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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, 2010

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, 2010, was approximately $314,394,099, based on the price at which the registrant's common stock was last sold on June 30, 2010 ($19.33).

As of February 28, 2011, the registrant had 29,021,460 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 2011 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, 2010, 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, AZD3480 (TC-1734), AZD1446 (TC-6683), TC-6987, TC-6499 or any of our other product candidates or programs, such as the target indication(s) for development, the size, design, population, conduct, objective 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 for TC-5214), for meeting with regulatory authorities, or, where applicable, for an advancement decision by AstraZeneca;
- the benefits that may be derived from any of our product candidates;
- 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,” “scheduled” or other comparable words identify forward-looking statements. Actual results, performance or experience may differ materially from those expressed or implied by forward-looking statements as a result of various important factors, including our critical accounting policies and risks and uncertainties relating, 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 Phase 3 clinical trials;
- 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;
- the significant control or influence that AstraZeneca has over the development of TC-5214, AZD3480 and AZD1446, including as to the timing, scope and design of clinical trials and as to the conduct at all of further development of AZD3480 in attention deficit/hyperactivity disorder, AZD1446 in Alzheimer’s disease or TC-5619 in Alzheimer’s disease;
- the conduct and results of clinical trials and non-clinical studies and assessments of TC-5214, AZD3480, AZD1446, TC-5619, TC-6987, TC-6499 or any of our other product candidates, including the performance of third parties engaged to execute them and difficulties or delays in subject enrollment and data analysis;
- our ability to establish additional strategic alliances, collaborations and licensing or other 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, the results or events indicated by the forward-looking statements may not occur. We caution you not to place undue reliance on any forward-looking statement.

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

PART I

Item 1. Business.

Overview

We are a biopharmaceutical company engaged in the design, discovery and development of 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 is thought to derive antidepressant activity by modulating the activity of various NNR subtypes. We are co-developing TC-5214 with AstraZeneca 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. Phase 3 clinical trials of TC-5214 are ongoing. In addition, we and AstraZeneca initiated a Phase 2b clinical trial of TC-5214 as a “switch” monotherapy in the first quarter of 2011.

TC-5619

TC-5619 is a novel small molecule that modulates the activity of the a7 NNR. In January 2011, we announced positive top-line results from a Phase 2 clinical trial of TC-5619 in cognitive dysfunction in schizophrenia. We are currently conducting a separate Phase 2 clinical trial of TC-5619 in attention deficit/hyperactivity disorder, or ADHD, in adults and we expect results from the trial to become available by the end of the first quarter of 2011. In addition, we are conducting clinical and non-clinical studies to support the potential advancement of TC-5619 into Phase 2 clinical development in Alzheimer’s disease.

AstraZeneca has the right to license TC-5619 and to further develop and potentially commercialize TC-5619 for various conditions characterized by cognitive impairment on terms specified in our cognitive disorders agreement with AstraZeneca, as it was amended in April 2010. We expect AstraZeneca to determine whether to exercise its license right in the first half of 2011.

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 has conducted several clinical studies

of AZD3480 in various cognitive disorders and we are in discussions with AstraZeneca regarding potential additional development of the product candidate as a treatment for ADHD. Whether AstraZeneca will decide to conduct any additional development of AZD3480 in ADHD is uncertain in light of reservations about the adequacy of the therapeutic margin to support development across the broad ADHD patient population. We expect AstraZeneca to make its decision in the first half of 2011. In addition, we have agreed with AstraZeneca on respective roles and financial and non-financial responsibilities for an additional clinical trial of AZD3480 in Alzheimer's disease. We have had a favorable meeting with the U.S. Food and Drug Administration, or FDA, regarding a potential development path for AZD3480 in Alzheimer's disease and are continuing to explore the practicability of conducting an Alzheimer's disease study in Europe.

AZD1446 (TC-6683)

AZD1446 is a novel small molecule that modulates the activity of the a4ß2 NNR and is under consideration for further development as a treatment for Alzheimer's disease under our cognitive disorders agreement with AstraZeneca. We discovered and advanced AZD1446 as part of a now completed preclinical research collaboration conducted under the agreement. AstraZeneca has completed three of four early-stage clinical studies expected to inform its decision as to whether to conduct further clinical development of AZD1446, and we expect AstraZeneca to make its decision in the third quarter of 2011.

TC-6987

TC-6987 is a novel small molecule that modulates the activity of the a7 NNR and is in development as a treatment for inflammatory disorders. In February 2011, we announced the initiation of two Phase 2 studies planned to help guide the selection of indications for which TC-6987 is best suited for later-stage development. One of the Phase 2 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). We are currently considering possible future development plans.

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 discover 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 our potential collaborator has particular expertise or that involve large primary care markets that must be served by large sales and marketing organizations. In entering into these alliances and collaborations, our goal will generally be to maintain co-promotion or co-commercialization rights for specialists, particularly in neurology and psychiatry, in the United

States and, potentially in some cases, other markets. Under our 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, to specified classes of physicians in the United States.

- *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 in an effort to apply our product pipeline to indications in which there is a significant medical need and commercial potential.

Our Product Development Pipeline

The following table summarizes our 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)	Phase 3 clinical trials as an adjunct therapy and Phase 2b clinical trial as a "switch" monotherapy ongoing;	AstraZeneca
TC-5619	Cognitive dysfunction in schizophrenia, ADHD and Alzheimer's disease	Phase 2 clinical trial in cognitive dysfunction in schizophrenia completed; separate Phase 2 clinical trial in ADHD in adults and additional studies to support potential Phase 2 clinical development in Alzheimer's disease ongoing	subject to AstraZeneca's right to license
AZD3480 (TC-1734)	Either or both of ADHD and Alzheimer's disease	Phase 2 clinical trial in adults with ADHD completed, with decision by AstraZeneca as to whether to advance into Phase 2b development expected in the first half of 2011; Targacept considering the practicability of conducting an additional clinical trial in Alzheimer's disease	AstraZeneca
AZD1446 (TC-6683)	Alzheimer's disease	Three of four early-stage clinical trials expected to inform an AstraZeneca advancement decision completed	AstraZeneca
TC-6987	One or more disorders characterized by inflammation	Separate Phase 2 clinical trials in asthma and Type 2 diabetes ongoing	Targacept
TC-6499	One or more gastrointestinal disorders	Exploratory Phase 2a clinical trial in subjects with constipation-predominant irritable bowel syndrome completed; Targacept considering possible future development plans	Targacept

Information regarding our research and development expenses for the fiscal years ended December 31, 2010, 2009 and 2008 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 thought to derive antidepressant activity by modulating the activity of various NNR subtypes and 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.

We are co-developing TC-5214 with AstraZeneca under our TC-5214 agreement with AstraZeneca. The initial global 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. The Phase 3 program, which we and AstraZeneca refer to as the RENAISSANCE Program, is designed to support the planned second half of 2012 filing of a new drug application, or NDA, with the FDA for TC-5214 as an adjunct therapy for major depressive disorder. The RENAISSANCE Program includes four multi-center, double blind, parallel group clinical trials, two with a fixed dose design and two with a flexible dose design, to evaluate the efficacy and tolerability of TC-5214 as an adjunct to continued SSRI or SNRI treatment. In the fixed dose trials, each subject receiving TC-5214 receives a set dosing regimen throughout the dosing period. In the flexible dose trials, each subject receiving TC-5214 initially receives a particular dosage, which can be increased at various times during the trial at the discretion of the applicable investigator based on how the subject tolerates and responds to the then-current dosage. The primary outcome measure for each of the four trials is change from double blind baseline for TC-5214 on the Montgomery-Asberg Depression Rating Scale, or MADRS, which is a scale on which the clinician evaluates the subject's depressed mood and other symptoms of depression and anxiety, as compared to placebo. 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 safety trial in which subjects receive TC-5214 or placebo for up to one year.

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, a renal impairment study, which is designed to evaluate the elimination of TC-5214 in subjects with impaired kidney function, and a drug-drug interaction study designed to assess the safety of TC-5214 when used together with particular drugs. We and AstraZeneca also initiated a Phase 2b clinical trial of TC-5214 as a "switch" monotherapy in February 2011.

AstraZeneca is responsible for 80% and we are responsible for 20% of the costs of the initial global clinical 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 initial 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 initial 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, an approved treatment for major depressive disorder marketed in the United States as Celexa, is a representative SSRI, which is the drug class most commonly prescribed for major depressive disorder.

The Phase 2b clinical trial was a two-phase study conducted at 20 sites in India and three sites in the United States. The first phase of the trial was "open label," which means both the subjects and the investigators knew what was being administered. In the first phase, 579 subjects received initial treatment with citalopram for eight

weeks, 20mg daily for the first four weeks and 40mg daily for the next four weeks. At the end of the eight weeks, subjects whose score on MADRS had improved less than 50 percent and was no lower than 17 and whose score on the Clinical Global Impression—Severity of Illness subscale, or CGI-S, which is a scale on which the clinician assesses how ill a subject is based on his or her total clinical experience, was no lower than 4 were considered partial or non-responders and eligible for the second phase of the trial.

The second phase of the trial was double blind and placebo controlled. In this phase, subjects continued their citalopram treatment and also received either add-on TC-5214 or add-on placebo for an additional eight weeks. The daily dosage of TC-5214 was initially 2mg and could be increased at the discretion of the investigator to 4mg and to 8mg based on how the subject tolerated and responded to the then-current dosage.

The primary outcome measure for the trial was mean change between add-on TC-5214 (TC-5214 + citalopram) and add-on placebo (placebo + citalopram) from double blind baseline as measured by the Hamilton Rating Scale for Depression-17, or HAM-D, which is another scale on which the clinician evaluates the subject's depressed mood and other symptoms of depression and anxiety, at week 16. The magnitude of clinical response on HAM-D was 6.0 points greater for the add-on TC-5214 arm (13.75 point improvement) than for the add-on placebo arm (7.75 point improvement), and the result was highly statistically significant in favor of TC-5214 ($p < 0.0001$) on an intent to treat basis. The results on all of the trial's secondary efficacy outcome measures, including MADRS, the Quick Inventory of Depressive Symptomatology – Self Reporting scale and assessments of irritability, disability, cognition, severity of illness and global improvement, were also highly statistically significant in favor of TC-5214 ($p < 0.0001$) on an intent to treat basis. The intent to treat dataset included 265 subjects in the second phase.

TC-5214 exhibited a favorable tolerability profile in the trial. The most frequent adverse events were headache, dizziness and constipation, and there was no clinically significant difference between the dose groups in discontinuations due to adverse events. There was one serious adverse event in the trial considered by the investigators to be related to study drug (either or both of citalopram and TC-5214), a seizure experienced by a study subject.

TC-5619

TC-5619 is a novel small molecule that modulates the activity of the a7 NNR. In a 2004 survey of 46 cognitive neuroscientists and neuropharmacologists conducted in connection with a National Institute of Mental Health initiative known as Measurement and Treatment Research to Improve Cognition in Schizophrenia, or MATRICS, a7 was selected more often than any other target as a target of interest in the development of treatments for cognitive dysfunction in schizophrenia.

