR WARRANTIES THAT ANY CLAIMS OF THE LICENSED PATENTS, ISSUED OR PENDING, ARE VALID, OR THAT THE MANUFACTURE, USE, SALE OR OTHER DISPOSAL OF THE LICENSED PRODUCTS, OR PRACTICE OF THE LICENSED METHODS DOES NOT OR WILL NOT INFRINGE UPON ANY PATENT OR OTHER RIGHTS NOT VESTED IN YALE.

(b) EXCEPT AS OTHERWISE EXPRESSLY PROVIDED IN ARTICLE 14.5, YALE MAKES NO, AND EXPRESSLY DISCLAIMS ALL, REPRESENTATIONS AND WARRANTIES WHATSOEVER WITH RESPECT TO THE LICENSED PATENTS, LICENSED PRODUCTS AND LICENSED METHODS, EITHER EXPRESS OR IMPLIED, INCLUDING, BUT NOT LIMITED TO, WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. LICENSEE SHALL MAKE NO STATEMENTS, REPRESENTATION OR WARRANTIES WHATSOEVER TO ANY THIRD PARTIES WHICH ARE INCONSISTENT WITH SUCH DISCLAIMER BY YALE. IN NO EVENT SHALL YALE, OR ITS TRUSTEES, DIRECTORS, OFFICERS, EMPLOYEES AND AFFILIATES, BE LIABLE FOR SPECIAL, INCIDENTAL, CONSEQUENTIAL OR INDIRECT DAMAGES OF ANY KIND, INCLUDING ECONOMIC DAMAGE OR INJURY TO PROPERTY AND LOST PROFITS, REGARDLESS OF WHETHER YALE SHALL BE ADVISED, SHALL HAVE OTHER REASON TO KNOW, OR IN FACT SHALL KNOW OF THE POSSIBILITY OF THE FOREGOING.

ARTICLE 15 NOTICES

15.1. Any payment, notice or other communication required by this Agreement (a) shall be in writing, (b) may be delivered personally or sent by reputable overnight courier with written verification of receipt or by registered or certified first class United States Mail, postage prepaid, return receipt requested, (c) shall be sent to the following addresses or to such other address as such party shall designate by written notice to the other party, and (d) shall be effective upon receipt:

FOR YALE:
Managing Director
YALE UNIVERSITY
Office of Cooperative Research
433 Temple Street
New Haven, CT 06511

FOR LICENSEE:
TARGACEPT, INC.
200 East First Street, Suite 300
Winston-Salem, NC 27101
Attn: VP, Business and Commercial Development
Attn: General Counsel

ARTICLE 16 LAWS, FORUM AND REGULATIONS, DISPUTE RESOLUTION

16.1. Any matter arising out of or related to this Agreement shall be governed by and in accordance with the substantive laws of the State of Connecticut, without regard to its conflicts of law principles, except where the federal laws of the United States are applicable and have precedence. Any dispute arising out of or related to this Agreement shall be brought in a court of competent jurisdiction in the State of Connecticut.

16.2. LICENSEE shall comply, and shall cause its AFFILIATES to comply and contract with its SUBLICENSEES to comply, in all material respects with all foreign and United States federal, state, and local laws, regulations, rules and orders applicable to the testing, production, transportation, packaging, labeling, export, sale and use of the LICENSED PRODUCTS and practice of the LICENSED METHODS. In particular, LICENSEE shall be responsible for assuring compliance with all United States export laws and regulations applicable to this LICENSE and LICENSEE's activities under this Agreement

16.3. Neither party shall institute a proceeding in any court or administrative agency to resolve a dispute arising out of or relating to this Agreement before that party has sought to resolve such dispute through direct negotiation with the other party. Notwithstanding the foregoing, either party may seek, without waiving any right or remedy under this Agreement, from any court having jurisdiction injunctive or provisional relief to protect the rights or property of that party pending resolution of the dispute.

ARTICLE 17 MISCELLANEOUS

17.1. This Agreement shall be binding upon and inure to the benefit of the parties and their respective legal representatives, successors and permitted assigns.