We have completed a Phase 2 clinical trial of TC-5619 in cognitive dysfunction in schizophrenia. In addition, we are currently conducting a separate Phase 2 clinical trial in ADHD in adults, as well as clinical and non-clinical studies to support the potential advancement of TC-5619 into Phase 2 clinical development in Alzheimer's disease. We expect that a decision as to whether to conduct Phase 2 clinical development of TC-5619 as a treatment for Alzheimer's disease will be made in the future.

TC-5619 is subject to our cognitive disorders agreement with AstraZeneca as a result of a process that we initiated under the agreement in 2007 and a related election made by AstraZeneca. AstraZeneca has the right to license TC-5619 and to further develop and potentially commercialize TC-5619 for various conditions characterized by cognitive impairment on terms specified in the agreement, as it was amended in April 2010. If AstraZeneca exercises its right to license TC-5619, the agreement provides for AstraZeneca to make a $30 million payment to us and to assume responsibility for and fund all future development (except for completion of our ongoing studies) and commercialization. In that event, we would be eligible to receive additional payments of up to $212 million, if development, regulatory, first commercial sale and first detail milestone events are achieved for three indications, as well as stepped double-digit royalties on any future TC-5619 product sales. We expect AstraZeneca to determine whether to exercise its license right in the first half of 2011.

Completed Phase 2 Trial in Cognitive Dysfunction in Schizophrenia

In January 2011, we announced positive top-line results from a Phase 2 clinical trial of TC-5619 in cognitive dysfunction in schizophrenia. The double blind, placebo controlled trial was conducted at seven sites in the United States and 12 sites in India. In the trial, 185 subjects meeting DSM-IV criteria for schizophrenia, with stable psychotic symptoms and taking a stable dose of an approved medication from the drug class known as atypical anti-psychotics (either quetiapine, marketed as Seroquel, or risperidone, marketed as Risperdal) were randomly assigned to receive either TC-5619 or placebo, together with continued treatment with the atypical antipsychotic, for 12 weeks. As planned, 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 efficacy outcome measure of the trial was change from baseline on the Groton Maze Learning task of the CogState Schizophrenia Battery, on each of three measurement dates as compared to placebo. The CogState Schizophrenia Battery is a computerized battery of neuropsychiatric tests that assess specific cognitive domains, and the Groton Maze Learning task is designed to assess executive function, which is the 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. 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 and for subjects at study sites in the United States as compared to subjects at study sites in India. There was no activity in non-tobacco users. Estimates of the prevalence of smoking amongst schizophrenia patients vary, with one study indicating as high as 80%. Each of the p-values noted above was derived after data log transformation, a commonly utilized technique where the data does not follow a normal distribution.

In addition, positive signals were observed in the trial on several secondary efficacy outcome measures, including Scale for Assessment of Negative Symptoms, an investigator assessment of improvement on the negative symptoms of schizophrenia, Clinical Global Impression – Global Improvement, an investigator assessment of overall response, and Subject Global Impression – Cognition scale, a patient self-assessment of cognitive change. Other secondary outcome measures of the trial, including a composite measure of the CogState Schizophrenia Battery, did not demonstrate a drug effect in the dataset that included all subjects.

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

Ongoing Phase 2 Trial in Adults with ADHD

We are currently conducting a Phase 2 clinical trial of TC-5619 in adults with ADHD. The trial is designed as a double blind, placebo controlled, parallel group study and is being conducted in the United States. In the trial, approximately 125 adult subjects are randomly assigned to one of two cohorts, TC-5619 or placebo, and dosed over a 12-week period. Subjects in the TC-5619 cohort receive 1mg doses of TC-5619 for the first four weeks, 5mg doses of TC-5619 for the next four weeks and 25mg doses of TC-5619 for the last four weeks. The primary efficacy outcome measure of the trial is change from baseline on the Conners Adult ADHD Rating Scale, a multimodal questionnaire assessment of symptoms and behaviors associated with ADHD in adults aged 18 and older, as compared to placebo. The trial also includes a number of secondary efficacy outcome measures. We expect results from the trial to become available by the end of the first quarter of 2011.

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 has completed Phase 2 clinical trials of AZD3480 in various indications characterized by cognitive impairment that have generated a range of efficacy results, including: (1) achievement of primary outcome measure(s) (a Phase 2 clinical trial conducted by us and AstraZeneca in adults with ADHD and our Phase 2 trial reported in 2006 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); (2) inconclusive (AstraZeneca's Phase 2b trial in mild to moderate Alzheimer's disease completed in 2008); (3) positive signals (our Phase 2a studies in AAMI and mild cognitive impairment, or MCI; and (4) failure to achieve primary outcome measures (AstraZeneca's Phase 2b trial in cognitive dysfunction in schizophrenia completed in 2008).

We are in discussions with AstraZeneca regarding potential additional development of AZD3480 as a treatment for ADHD. Whether AstraZeneca will decide to conduct additional development of AZD3480 in ADHD is uncertain in light of reservations about the adequacy of the therapeutic margin to support development across the broad ADHD patient population. We expect AstraZeneca to make its decision in the first half of 2011.

In addition, we have agreed with AstraZeneca on respective roles and financial and non-financial responsibilities for an additional clinical trial of AZD3480 in Alzheimer's disease. We have had a favorable meeting with the FDA regarding a potential development path for AZD3480 in Alzheimer's disease and are continuing to explore the practicability of conducting an Alzheimer's disease study in Europe. If an Alzheimer's disease study proceeds, we would be responsible for funding the study but would be entitled to receive up to $5.7 million in additional payments from AstraZeneca, with the last tranche being payable to us upon first dosing in the United States and Europe.

Completed Phase 2 Trial in Adults with ADHD

In 2009, we and AstraZeneca completed a Phase 2 clinical trial of AZD3480 in adults with ADHD. The trial was a double blind, placebo controlled crossover study conducted at Fletcher Allen Health Care, an affiliate of University of Vermont College of Medicine. Subjects were non-smoking males and females between the ages of 18 and 65 who were diagnosed with ADHD based on *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition*, or DSM-IV, criteria and had a baseline score of at least 4 on CGI-S. Each subject received 5mg AZD3480, 50mg AZD3480 and placebo daily for two weeks, in random order, with the three dosing periods separated by three-week periods without any dosing to minimize carryover effects. As a result, each subject served as his or her own control.

The primary outcome measure for the trial was the change in total symptom score on the Conners Adult ADHD Rating Scale—Investigator Rating, or CAARS-INV, a scale that takes into account nine domains thought to encompass a range of ADHD manifestations in adults, following two weeks dosing with AZD3480 as compared to two weeks dosing with placebo. In the trial, the subjects' symptoms of ADHD as measured by CAARS-INV improved with 50mg AZD3480, and the result was statistically significant ($p < 0.01$) on an intent to treat basis. Statistically significant results were also achieved at 50mg AZD3480 on some, but not all, of the secondary outcome measures in the study, including Stop Signal Reaction Time, a computerized assessment of behavioral inhibition, which is a core cognitive deficit of ADHD. AZD3480 was well tolerated in the study, and there were no serious adverse events.

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

In 2008, AstraZeneca completed two Phase 2b double blind, placebo controlled, dose finding clinical trials of AZD3480, one in mild to moderate Alzheimer's disease and one in cognitive dysfunction in schizophrenia. The trial in mild to moderate Alzheimer's disease, known as the "Sirocco" trial, was conducted at 84 sites in Western Europe, Eastern Europe and Canada. In the Sirocco trial, 567 subjects who were between 60 and 85

years old and diagnosed with probable Alzheimer's disease classified as mild or moderate in severity were randomly assigned to one of three dose groups of AZD3480, to the active comparator donepezil (the most commonly prescribed drug for Alzheimer's disease), or to placebo and dosed over a 12-week period. The primary outcome measure of the trial was change from baseline after 12 weeks on the Alzheimer's Disease Assessment Scale-cognitive subscale, or ADAS-Cog. Some of the secondary outcome measures of the trial included the Alzheimer's Disease Cooperative Study—Clinical Global Impression of Change, or ADCS-CGIC, which is a 7-point clinician assessment of change in behavior and the ability to function, the Mini Mental State Examination, or MMSE, which is a quantitative, 30-point cognition scale, and a computer-based test battery developed by CDR Ltd. to test cognitive function.

The results of the Sirocco trial were inconclusive. Neither the active comparator donepezil nor AZD3480 met the trial's criteria for statistical significance on the primary outcome measure, ADAS-Cog. 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 Phase 2b Clinical Trial in Cognitive Dysfunction in Schizophrenia

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

Completed Phase 2 Clinical Trial in AAMI Reported in 2006

In 2006, we reported results from a double blind, placebo controlled Phase 2 clinical trial of AZD3480 in AAMI in the United States. We recruited 193 subjects between the ages of 50 and 80, who were classified with AAMI based on inclusion criteria reflecting both subjective and objective memory impairment, to participate in the trial. The trial assessed the effects of 25mg AZD3480 and 50mg AZD3480 on various aspects of cognitive function using the CDR test battery. We tested each subject at various time points prior to the first day of the 16-week dosing period to establish baseline. We tested subjects again at eight weeks and on the last day of the 16-week dosing period. The CDR test battery includes measures of attention, speed of cognitive processes and memory that assess the ability to react to stimuli, recognize words and pictures and recall words. These measures are then used to make composite assessments on five factors —power of attention, continuity of attention, working or short-term memory, episodic or long-term memory and speed of memory.

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

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

On an intent to treat basis, subjects in the 50mg AZD3480 dose group showed improvement as compared to subjects in the placebo dose group on all three co-primary efficacy endpoints and subjects in the 25mg AZD3480 dose group showed improvement as compared to subjects in the placebo dose group on the power of attention endpoint. These results were statistically significant, with p-values less than 0.05.

Previously Completed Phase 2 Clinical Trials in AAMI and MCI

Prior to the Phase 2 clinical trial of AZD3480 in AAMI described above, we completed two double blind, placebo controlled, crossover design Phase 2 clinical trials of AZD3480, one in AAMI and one in MCI. In the AAMI trial, we evaluated four doses of AZD3480, 50mg, 100mg, 125mg and 150mg. In the MCI trial, we evaluated two doses of AZD3480, 50mg and 100mg. Each trial assessed the effects of AZD3480 on various aspects of cognitive function using the CDR test battery before dosing and at various time points after dosing on the first and last day of each dosing period.

In both trials, AZD3480 demonstrated positive effects at some dose levels with respect to some measures of cognition tested, but did not demonstrate positive effects as to all measures at all dose levels and placebo showed superior effects to AZD3480 as to some measures at some dose levels. The results of the AAMI trial were most favorable in the 50mg AZD3480 dose group and were less pronounced in the other dose groups. The results of the MCI trial were more favorable in the 100mg AZD3480 dose group, as the results in the 50mg AZD3480 dose group did not favor AZD3480 on any measure.

AZD1446 (TC-6683)

AZD1446 (TC-6683) is a novel small molecule that modulates the activity of the a4ß2 NNR and is under consideration for further development as a treatment for Alzheimer's disease under our cognitive disorders agreement with AstraZeneca. We discovered and advanced AZD1446 as part of a now completed preclinical research collaboration that we and AstraZeneca conducted under the agreement. AstraZeneca is responsible for conducting and funding the development and potential future commercialization of AZD1446 and has completed three of four early-stage clinical studies expected to inform its decision as to whether to advance the product candidate, including:

- a trial in adults with ADHD in which AZD1446 did not improve core symptoms of ADHD, as compared to placebo, as measured by the primary outcome measure (CAARS-INV), but showed signals of a drug effect in non-nicotine using subjects (but not 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 which 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; and

- a trial designed to explore the effects of a single dose of AZD1446 in healthy volunteers with drug-induced cognitive impairment in which pro-cognitive signals were observed on various secondary outcome measures but neither AZD1446 nor the positive comparator donepezil demonstrated a statistically significant effect on an assessment of reversal of a drug-induced effect on brain waves associated with attention, which was the primary outcome measure.

A fourth study, which has not completed, is designed to evaluate the effect of AZD1446 and donepezil on brain response in subjects with Alzheimer's disease as assessed by electroencephalography (EEG). We expect AstraZeneca to decide whether to conduct further development of AZD1446 as a treatment for Alzheimer's disease in the third quarter of 2011.

TC-6987

TC-6987 is a novel small molecule that modulates the activity of the a7 NNR. We have completed Phase 1 clinical development and have ongoing separate Phase 2 studies planned to help guide the selection of indications for which TC-6987 is best suited for later-stage development. One of the Phase 2 studies is in asthma and the other is in Type 2 diabetes. Both studies were designed to include a number of different efficacy measures that would show anti-inflammatory effects of TC-6987 and inform potential future development.

Ongoing Phase 2 Trial in Asthma

The Phase 2 clinical trial in asthma is a multicenter, double blind, placebo controlled, parallel group study being conducted in the United States. The study is planned to enroll approximately 90 adult subjects with asthma mild to moderate in severity. The study design provides for subjects to undergo a four-week wash-out period during which they receive a low-dose inhaled corticosteroid and cease taking their current asthma medication 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 end of dosing for subjects receiving TC-6987 as compared to placebo designated as the primary efficacy outcome measure. The study also includes assessments of safety, tolerability and pharmacokinetics of TC-6987.

Ongoing Phase 2 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. The study is planned to enroll approximately 120 adult subjects with Type 2 diabetes. The study design includes a one-week screening period followed by a four-week washout period during which subjects cease taking their current medication for Type 2 diabetes 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 (a metabolic measurement used to expose problems with insulin function) from baseline to end of dosing for subjects receiving TC-6987 as compared to placebo designated as the primary efficacy 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). We are currently considering possible future development plans. As previously disclosed, we are no longer developing TC-6499 as a treatment for pain.

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, cognitive dysfunction in schizophrenia, ADHD, Alzheimer's disease and inflammatory disorders (currently asthma and Type 2 diabetes).

Major depressive disorder is characterized by a combination of symptoms that interfere with a person's ability to work, sleep, study, eat and enjoy once-pleasurable activities. It is disabling and can prevent a person from functioning normally. The market research firm Decision Resources estimated that approximately 42.4 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 2009. The Sequenced Treatment Alternatives to Relieve Depression, or STAR*D, study undertaken by the National Institute of Mental Health between 2001 and 2006 showed the inadequacy of currently available therapies for major depressive disorder. In the first phase of the STAR*D study, approximately 2,800 persons with major depressive disorder were given the representative SSRI citalopram for 12 to 14 weeks. Only about one-third of the participants became symptom free, which is referred to as achieving "remission," and about 10-15 percent more responded, but did not reach remission.

Schizophrenia is a chronic, severe and disabling form of psychosis. In addition to symptoms such as delusions, hallucinations, the inability to disregard familiar stimuli, sometimes referred to as sensory gating, disorganized speech, grossly disorganized or catatonic behavior and prolonged loss of emotion, feeling, volition or drive, schizophrenia is often marked by impairment in cognitive functions, such as attention, vigilance, memory, and reasoning. Decision Resources estimated that there were approximately 4.6 million people with schizophrenia in the world's seven major pharmaceutical markets in 2009. 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 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. For an adult to be diagnosed with ADHD, the ADHD symptoms must have begun during childhood and continued throughout adulthood. Decision Resources estimated that there were approximately 23.3 million adults and 21.6 million children with ADHD in the world's seven major pharmaceutical markets in 2009. 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 debilitating brain disorder for which there is no cure. Decision Resources estimated that there were approximately 9.7 million people with Alzheimer's disease in the world's seven major pharmaceutical markets in 2009. The disease progresses in stages from mild to moderate to severe and gradually destroys a person's memory and ability to learn, reason, make judgments, communicate and carry out daily activities. Mild Alzheimer's disease is characterized by mild forgetfulness and difficulty acquiring basic information and communicating. Patients generally exhibit the symptoms of mild Alzheimer's disease for two to four years before progressing to the moderate stage. Moderate Alzheimer's disease is characterized by forgetfulness, failure to recognize friends and family, disorientation regarding time

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

Asthma is a chronic inflammatory disorder of the lungs and airways characterized by recurring periods of wheezing, chest tightness, shortness of breath and coughing, which 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 has estimated that there were approximately 65 million people with asthma in the world's seven major pharmaceutical markets in 2009.

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 be largely the result of excess body weight and physical inactivity. According to the World Health Organization, approximately 198 million people worldwide have Type 2 diabetes, representing about 90% of all diabetics. Deaths related to complications from the disease are expected to double between 2005 and 2030.

Our Preclinical Research Programs

In addition to our clinical-stage product candidates, we focus preclinical research efforts in areas in which we believe NNRs can be exploited for medical benefit and for which we believe we can efficiently develop marketable product candidates. We have research programs targeting the design and development of (1) nicotinic channel modulators, which we believe have potential therapeutic application for a number of indications, (2) compounds that act on the a7 NNR for the treatment of disorders characterized by cytokine-mediated inflammation and (3) Parkinson's disease. We have been awarded two grants from The Michael J. Fox Foundation for Parkinson's Research. One of the grants is to test the potential of compounds that modulate NNRs to address abnormal involuntary movements, or dyskinesias, that are a side effect of levodopa treatment, and the other is 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. 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 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 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 has been approved for marketing since the 1950s, and 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. 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 initial global clinical program includes development of TC-5214 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 initial 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 initial 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 initial 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 initial 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 (e.g., receipt of regulatory approval of the applicable indication or formulation).

AstraZeneca is responsible under the agreement for executing and funding the costs of global commercialization of TC-5214, 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 and has assumed our rights and obligations under our applicable agreements with third parties.

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 clinical trial of a compound as an adjunct (or add-on) to antidepressant treatment for major depressive disorder, or to commercialize such a compound, subject to certain exceptions that include, among others, AstraZeneca's right to develop and commercialize quetiapine (marketed by AstraZeneca as Seroquel XR) 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 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 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 ADHD, Alzheimer's disease, 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.

We or AstraZeneca has conducted several clinical studies of AZD3480 in various cognitive disorders and we are in discussions with AstraZeneca regarding potential additional development of the product candidate as a treatment for ADHD. Whether AstraZeneca will decide to conduct any additional development of AZD3480 in ADHD is uncertain in light of reservations about the adequacy of the therapeutic margin to support development across the broad ADHD patient population. We expect AstraZeneca to make its decision in the first half of 2011. In addition, we are exploring the practicability of conducting an additional clinical trial of AZD3480 in Alzheimer's disease and have agreed with AstraZeneca on respective roles and financial and non-financial responsibilities for such a study.

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 it is under consideration for further development as a treatment for Alzheimer's disease. AstraZeneca has completed three of four early-stage clinical studies expected to inform its decision as to whether to advance AZD1446, and we expect AstraZeneca to make its decision in the third quarter of 2011.

As a result of a process that we initiated under the agreement and a related election made by AstraZeneca, TC-5619 is also subject to the agreement. AstraZeneca has the right to license TC-5619 and to further develop and potentially commercialize TC-5619 for various conditions characterized by cognitive impairment on terms specified in the agreement, as it was amended in April 2010. We expect AstraZeneca to determine whether to exercise its license right in the first half of 2011.

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 $103 million, if development, regulatory and first commercial sale milestone events for AZD3480 are achieved only for ADHD, and stepped double-digit royalties on any future AZD3480 product sales for any indication. We are also eligible to receive other payments if we proceed with another Alzheimer's disease study of AZD3480, AstraZeneca subsequently advances AZD3480 into later-stage development for Alzheimer's disease and development, regulatory and first commercial sale milestone events for AZD3480 are achieved for Alzheimer's disease. The aggregate amount of contingent milestone payments that we are eligible to receive with respect to Alzheimer's disease and ADHD is $197 million. If AZD3480 is developed under the agreement for an indication in addition to Alzheimer's disease and ADHD, we would also be eligible to receive payments of up to $52 million 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 only 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.

If AstraZeneca licenses TC-5619, the agreement provides for AstraZeneca to make a $30 million payment to us. In that event, we would be eligible to receive additional payments of up to $212 million, if development, regulatory and first commercial sale and first detail milestone events are achieved for three indications, as well as stepped double-digit royalties on any future TC-5619 product sales.

AstraZeneca's obligation to pay royalties to us for each compound subject to the collaboration expires on a country-by-country basis on the later of expiration of our patent rights that provide exclusivity for that compound in that country or 12 years after the first commercial sale in that country of either that compound or any related compound that meets specified criteria. If AstraZeneca obtains a patent covering the composition of a compound that is derived within a specified period from a compound that is subject to the collaboration, the term of AstraZeneca's patent would also be taken into account in determining the term of AstraZeneca's obligation to pay royalties to us for that derived compound. The U.S. patent rights to the chemical genus that includes TC-5619 expire in 2019 and the U.S. patent rights to a method of using a racemic mixture that includes TC-5619 to treat schizophrenia expire in 2025. The foreign patent rights that have issued and correspond to our issued U.S. patent rights expire in 2024. We also have a pending U.S. patent application with respect to TC-5619 specifically and to a particular salt form of TC-5619 that, if issued as patents, would expire in 2028. 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. In addition, we 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, AZD1446 or, if licensed by AstraZeneca, TC-5619 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. If we proceed to conduct another Alzheimer's disease study of AZD3480, we would be responsible for funding the study but would be entitled to receive up to $5.7 million in additional payments from AstraZeneca, with the last tranche being payable to us upon first dosing in the United States and Europe. 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. If AstraZeneca licenses TC-5619, it would assume responsibility for and fund all future development (except for completion of our ongoing studies) and commercialization of TC-5619.

Exclusivity Rights and Restrictions. Neither we nor AstraZeneca are permitted outside of the collaboration to develop or commercialize compounds that act on the a4ß2 NNR and meet pre-defined criteria for ADHD, Alzheimer's disease, 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 right to license TC-5619. If we do not offer this right to AstraZeneca for a compound that meets pre-defined criteria for any NNR other than the a4ß2 NNR, we are generally not permitted to develop or commercialize the compound for any indication for which AstraZeneca has development and commercialization rights under the agreement.