17.2. This Agreement constitutes the entire agreement of the parties relating to the LICENSED PATENTS, LICENSED PRODUCTS and LICENSED METHODS, and all prior representations, agreements and understandings, written or oral (including, without limitation, the various draft term sheet proposals exchanged between the parties), are merged into it and superseded by this Agreement.

17.3. The provisions of this Agreement shall be deemed separable. If any part of this Agreement is rendered void, invalid, or unenforceable, such determination shall not affect the validity or enforceability of the remainder of this Agreement unless the part or parts which are void, invalid or unenforceable shall substantially impair the value of the entire Agreement as to either party.

17.4. Paragraph headings are inserted for convenience of reference only and do not form a part of this Agreement.

17.5. No person not a party to this Agreement, including any employee of either party to this Agreement, shall have or acquire any rights by reason of this Agreement. Nothing contained in this Agreement shall be deemed to constitute the parties partners with each other or any third party.

17.6. This Agreement may not be amended or modified except by written agreement executed by each of the parties. This Agreement is personal to LICENSEE and shall not be assigned by LICENSEE without the prior written consent of YALE, except no such consent shall be required in connection with any assignment by LICENSEE to an AFFILIATE or to a successor of all or substantially all of the business of LICENSEE to which this Agreement relates. Any attempted assignment in contravention of this Article 17.6 shall be null and void and shall constitute a material breach of this Agreement.

17.7. Neither LICENSEE nor any SUBLICENSEE or assignee will create, assume or permit to exist any lien, pledge, security interest or other encumbrance on this Agreement or any sublicense.

17.8. The failure of either party to enforce at any time, or for any period of time, any provision of this Agreement shall not be construed as a waiver of either such provision or of the right of such party thereafter to enforce each and every provision of this Agreement.

17.9. This Agreement may be executed in any number of counterparts and either party may execute any such counterpart, each of which when executed and delivered shall be deemed to be an original and all of which counterparts taken together shall constitute but one and the same instrument.

IN WITNESS to their Agreement, the parties have caused this Agreement to be executed in duplicate originals by their duly authorized representatives.

YALE UNIVERSITY

By: /s/ Jonathan Soderstrom

E. Jonathan Soderstrom, Ph.D.
Managing Director, Office of Cooperative Research

Date: 18 Jan 2007

TARGACEPT, INC.

By: /s/ Jeffrey C. Brennan

Name: Jeffrey C. Brennan
Title: Vice President, Business and Commercial Development

Date: January 22, 2007

Appendix A

LICENSED PATENTS

U.S. Patent Application 10/585,562 “Mecamylamine and Other Nicotinic Antagonists for Augmentation of SSRI, MAOIs, TCA and Other Antidepressants”.

U.S. provisional applications 60/534,532 and 60/627,250

PCT/US2005/000083 (Publication No. WO05067909A1)

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 Statements (Form S-8 No. 333-160331 and Form S-8 No. 333-133881) pertaining to the Targacept, Inc. 2006 Stock Incentive Plan, and
- Registration Statement (Form S-3 No. 333-171346) of Targacept, Inc.;

of our reports dated March 06, 2012, 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) of Targacept, Inc. for the year ended December 31, 2011.

/s/ Ernst & Young LLP

Raleigh, North Carolina
March 06, 2012

EXHIBIT 31.1

CERTIFICATION 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

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(s) 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(s) 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 6, 2012

By: /s/ J. DONALD DEBETHIZY

J. Donald deBethizy
President and Chief Executive Officer
(Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION 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

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(s) 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(s) 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 6, 2012

By: /s/ ALAN A. MUSSO

Alan A. Musso
Senior Vice President, Finance and Administration, Chief Financial Officer and Treasurer
(Principal Financial and Accounting Officer)

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 year ended December 31, 2011 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, as amended; 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 6, 2012

By: /s/ J. DONALD DEBETHIZY

J. Donald deBethizy
President and Chief Executive Officer
(Principal 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 year ended December 31, 2011 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Alan A. Musso, Senior Vice President, Finance and Administration, 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, as amended; 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 6, 2012

BY: /s/ ALAN A. MUSSO

Alan A. Musso
Senior Vice President, Finance and Administration, Chief Financial Officer and Treasurer
(Principal Financial and Accounting Officer)