If we offer a compound to AstraZeneca, AstraZeneca could license the compound from us, together with metabolites of the compound and derivatives and other compounds related to the compound that meet specified criteria, on terms specified in the agreement. Alternatively, as in the case of TC-5619, AstraZeneca could negotiate a development plan with us pursuant to which we would conduct development intended to provide a pre-defined indication of efficacy. AstraZeneca could license the compound from us after we complete the additional development. For each compound licensed by AstraZeneca through this process, we are eligible to receive an exercise fee and other payments 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, 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

On July 27, 2007, we entered into a product development and commercialization agreement with SmithKlineBeecham Corporation and Glaxo Group Limited, which we refer to collectively 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, in late February 2011, we received notice of termination of the agreement from GlaxoSmithKline. By the terms of the agreement, the termination becomes effective in late 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 28, 2011, our patent estate included 58 patents issued in the United States, 75 patent applications pending in the United States and approximately 600 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 family of compounds that includes TC-5619	August 2019
	Composition of matter for a racemic mixture that includes TC-5619	March 2019
	Methods of use of a racemic mixture that includes TC-5619 for treatment of schizophrenia	November 2025
AZD3480 (TC-1734)	Composition of matter for AZD3480	July 2018
	Composition of matter for a family of compounds that includes AZD3480	April 2016
	Methods of use of a family of compounds that includes AZD3480 for treatment and prevention of CNS disorders	February 2017
	Methods of use for AZD3480 for treatment and prevention of CNS disorders	July 2018
	Composition of matter for the preferred salt (p-hydroxybenzoate) of AZD3480	August 2026
TC-6987	Composition of matter for a family of compounds that includes TC-6987	August 2019
TC-6499	Composition of matter for TC-6499; composition of matter for a family of compounds that includes TC-6499	February 2024

In addition to these patents, for some of these product candidates we have later-expiring patents that cover a particular form or composition, use as part of combination therapy or method of preparation or use, as well as other pending patent applications. These issued patents, including any patents that issue from the pending applications, could provide additional or a longer period of protection. We also have patent applications pending that seek equivalent or substantially comparable protection for our product candidates in jurisdictions internationally that we consider key pharmaceutical markets.

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

License Agreements

In addition to the agreements governing our collaborations with AstraZeneca, we consider the following license agreements to be important to our business as of March 11, 2011.

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 to R.J. Reynolds Tobacco Company UKRF's rights to inventions that resulted in patents related to AZD3480. These patents were subsequently assigned by RJR to us in August 2000, 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 alpha7 or other nicotinic receptors, as well as the use of modulators of the a7 NNR to treat 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 for target indications for which our potential collaborator has particular expertise or that involve large primary care markets that must be served by large sales and marketing organizations. In entering into these alliances and collaborations, our goal will generally be to maintain co-promotion or co-commercialization rights in the United States and, in some cases, other markets. In order to implement this aspect of our strategy successfully, we must 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 approximately $31,000 in 2010, $140,000 in 2009 and $170,000 in 2008.

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 as examples Roche, with a compound in Phase 2 development for Alzheimer's disease, and Abbott Laboratories, with one compound in Phase 2 development for ADHD and a second compound in Phase 1 development for cognitive disorders. Other companies that we believe have active NNR-based programs include AstraZeneca, Eli Lilly, Sanofi-Aventis, Bristol-Myers Squibb, GlaxoSmithKline, Johnson & Johnson, Novartis, NeuroSearch A/S, Solvay, Servier, CoMentis, EnVivo Pharmaceuticals, Galantos Pharma, Proximagen, Psychogenics, AGI Therapeutics, 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 enter the CNS market, whether independently or by alliance or acquisition.

In addition, there are several pharmaceutical companies in the United States and globally that currently market and sell drugs for indications that we are targeting. We believe that the primary competitive products for use in indications that we are currently targeting with our most advanced product candidates include:

- 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/Seroxar from GlaxoSmithKline, Zoloft from Pfizer, Celexa and Lexapro from Forest Laboratories, dual uptake inhibitors such as Effexor from Wyeth and Cymbalta from Eli Lilly, and the SSRI and $5HT_{1A}$ receptor partial agonist Viibryd from Clinical Data (under agreement to be acquired by Forest Laboratories);
- for ADHD, stimulants such as Adderall XR and Vyanase from Shire, Concerta from Johnson & Johnson and Ritalin LA from Novartis, and Strattera, a non-stimulant acting as a norepinephrine reuptake inhibitor, from Eli Lilly;
- for mild to moderate Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer/Eisai, Razadyne from Johnson & Johnson and Exelon from Novartis; in addition, Namenda from Forest Laboratories, which acts by regulating the neurotransmitter glutamate, is marketed for moderate to severe Alzheimer's disease;
- for 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; and

- 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.

There is currently no approved product for cognitive dysfunction in schizophrenia. There are however multiple third-party product candidates currently in clinical development for cognitive dysfunction in schizophrenia, including at least one modulator 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, record-keeping, promotion, advertising, distribution, marketing and export and import of drugs such as those we are developing. Our product candidates must be approved by 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 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, must review and approve the plan for any clinical trial before it commences at any institution. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and 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.

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.

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

U.S. Review and Approval Processes

The results of product development, preclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical chemistry tests, proposed labeling, and other relevant information, are submitted to the FDA as part of an NDA requesting approval to market the drug as a 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 product and establishment user 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 accepting it for filing. The FDA may request additional information rather than accept an NDA for filing. In this event, the NDA must be resubmitted with the additional information. The resubmitted application also is subject to review before the FDA accepts it for filing. The FDA may refuse to file the NDA. If the submission is accepted for filing, the FDA begins an in-depth substantive review to determine, among other things, whether a product is safe and effective for its intended use and whether its manufacturing is cGMP-compliant to assure and preserve the product's identity, strength, quality and purity. In that regard, the FDA will inspect the facility or facilities where the product is manufactured before approving an NDA.

Under current performance goals, the FDA has either six or 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, 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 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, for example, for new indications, dosages, or strengths of an existing drug. This three-year exclusivity covers only the conditions associated with the new clinical investigations and does not prohibit the FDA from approving ANDAs for drugs containing the original active agent. Five-year and three-year exclusivity will not delay the submission or approval of a full NDA; however, an applicant submitting a full NDA would be required to conduct or obtain a right of reference to all of the preclinical studies and adequate and well-controlled clinical trials necessary to demonstrate safety and effectiveness.

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

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

Under European Union regulatory systems, we may submit marketing authorization applications either under a centralized or a decentralized procedure. The centralized procedure, which is compulsory for medicines produced by certain biotechnological processes and optional for those which are highly innovative, provides for the grant of a single marketing authorization that is valid for all European Union member states. For drugs without approval in any member state, the decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state, known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials (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.

Reimbursement

Sales of pharmaceutical products depend in significant part on the availability of third-party reimbursement. Third-party payors include government health administrative authorities, managed care providers, private health insurers and other organizations. These third-party payors are increasingly challenging the price and examining

the cost-effectiveness of medical products and services, 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 for which we or any collaborator of ours receives marketing approval. 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 for which we or any collaborator of ours receives marketing approval on a competitive and profitable basis.

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

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

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

In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their 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.

Employees

As of February 28, 2011, we had 132 employees, 47 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.

Our trademarks and service marks include Targacept®, Pentad™, NNR Therapeutics™, TRIDMAC™ and Building Health, Restoring Independence℠. 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 sustain profitability or, if we do sustain profitability, we may not grow it.

We were incorporated in 1997 and operated as a wholly owned subsidiary of R.J. Reynolds Tobacco Company until August 2000. We have a limited operating history. As of December 31, 2010, we had an accumulated deficit of $218.4 million. We had net income of $10.9 million for the year ended December 31, 2010, net loss of $39.4 million for the year ended December 31, 2009 and net loss of $25.7 million for the year ended December 31, 2008. 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 sustain profitability.

We derived a substantial portion of our revenue for 2010, 2009 and 2008 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;
- the progress of, and outcomes from, Phase 3 clinical development of TC-5214 and the amount and timing of development costs for TC-5214 payable by us;
- if the outcome of Phase 3 clinical development of TC-5214 is favorable, whether we elect to exercise our co-promotion rights;
- whether AstraZeneca exercises its right to license TC-5619;

- whether and to what extent AstraZeneca determines to continue clinical development of one or both of AZD3480 and AZD1446 and, if so, milestone events are achieved under our cognitive disorders agreement with AstraZeneca that we entered into in December 2005; and
- whether we establish additional strategic alliances, collaborations and licensing or other arrangements, or pursue and complete any merger and acquisition transactions, on terms favorable to us.

Sources that contributed to our revenue for any particular year may not continue. In particular, the term of the preclinical research collaboration focused in cognition that we had been conducting with AstraZeneca under our cognitive disorders agreement with AstraZeneca expired in January 2010. We had received an aggregate of $26.5 million in research fees from AstraZeneca as of December 31, 2009, and research fee revenue generated from the preclinical research collaboration represented 21% of our net operating revenues for the year ended December 31, 2009 and 45% of our net operating revenues for the year ended December 31, 2008. In addition, 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 be profitable. 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 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 sustain profitability or, if we do sustain profitability, we may not grow it.*";
- the progress of, and outcomes from, Phase 3 clinical development of TC-5214 and the amount and timing of development costs for TC-5214 payable by us;
- the scope, progress, duration, results and costs of clinical trials, as well as non-clinical studies and assessments, of our product candidates;
- 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 and manufacturing costs and costs to establish sales and marketing functions;
- the costs, timing and outcomes of regulatory reviews or other regulatory actions;
- the number and characteristics of product candidates that we pursue;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending intellectual property-related claims;
- the costs of manufacturing-related services for our product candidates in clinical and late preclinical development;
- the rate of technological advancements for the indications that we target;

- the costs to satisfy our obligations under existing and potential future alliances and collaborations;
- the timing, receipt and amount of sales or royalties, if any, from our potential products; and
- the extent and scope of our general and administrative expenses.

In addition, we may seek additional capital due to market conditions or strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders may be diluted and the terms 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.

Our plans provide for us 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 at least through the end of 2013. 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 funds if and when needed may be materially and adversely affected by challenging U.S. and global financial markets and additional funds may not be available on terms that are acceptable to us, or at all. If adequate funds are not available on a timely basis, we may:

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

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

Our success depends substantially on our most advanced product candidates, which are still under development. If we 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); TC-5619 (for which a Phase 2 clinical trial has been completed in cognitive dysfunction in schizophrenia and a separate Phase 2 clinical trial in adults with ADHD and additional studies to support potential advancement into a Phase 2 clinical trial in Alzheimer’s disease are ongoing); AZD3480 and AZD1446 (each of which is at the Phase 2 clinical development stage, with any future development by AstraZeneca uncertain); and TC-6987 (which is currently being studied in separate Phase 2 trials in asthma and Type 2 diabetes).

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, if at all. 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 the completed Phase 2b clinical trial of TC-5214 as an adjunct therapy for major depressive disorder are not replicated in Phase 3 clinical trials, 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, such as our completed Phase 2b clinical trial of TC-5214 as an adjunct therapy for major depressive disorder, may not be replicated in later clinical trials that involve different numbers of subjects, different dosing regimens and durations, different subject populations and other differences in design or execution.

Our completed Phase 2b clinical trial of TC-5214 as an adjunct therapy for major depressive disorder was limited to subjects who did not respond adequately to the antidepressant citalopram. The ongoing Phase 3 development program for TC-5214 includes subjects who do not respond adequately to citalopram or any one of several other antidepressant therapies. It is possible that this difference in subject population, or any other difference in design between one or more of the ongoing Phase 3 clinical trials of TC-5214 and our completed Phase 2b clinical trial, will impact the likelihood that the favorable results achieved in the completed Phase 2b clinical trial will be replicated in Phase 3.

Furthermore, our completed Phase 2b clinical trial was conducted primarily in India and the ongoing Phase 3 development program is being conducted at investigative sites worldwide, including a significant number in the United States and Western Europe. 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. As a result, clinical trial subjects in India may be less likely to discontinue participation from a clinical trial or to report adverse events experienced, either of which may impact the likelihood that the favorable results achieved in the completed Phase 2b clinical trial will be replicated. If the favorable results achieved in our completed Phase 2b clinical trial of TC-5214 are not replicated in future clinical trials, 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 safety study in which patients receive TC-5214 or placebo for up to one year, as well as multiple Phase 1 clinical trials—including a QTc study, which is designed to confirm that various doses of TC-5214 do not disturb the electrical activity of the heart, a renal impairment study, which is designed to evaluate the elimination of TC-5214 in subjects with impaired kidney function, 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. 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 applicable foreign regulatory authorities could limit the patient population for which TC-5214 is approved, which could materially and adversely affect its commercial potential.

If the ongoing fixed dose clinical trials included in the Phase 3 development program for TC-5214 do not result in the determination of an effective dose range for TC-5214, or if an effective dose range is determined but does not provide a sufficient safety margin, we and AstraZeneca may not obtain the regulatory approvals required to market and sell TC-5214.

Our completed Phase 2b clinical trial of TC-5214 as an adjunct therapy for major depressive disorder utilized a flexible dose design. “Flexible dose” means that each subject who received TC-5214 initially received

a particular dosage (1mg twice per day), which could be increased (to 2mg and 4mg, in each case twice per day) at various times during the trial at the discretion of the applicable investigator based on how the subject tolerated and responded to the then-current dosage. Accordingly, the completed Phase 2b clinical trial was not designed to establish statistically the specific dosage at which TC-5214 had positive effects.

Two of the clinical trials in the Phase 3 development program for TC-5214 also utilize a flexible dose design, but two other trials in the program utilize a fixed dose design. A “fixed dose” design means that subjects in the trial receiving TC-5214 receive a set dosage regimen throughout the dosing period. Prior to initiation of the Phase 3 development program, neither we nor AstraZeneca had ever conducted a fixed dose 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.

In addition, in a Phase 1 multiple rising dose clinical trial completed by AstraZeneca in healthy volunteers, the tolerability profile of TC-5214 was less favorable at the highest dose tested as compared to the other doses. If, upon completion of the fixed dose Phase 3 clinical trials, the highest dosage evaluated in the trials (4mg twice per day) is the only effective dosage, the United States Food and Drug Administration, or FDA, or foreign regulatory authorities may not determine there to be a sufficient margin of safety to support approval to market and sell TC-5214.

If, notwithstanding the favorable results of our completed Phase 2b flexible dose clinical trial of TC-5214, the fixed dose clinical trials included in the Phase 3 development program do not result in the determination of an effective dose range for TC-5214 as an adjunct treatment for major depressive disorder, or if an effective dose range is determined but does not provide a safety margin that the FDA or foreign regulatory authorities determine to be sufficient, we and AstraZeneca may not obtain the regulatory approvals required to market and sell TC-5214, even if favorable results are obtained in the flexible dose clinical trials included in the Phase 3 development program.

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 and the ability of us and AstraZeneca to exclude third parties from marketing TC-5214 themselves 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 a new drug application, or 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 approved by the FDA. 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 re-authorized by the U.S. Congress. It is uncertain whether the statutory provision will be re-authorized. If we and AstraZeneca are unable to complete the Phase 3 development program for TC-5214 in time to submit an NDA for TC-5214 on or before September 30, 2012, whether because of delays that have been experienced in subject enrollment or for any other reason, 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 three years of exclusivity 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 designs, endpoints and outcomes of clinical trials that will be required to obtain regulatory approval of a drug to treat cognitive dysfunction in schizophrenia are uncertain, and we and, if AstraZeneca exercises its license right, AstraZeneca may never receive the regulatory approvals required to market and sell TC-5619 as a treatment for cognitive dysfunction in schizophrenia.

There is currently no product approved in the United States or Europe specifically for the treatment for cognitive dysfunction in schizophrenia. Accordingly, there is not a well-developed development path that, with clinical success, would be reasonably assured of receiving regulatory approval. If the FDA or any foreign regulatory authority determines that the designs or endpoints of any future clinical trials of TC-5619 as a treatment for cognitive dysfunction in schizophrenia that we or, if AstraZeneca exercises its license right, AstraZeneca conducts are not sufficient to support regulatory approval, we and, if AstraZeneca exercises its license, AstraZeneca would not receive the approval required to market and sell TC-5619 as a treatment for cognitive dysfunction in schizophrenia even if the outcomes from the trials are positive.

The positive findings in our completed Phase 2 trial of TC-5619 in cognitive dysfunction in schizophrenia may not be replicated in later clinical trials and, even if replicated, may not be sufficient to obtain required regulatory approvals.

In our completed Phase 2 trial of TC-5619 in cognitive dysfunction in schizophrenia, TC-5619 met the protocol criteria for a positive result on the primary efficacy outcome measure and positive signals were observed on some secondary efficacy outcome measures. However, TC-5619 did not demonstrate positive effects as to all of the trial's efficacy outcome measures and all evaluation dates and the results varied by geography and by whether patients used tobacco. Moreover, the favorable findings in the trial may not be replicated in any later clinical trials of TC-5619 as a treatment of cognitive dysfunction in schizophrenia that involve a large number of subjects and a long duration of dosing. If the favorable findings in the completed Phase 2 trial are not replicated in later clinical trials of TC-5619, we and, if AstraZeneca exercises its right to license TC-5619, AstraZeneca, will not obtain the regulatory approval required to market and sell TC-5619 as a treatment for cognitive dysfunction in schizophrenia.

If AstraZeneca determines to conduct additional development of AZD3480 as a treatment for ADHD but the favorable results of the completed Phase 2 clinical trial of AZD3480 in adults with ADHD are not replicated in future clinical trials, we and AstraZeneca will not obtain the regulatory approvals required to market and sell AZD3480 as a treatment for ADHD.

Whether AstraZeneca will decide to conduct any additional development of AZD3480 as a treatment for ADHD is uncertain in light of reservations about the adequacy of the therapeutic margin to support development across the broad ADHD patient population. Even if AstraZeneca determines to advance AZD3480 in ADHD, the

favorable results in the completed Phase 2 clinical trial of AZD3480 in adults with ADHD may not be replicated in later clinical trials. The completed Phase 2 clinical trial of AZD3480 in adults with ADHD was conducted at a single site with only 24 completed subjects and used a crossover trial design in which subjects received each treatment (5mg AZD3480, 50mg AZD3480 and placebo) and in each case for only two weeks. Because subjects received each treatment, each subject served as his or her own control. It is likely that, if there are future clinical trials of AZD3480 in adults with ADHD, they would be substantially larger, conducted at several sites and over a longer duration and use a parallel group design with placebo as a control such that each subject receives a particular dosing regimen of AZD3480 or placebo, but not both. It is possible that any of these differences or any other difference in trial design will impact the likelihood that the favorable results achieved in the completed Phase 2 clinical trial of AZD3480 in adults with ADHD would not be replicated in future clinical trials. If the favorable results achieved in the completed Phase 2 clinical trial of AZD3480 in adults with ADHD are not replicated, if future clinical trials otherwise do not establish the safety and efficacy of AZD3480 as a treatment for ADHD or if no further clinical trials of AZD3480 in ADHD are conducted, we and AstraZeneca will not obtain the regulatory approvals required to market and sell AZD3480 as a treatment for ADHD.

If AstraZeneca determines to conduct any additional development of AZD3480 as a treatment for ADHD and if the favorable results of the completed Phase 2 clinical trial of AZD3480 in adults with ADHD are not replicated in future clinical trials in children and adolescents, the commercial potential of AZD3480 would be materially and adversely affected.

If AstraZeneca determines to advance AZD3480 in ADHD, the results of the completed Phase 2 clinical trial of AZD3480 in adults with ADHD may not be predictive of results that would be obtained in any future clinical trials of AZD3480 in children or adolescents with ADHD. A drug that has positive effects in adults may not necessarily have positive effects in younger patients. Children with ADHD tend to exhibit more hyperactivity than do adults with ADHD, and it is possible that this or any other difference in the characteristics of the disorder between adults and children would cause the results of the completed Phase 2 clinical trial adults with ADHD to be not predictive of results obtained in future clinical trials in children or adolescents with ADHD, if conducted at all. Even if the favorable results in the completed Phase 2 clinical trial of AZD3480 in adults with ADHD are replicated in any future clinical trials of AZD3480 in adults with ADHD, if the results are not also replicated in any future clinical trials of AZD3480 in children or adolescents with ADHD, the FDA or applicable foreign regulatory authorities could limit the patient population for which AZD3480 is approved to adults. In that event, the commercial potential of AZD3480 would be materially and adversely affected.

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 or effective;
- 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 will 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. 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 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, ADHD, Alzheimer’s disease and cognitive dysfunction in schizophrenia. 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 candidates 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 third-party contractors to us or any applicable collaborator of ours 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 emphasis placed on ensuring a rigorous adherence to the trial protocol, the availability of effective treatments for the relevant disease and the eligibility criteria for the clinical trial. Delays in subject enrollment can result in increased costs and longer development times. The failure to enroll subjects in a clinical trial could delay the completion of the clinical trial beyond our current expectations. For example, in part due to initiatives that we and AstraZeneca implemented to assure that only patients meeting the criteria for initial and continued inclusion in the Phase 3 clinical trials of TC-5214 participate in the trials, we and AstraZeneca have experienced unexpected enrollment delays and enrollment for some of the Phase 3 clinical trials is tracking behind projections. We do not yet know whether the steps we and AstraZeneca have taken to address these enrollment delays will be successful.

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 applicable foreign regulatory authorities may require more preclinical or clinical data for any of our product candidates or more time to evaluate that data than we currently anticipate because drugs that act on NNRs are not a well established class of drugs, 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, in February 2008, the FDA issued a public health advisory with regard to Pfizer's aid to smoking cessation product, Chantix. In July 2009, the FDA announced that it would require each of Chantix and Zyban, which is GlaxoSmithKline's aid to smoking cessation product, to include a boxed warning on its prescribing information. The warning makes more 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. The warning also states that the health benefits of quitting smoking are immediate and substantial and that the risks of the drug should be weighed against the benefits of use. 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.

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.

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 causes adverse medical experiences or becomes associated with any third-party product that is associated with adverse medical experiences such as those 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.*" for Chantix, 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 and fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success.

Because we have 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, we may relinquish valuable rights to that product candidate through collaboration, licensing or other royalty arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights.

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

A key element of our strategy is to develop and commercialize drugs that selectively target specific NNR subtypes. 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 December 2009 collaboration with AstraZeneca.

We entered into our collaboration with AstraZeneca for TC-5214 in December 2009. We cannot predict the ultimate success of the collaboration. The collaboration 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. We and AstraZeneca have agreed on an initial development program for TC-5214 for major depressive disorder, but AstraZeneca has the authority to make changes to the initial program and also has decision-making authority for many other matters in our collaboration. In addition, AstraZeneca 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 time 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 initial development program of 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, the development and potential commercialization of TC-5214 would be delayed. This would result in a delay in 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.

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.

If AstraZeneca terminates our TC-5214 agreement at any time, for any reason, it would negatively impact our development of TC-5214 and materially harm our business and could accelerate our need for additional capital. In particular, we would have to fund any further clinical development and commercialization of TC-5214 on our own, 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 one or more 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.

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

If AstraZeneca exercises its right to license TC-5619, AstraZeneca would become generally responsible for conducting and funding substantially all future development and regulatory approval activities for TC-5619 and

have significant control over the conduct and timing of development efforts with respect to TC-5619, including whether to conduct Phase 2 development of TC-5619 as a treatment for Alzheimer's disease either alone or in addition to further development in either or both of cognitive dysfunction in schizophrenia and ADHD. If AstraZeneca were to fail to devote sufficient financial and other resources to the development of TC-5619, whether in favor of an internal product candidate or for any other reason, the development and potential commercialization of TC-5619 would be delayed. This would result in a delay in milestone payments and, if regulatory approval to market and sell TC-5619 is obtained, royalties that we could receive on any future TC-5619 product sales.

The successful development and commercialization of AZD3480 and AZD1446 depends substantially on our December 2005 collaboration with AstraZeneca, and AstraZeneca may decide not to conduct any further development of either or both of AZD3480 and AZD1446.

Our collaboration with AstraZeneca focused on cognitive disorders involves a complex allocation of rights, provides for milestone payments to us based on the achievement of specified development, regulatory and first commercial sale milestone events and provides us with royalty-based revenue if AZD3480, AZD1446 or another product candidate subject to the collaboration is successfully commercialized. AstraZeneca has decision-making authority for most matters in our collaboration, including, provided it meets its diligence obligations under the agreement, whether to proceed with further development and potential commercialization of any particular product candidate in the collaboration and, if so, for what indication(s). In particular, as long as AstraZeneca meets its diligence obligations under the agreement, AstraZeneca has decision-making authority with regard to whether to proceed with further development of either or both of AZD3480 in ADHD and AZD1446 in Alzheimer's disease, although we are exploring the practicability of conducting an additional clinical trial of AZD3480 in Alzheimer's disease and have agreed with AstraZeneca on respective roles and financial and non-financial responsibilities if we proceed to conduct such a study.

We are in discussions with AstraZeneca regarding potential additional development of AZD3480 as a treatment for ADHD. Whether AstraZeneca will decide to conduct additional development of AZD3480 in ADHD is uncertain in light of reservations about the adequacy of the therapeutic margin to support development across the broad ADHD patient population. In addition, AstraZeneca is currently considering whether to conduct further clinical development of AZD1446 as a treatment for Alzheimer's disease. If at any time AstraZeneca decides not to conduct further development of one 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 be permitted to conduct development of the affected product candidate(s) independently or with another collaborator and would not benefit from any commercial potential of the affected product candidate(s). An exception to this restriction is that we are entitled to conduct an additional clinical trial of AZD3480 in Alzheimer's disease. Even if we proceed to conduct an additional clinical trial of AZD3480 in Alzheimer's disease, whatever the outcome, AstraZeneca may decide not to conduct any further development of AZD3480 beyond our study, in which case we would likewise not benefit from any commercial potential of AZD3480.

If AstraZeneca decides to conduct further development of either or both of AZD3480 in ADHD and AZD1446 in Alzheimer's disease, AstraZeneca would have significant control and we would have little control over the conduct and timing of development efforts. 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 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. If AstraZeneca terminates our agreement at any time, for any reason, it may negatively impact the development of AZD3480 and AZD1446. In particular, we would have to fund any further clinical development and commercialization of AZD3480 and AZD1446 on our own, seek another collaborator or licensee for clinical development and commercialization or abandon the development and commercialization of AZD3480 and AZD1446.

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 for target indications for which our potential collaborator has particular expertise or that represent large primary care markets that must be served by large sales and marketing organizations. Our ability to generate revenue from our alliances and collaborations will depend on our collaborators' abilities to establish the safety and efficacy of our product candidates, to obtain regulatory approvals and to achieve market acceptance. Strategic alliances and collaborations involving our product candidates, including our 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, in late February 2011, we received from GlaxoSmithKline notice of termination of our alliance agreement.

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

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 a4ß2 NNR that we may in the future seek to exploit for any condition characterized by cognitive impairment for which AstraZeneca has development and commercialization rights under our agreement. We made such an offer with respect to TC-5619, which following a process under our agreement led to AstraZeneca's right to license TC-5619. However, if we do not offer a compound that meets pre-defined criteria for any NNR other than the a4ß2 NNR to AstraZeneca, we are generally not permitted to develop or commercialize the compound for any of these indications. 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 clinical trial, or to commercialize, a compound as an adjunct therapy for major depressive disorder. 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 with AstraZeneca 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, clinical trials and 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, 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 some cases such as the Phase 3 clinical program for TC-5214, 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. Language barriers and the limited experience of some clinical investigators in India 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, AZD1446 and, if it licenses TC-5619, TC-5619 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; 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.* may in some cases make it more difficult to obtain a patent, or to withstand a validity challenge to any issued patent, for pharmaceutical products that have a relationship to other pharmaceutical products, such as single enantiomers of a previously approved racemate like TC-5214, combination products or specific salt forms. 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 and we license patent rights from Cornerstone Therapeutics Inc. that cover the use of modulators of the a7 NNR to treat inflammatory disorders. 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 AstraZeneca (with respect to TC-5214) or any other present or future collaborator of ours to which we out-license patents rights that we have in-licensed from a third party or for any other reason, 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 there are at least two companies that are currently developing mecamylamine—AGI Therapeutics Ltd., which we believe is developing mecamylamine for chemotherapy-induced diarrhea, and Cary Pharmaceuticals Inc., which we believe is developing mecamylamine in a fixed dose combination with bupropion as a smoking cessation aid. In addition, mecamylamine is the active ingredient in our approved product Inversine, 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 be similarly sued by third parties. We may also become subject to interference or opposition proceedings conducted in the patent and trademark offices of various countries to determine our entitlement to patents. The defense and prosecution of intellectual property suits, interference proceedings and related legal and administrative proceedings, if necessary, would be costly and divert our technical and management personnel from conducting our business. Moreover, we may not prevail in any of these suits. An adverse determination of any litigation or proceeding could put our patents at risk of being invalidated or narrowly interpreted and our patent applications at risk of not being issued and could prevent us from protecting our rights, particularly in countries where the laws may not protect such rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that disclosure of some of our confidential information could be compelled and the information compromised. In addition, during the course of this kind of litigation, there could be public announcements of the results of hearings, motions or other interim proceedings or developments that, if perceived as negative by securities analysts or investors, could have a 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 infringed, unless we can obtain a license from the patent holder. Any necessary license may not be available on acceptable terms or at all, particularly if the third party is developing or marketing a product competitive with the infringing product. Even if we are able to obtain a license, the rights may be nonexclusive, which would give our competitors access to the same intellectual property.

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

Any successful infringement action brought against us may also 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 regulatory authorities in other countries.

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

We currently have limited sales, marketing and distribution experience and no internal sales or distribution capabilities. If we are unable to enter into alliances and collaborations or other arrangements with third parties to market and sell our product candidates or to develop our own internal marketing capability, 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 with sales and distribution characteristics requiring a large sales force. There are risks involved with establishing our own sales force and marketing and distribution capabilities, as well as in entering into arrangements with third parties to perform these services. Developing our own sales force would be expensive and time-consuming and could delay any product launch. We may not be successful in entering into arrangements with third parties on terms that are favorable to us or at all. Also, we have little control over AstraZeneca and would have little control over such other third parties, 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 that is successfully developed will also depend in part on the extent to which coverage and adequate payment is available from government health administration authorities, 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 to the patient 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, as amended by the Health Care and Education Affordability Reconciliation Act, or the Healthcare Reform Act, was enacted in 2010. This law substantially changes the way health care is financed by both governmental and private insurers. The Healthcare Reform Act contains a number of provisions that are expected to impact our business and operations, some of which in ways we cannot currently predict, including those governing enrollment in federal healthcare programs, reimbursement changes and fraud and abuse, which will impact existing government healthcare programs and will result in the development of new programs.

Additional provisions of the Healthcare Reform Act, may negatively affect our potential revenues in the future. For example, the Healthcare Reform Act imposes a non-deductible excise tax on pharmaceutical manufacturers or importers that sell branded prescription drugs to U.S. government programs, which we believe

will increase the cost of any of our product candidates that receives regulatory approval. In addition, as part of the Healthcare Reform Act's provisions closing a funding gap that currently exists in the Medicare Part D prescription drug program (commonly known as the "donut hole"), we will also be required to provide a 50% discount on branded prescription drugs sold to beneficiaries who fall within the donut hole.

Beyond the Healthcare Reform Act, there have been a number of 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, which became effective in February 2009, provides funding for the federal government to compare the effectiveness of different treatments for the same illness. While the specific effects that the Healthcare Reform Act, implementing regulations, the American Recovery and Reinvestment Act of 2009 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 or a decision by a third-party payor to not cover any of our product candidates that is successfully developed could reduce prescriptions by physicians of the product candidate and have 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, with a compound in Phase 2 development for Alzheimer's disease, and Abbott Laboratories, with one compound in Phase 2 development for ADHD and a second compound in Phase 1 development for cognitive disorders. Other companies that we believe have active NNR-based programs include AstraZeneca, Eli Lilly, Sanofi-Aventis, Bristol-Myers Squibb, GlaxoSmithKline, Johnson & Johnson, Novartis, NeuroSearch A/S, Solvay, Servier, CoMentis, EnVivo Pharmaceuticals, Xytis, Galantos Pharma, Proximagen, Psychogenics, AGI Therapeutics, 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 enter the CNS market, 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 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 Clinical Data (under agreement to be acquired by Forest Laboratories);
- for ADHD, stimulants such as Adderall XR and Vyanase from Shire, Concerta from Johnson & Johnson and Ritalin LA from Novartis, and Strattera, a non-stimulant acting as a norepinephrine reuptake inhibitor, from Eli Lilly;
- for mild to moderate Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer/Eisai, Razadyne from Johnson & Johnson and Exelon from Novartis; in addition, Namenda from Forest Laboratories, which acts by regulating the neurotransmitter glutamate, is marketed for moderate to severe Alzheimer's disease;
- for 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; and

- 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.

There is currently no approved product for cognitive dysfunction in schizophrenia. There are however multiple third-party product candidates currently in clinical development for cognitive dysfunction in schizophrenia, including at least one modulator 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 or eventual adjudication, could be costly and significantly divert management's attention from conducting our business or materially and adversely affect our reputation and the demand for our products.

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

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

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

If any promotional activities that we undertake fail to comply with the regulations and guidelines of the FDA and 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 similar regulatory authorities in other countries. Regulatory authorities generally do not regulate the behavior of physicians in their choice of treatments. Regulatory authorities do, however, restrict communications on the subject of off-label use. Companies cannot actively promote approved drugs for off-label uses but may in some jurisdictions and under specified conditions disseminate articles published in peer-reviewed journals that discuss off-label uses of approved products to physicians. To the extent allowed, we may in the future disseminate peer-reviewed articles on our products to physicians. 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 and Managing Growth

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

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

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

We may encounter difficulties in managing our growth, which could have a material adverse effect on our business.

The number of our employees and the scope of our operations have grown over the last several years. Any continued growth could place a significant strain on our managerial, operational and financial resources. To manage our growth, we must continue to implement and improve our managerial, operational and financial systems and controls and reporting processes and procedures. We may not be able to manage our growth effectively. Moreover, if our existing systems and internal controls over financial reporting are not implemented properly or are not adequate, we could be exposed to an increased risk of incurring financial or accounting irregularities or fraud, which would cause our stock price to suffer.

Risks Related to Our Common Stock

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

We expect that the trading price of our common stock is likely to be highly volatile in response to factors that are beyond our control. The stock market in general has experienced extreme price and volume fluctuations. The market prices of securities of pharmaceutical, biopharmaceutical and biotechnology companies have been extremely volatile and have experienced fluctuations that have often been unrelated or disproportionate to 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;

- whether AstraZeneca exercises its right to license TC-5619;
- whether and to what extent AstraZeneca determines to continue clinical development of one or both of AZD3480 or AZD1446 and, if so, milestone events are achieved under our cognitive disorders agreement with AstraZeneca;
- whether we proceed with an additional clinical trial of AZD3480 in Alzheimer's disease;
- the scope, progress, duration, results and cost of clinical trials, as well as non-clinical studies and assessments, of 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 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;
- our ability to establish strategic alliances, collaborations and licensing or other arrangements on terms favorable to us;
- whether we pursue and complete any in-licensing, merger and acquisition and other business combination or corporate partnering opportunities and, if so, the terms of any transaction;
- the cost, timing and outcomes of regulatory approvals or other regulatory actions;
- the number and characteristics of product candidates that we pursue;
- general and industry-specific economic conditions that may affect the research and development expenditures of AstraZeneca or any of our potential future collaborators;
- the expiration or termination of agreements with AstraZeneca or any potential future collaborator, or the execution of new agreements; and
- general conditions in the pharmaceutical, biopharmaceutical or biotechnology industries or in the U.S. or global credit or financial markets.

Due to fluctuations in our operating results, a period-to-period comparison of our results of operations may not be a good indication of our future performance. 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.

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

Our executive officers, directors and 10% or greater stockholders beneficially own or control approximately 42% of the outstanding shares of our common stock, based on the shares outstanding as of February 28, 2011. Accordingly, our executive officers and directors and these principal stockholders have substantial control over the outcome of corporate actions requiring stockholder approval, including the election of directors, any merger, consolidation or sale of all or substantially all of our assets or any other significant corporate transactions, as well as our management and affairs. The concentration of ownership may also delay or prevent a change of control of us at a premium price if these stockholders oppose it, even if it would benefit our other stockholders.

Provisions of our collaboration agreements with AstraZeneca and provisions of our charter, bylaws and 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 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 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 be elected at one time;
- authorize our board of directors to issue without stockholder approval blank check preferred stock that, if issued, could operate as a “poison pill” to dilute the stock ownership of a potential hostile acquirer 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 have a renewal option for an additional five-year term at a rental rate to be mutually determined between us and the landlord. 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. (Removed and Reserved).

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:

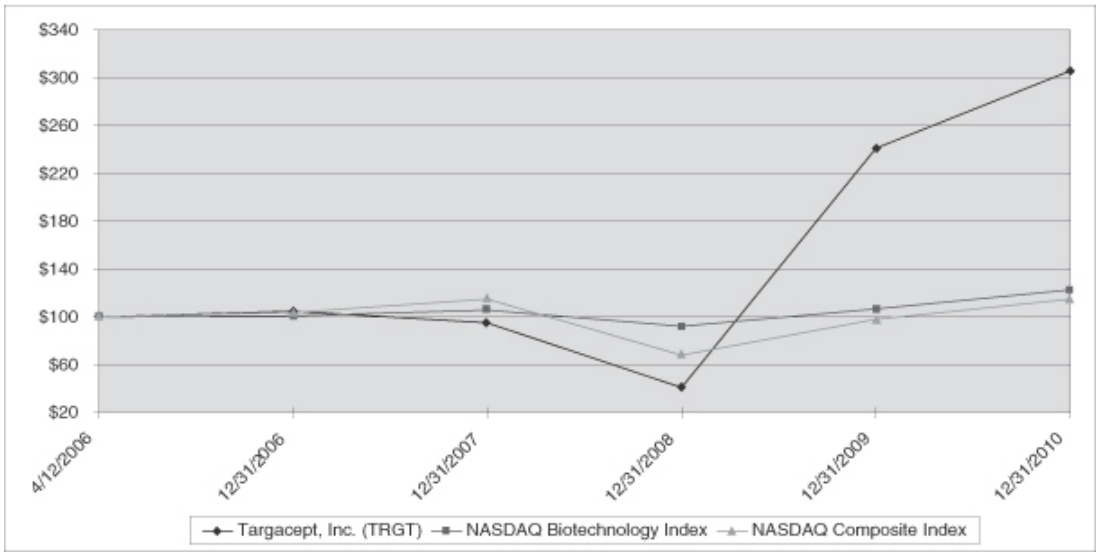
	Common Stock	
	High	*Low*
2009:		
First Quarter	$ 3.94	$ 2.00
Second Quarter	$ 4.17	$ 2.26
Third Quarter	$21.84	$ 2.00
Fourth Quarter	$24.50	$17.59
2010:		
First Quarter	$21.35	$18.29
Second Quarter	$25.00	$19.25
Third Quarter	$23.59	$17.80
Fourth Quarter	$27.65	$20.50

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 April 12, 2006 (the date our common stock was first publicly traded) in each of our common stock, the NASDAQ Composite Index and the NASDAQ Biotechnology Index and the reinvestment of any dividends. We have not paid any dividends on our common stock and do not include dividends in the representation of our performance. The performance shown for any prior period does not predict the performance to be expected for the current period or any future period.

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



	Cumulative Total Return					
	4/12/06	12/31/06	12/31/07	12/30/08	12/30/09	12/31/10
Targacept, Inc.	100	105	95	41	241	306
NASDAQ Biotechnology Index	100	101	106	92	107	123
NASDAQ Composite Index	100	104	115	68	98	115

Stockholders

As of February 28, 2011, there were approximately 57 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 28, 2011, 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 3,075.

Dividends

We have never declared or paid cash dividends on any of our shares of capital stock. We currently intend to retain future earnings, if any, to finance the expansion and growth of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion

of our board of directors and will depend on our financial condition, results of operations, capital requirements and other factors that our board of directors deems relevant. In addition, the terms of any future debt or credit facility may preclude us from paying dividends.

Calculation of Aggregate Market Value of Non-Affiliate Shares

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

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

None.

Item 6. Selected Financial Data.

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

We derived the statements of operations data for the years ended December 31, 2010, 2009, and 2008 and the balance sheet data as of December 31, 2010 and 2009 from our audited financial statements included in this annual report. We derived the statements of operations data for the years ended December 31, 2007 and 2006 and the balance sheet data as of December 31, 2008, 2007, and 2006 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,				
	2010	2009	2008	2007	2006
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Net operating revenues	$ 85,713	$ 25,062	$ 20,085	$ 11,576	$ 27,537
Operating expenses:					
Research and development	64,546	40,179	40,981	34,620	21,788
General and administrative	8,052	8,167	6,499	8,013	5,696
License fees and royalties	—	16,350	—	—	—
Cost of product sales	—	691	749	715	457
Total operating expenses	72,598	65,387	48,229	43,348	27,941
Income (loss) from operations	13,115	(40,325)	(28,144)	(31,772)	(404)
Interest and dividend income	1,463	1,050	2,734	3,837	2,584
Interest expense	(153)	(217)	(251)	(138)	(83)
Income (loss) before income taxes	14,425	(39,492)	(25,661)	(28,073)	2,097
Income tax (expense) benefit	(3,526)	88	—	—	—
Preferred stock accretion	—	—	—	—	(3,333)
Net income (loss) attributable to common stockholders	$ 10,899	$ (39,404)	$ (25,661)	$ (28,073)	$ (1,236)
Basic net income (loss) attributable to common stockholders per share	$ 0.38	$ (1.54)	$ (1.04)	$ (1.42)	$ (0.09)
Diluted net income (loss) attributable to common stockholders per share	$ 0.36	$ (1.54)	$ (1.04)	$ (1.42)	$ (0.09)
Weighted average common shares outstanding—basic	28,543,408	25,636,419	24,664,169	19,720,732	13,595,523
Weighted average common shares outstanding—diluted	30,150,324	25,636,419	24,664,169	19,720,732	13,595,523

	As of December 31,				
	2010	2009	2008	2007	2006
			(in thousands)		
Balance Sheet Data:					
Cash, cash equivalents and investments	$ 252,509	$ 111,066	$ 88,363	$ 87,040	$ 54,190
Working capital	119,422	213,269	78,174	77,217	69,903
Total assets	262,787	319,379	98,551	98,965	81,368
Long-term debt, net of current portion	1,349	1,966	3,408	1,686	816
Accumulated deficit	(218,401)	(229,300)	(189,896)	(164,235)	(136,162)
Total stockholders' equity	91,847	68,991	57,373	51,584	64,999

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes included in this annual report. In addition to historical information, the following discussion contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results, performance or experience could differ materially from those indicated by any forward-looking statement due to various important factors, risks and uncertainties, including, but not limited to, those set forth under "Cautionary Note Regarding Forward-Looking Statements," 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, AZD3480 (TC-1734), AZD1446 (TC-6683) and TC-6987, 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, we and AstraZeneca have jointly designed an initial program that includes development of TC-5214 as an adjunct therapy and as a "switch" monotherapy, in each case in patients with major depressive disorder, or MDD, who do not respond adequately to initial antidepressant treatment. AstraZeneca is responsible for 80% and we are responsible for 20% of the cost of the initial 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 initial 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 initial 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 initial 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 global commercialization of TC-5214.

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;
- we conducted and funded the development of TC-5619 to date; AstraZeneca has the right to license TC-5619 and, if it exercises its right, would assume responsibility for and fund all future development (except for completion of our ongoing studies) and commercialization of TC-5619;
- 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 exploring the practicability of conducting an additional clinical trial of AZD3480 in Alzheimer's disease and have agreed with AstraZeneca on respective roles and financial and

non-financial responsibilities for such a study; we have received $500,000 and, if an Alzheimer's disease study proceeds, we would be responsible for funding the study but would be entitled to receive up to $5.7 million in additional payments from AstraZeneca, with the last tranche being payable upon first dosing in the United States and Europe; 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 services rendered in the preclinical research collaboration.

In addition to our two collaboration agreements with AstraZeneca, we entered into a product development and commercialization agreement with GlaxoSmithKline in July 2007 that was designed to discover, develop and market product candidates that selectively target specified NNR subtypes in five therapeutic focus areas. In late February 2011, we received notice of termination of the agreement from GlaxoSmithKline. By the terms of the agreement, the termination becomes effective in late 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 RJR. In August 2000, we became an independent company when we issued and sold stock to venture capital investors. Since our inception, we have had limited revenue from product sales and have funded our operations principally through the sale of equity securities, revenue from collaboration agreements, grants and equipment and building lease incentive financing. We have devoted substantially all of our resources to the discovery and development of our product candidates and technologies, including the design, conduct and management of preclinical and clinical studies and related manufacturing, regulatory and clinical affairs, as well as intellectual property prosecution.

We generated net income for the year ended December 31, 2010, and for three quarterly periods within the year, due primarily to recognition into revenue of a portion of the upfront payment received under our TC-5214 agreement with AstraZeneca. We also generated net income for two other quarterly periods since inception, in each case due primarily to the achievement in each period of a single milestone event related to AZD3480 under our cognitive disorders agreement with AstraZeneca. Except for these periods, we have never been profitable and 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. As of December 31, 2010, we had an accumulated deficit of $218.4 million. Clinical trials and preclinical studies are 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 submission of an NDA to the FDA. As of December 31, 2010, we had $127.0 million of the upfront payment remaining to be recognized into revenue. We are eligible under our TC-5214 agreement with AstraZeneca 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.

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 are recognizing into revenue on a straight-line basis over the estimated period of our research and development obligations related to TC-5619. Pursuant to a September 2010 amendment to our cognitive disorders agreement with AstraZeneca related to a potential additional clinical trial of AZD3480 in Alzheimer's disease, we received an additional $500,000 payment in October 2010, 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 potential study.

As of December 31, 2010, we had received $82.6 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 deferred recognition of an aggregate of $21.5 million of the amounts received under our cognitive disorders agreement with AstraZeneca and are recognizing these deferred amounts into revenue over the periods discussed in Note 12 to our audited financial statements for the year ended December 31, 2010 included in this annual report. As of December 31, 2010, we had $7.0 million of amounts received under our cognitive disorders agreement with AstraZeneca remaining to be recognized into revenue.

As of December 31, 2010, we had also received $45.0 million in aggregate payments under our alliance agreement with GlaxoSmithKline, of which we initially deferred recognition of $29.5 million that we were recognizing into revenue over the period discussed in Note 12 to our audited financial statements for the year ended December 31, 2010 included in this annual report. As a result of our receipt in late February 2011 of notice of termination of the agreement, we expect to recognize the remaining $18.4 million into revenue in the first quarter of 2011.

Under our cognitive disorders agreement with AstraZeneca, we are eligible to receive other payments of up to $103.0 million, if development, regulatory and first commercial sale milestone events for AZD3480 are achieved only for ADHD, up to $145.0 million if we proceed with another Alzheimer's disease study of AZD3480, AstraZeneca subsequently advances AZD3480 into later-stage development for Alzheimer's disease and development, regulatory and first commercial sale milestone events are achieved for Alzheimer's disease, and up to $197.0 million if both ADHD and Alzheimer's disease are successfully pursued. If AZD3480 is developed for an indication in addition to Alzheimer's disease and ADHD, 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.

With regard to AZD1446, we are eligible under our cognitive disorders agreement with AstraZeneca to receive payments of up to $73.0 million, if development, regulatory and first commercial sale milestones are achieved only for Alzheimer's disease, as well as 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 $35.0 million for each such indication, if development, regulatory, first commercial sale and first detail milestone events are achieved.

In addition, if AstraZeneca licenses TC-5619, our cognitive disorders agreement with AstraZeneca provides for AstraZeneca to make a $30.0 million payment to us and to assume responsibility for and fund all future development (except for completion of our ongoing studies) and commercialization. In that event, we would be eligible to receive additional payments of up to $212.0 million, if development, regulatory, first commercial sale and first detail milestones are achieved for three indications, as well as stepped double-digit royalties on any future TC-5619 product sales.

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 Inversine. Sales of Inversine generated net revenue of $473,000 and $718,000 for the years ended December 31, 2009 and 2008, respectively.

From time to time we seek and are awarded grants or work to be performed under grants awarded to third-party collaborators from which we derive revenue. As of December 31, 2010 we have been awarded two grants from The Michael J. Fox Foundation for Parkinson's Research, or MJFF. One of the grants is to fund preclinical research involving the use of compounds that modulate NNRs to address Levodopa-induced abnormal involuntary movements, known as dyskinesias, and we have received aggregate payments of $641,000 from MJFF since August 2009 in connection with this grant. The other grant is to fund research to identify NNR-related biomarkers relevant to Parkinson's disease, and we have received an aggregate of $304,000 from MJFF in connection with this grant. In addition, as of December 31, 2010, 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%, 61% and 85% of our total operating expenses for the years ended December 31, 2010, 2009, and 2008, 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 2010 and 2008 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 initial 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 that are in development. Our current and future expenditures on preclinical and clinical development programs are subject to numerous uncertainties in timing and cost to completion. We 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 AstraZeneca will exercise its option to license TC-5619, whether any of our product candidates will be subject to future alliances or collaborations or how any such arrangements would affect our development plans or capital requirements. Because of this uncertainty, and because of the numerous uncertainties related to clinical trials and related activities as described above, we are unable to determine the duration and completion costs of our research and development programs or whether or when we will generate revenue from the commercialization and sale of any of our product candidates in development.

General and Administrative Expenses

General and administrative expenses consist principally of salaries and other related costs for personnel in executive, finance, 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 incurred net operating losses through December 31, 2009 and have not paid federal, state or foreign income taxes for any period through December 31, 2009. For the year ended December 31, 2010, we recognized $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, 2010, we had net operating loss carryforwards of $39.0 million for federal income tax purposes and $76.2 million for state income tax purposes. We also had research and development income tax credit carryforwards of $9.6 million for federal income tax purposes and $1.0 million for state income tax purposes as of December 31, 2010. The federal net operating loss carryforwards begin to expire in 2021. The state net operating loss carryforwards begin to expire in 2016. 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 because it is uncertain whether we will be eligible to use or 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 agency-backed certificates, corporate debt securities that are rated at least A quality or equivalent and certificates of deposits. Our investments in marketable securities of $86.7 million at December 31, 2010 are recorded at quoted market prices.

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

Critical Accounting Policies and Estimates

Our management’s discussion and analysis of our financial condition and results of operations are based on our 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, 2010 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: upfront fees, which may include initial payments upon commencement of the contractual relationship, payment representing a common stock purchase premium or payment to secure a right for a future license; research fees for ongoing research and development; payments associated with the achievement of discovery, development, regulatory and commercial milestone events; and rights to receive royalties based on specified percentages of any net product sales. In determining the accounting for collaboration and alliance agreements, we 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 stand-alone basis and there is objective and reliable evidence of that fair value, we treat the deliverable as a separate unit of accounting. If an agreement does not have multiple deliverables that meet these criteria, we consider the agreement to have one unit of accounting. If an agreement involves separate units of accounting, we then determine how to allocate amounts received under the agreement among the separate units, based on the respective fair value of each unit and the revenue recognition applicable to each unit. If an agreement involves a single unit of accounting, 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 over the estimated development period for the applicable licensed product candidate(s). The period over which we recognize the revenue may be adjusted from time to time to take into account any delays or acceleration in the development of the applicable product candidate or any extension or shortening of the applicable performance period. Any such delay or acceleration in the development of a product candidate, or extension or shortening of a performance period, could result in further deferral of revenue or acceleration in the recognition of deferred revenue. As of December 31, 2010, all amounts that we have received from AstraZeneca and GlaxoSmithKline are non-refundable.

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

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

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

If any of these conditions are not met, we 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.

Under our TC-5214 agreement with AstraZeneca, we received an upfront payment of $200.0 million. We recorded such amount as deferred revenue and commenced in December 2009 recognizing the payment ratably over the estimated development period for TC-5214 to submission of an NDA to the FDA.

We have received various payments under our cognitive disorders agreement with AstraZeneca as discussed below.

- We received an initial fee of $10.0 million in February 2006. Based on the agreement terms and consideration of fair value, we allocated $5.0 million of the initial fee to the preclinical research collaboration. Upon effectiveness of the agreement in January 2006, we commenced recognizing the $5.0 million as revenue over the planned four-year term of the research collaboration. We deferred recognition of the remaining $5.0 million of the initial fee, which we allocated to the AZD3480 license grants, until AstraZeneca made its determination in December 2006 to proceed with further development of AZD3480. Beginning in January 2007, we commenced recognizing the previously deferred $5.0 million of the initial fee ratably over the expected remaining development period for AZD3480.
- We received a $2.0 million payment from AstraZeneca in November 2007 to secure the right to license TC-5619 following our completion of an agreed development plan. Beginning in November 2007, we commenced recognizing the $2.0 million payment ratably over the estimated period of our research and development obligations for TC-5619.
- We received an $11.0 million payment from AstraZeneca in May 2010 in connection with an amendment to the agreement to modify the terms applicable to TC-5619. In conjunction with the amendment, we and AstraZeneca agreed to an expanded development program for TC-5619 and AstraZeneca maintained its option to license TC-5619. Beginning in May 2010, we commenced recognizing the $11.0 million payment ratably over the estimated period of our research and development obligations for TC-5619.
- We received a $500,000 payment from AstraZeneca in October 2010 in connection with an amendment to the agreement to provide for a potential additional clinical trial of AZD3480 in Alzheimer’s disease. Beginning in October 2010, we commenced recognizing the $500,000 payment ratably over the estimated period of our performance obligations with respect to the potential study.
- We received cumulative research fees of $26.5 million since inception of the agreement. We recognized all of these fees as the research was performed and related expenses were incurred.
- We received payments from AstraZeneca upon achievement of milestone events related to the development of product candidates in the aggregate amount of $34.6 million since inception of the agreement. We recognized the full amount of each payment as revenue upon achievement of the corresponding milestone event because the event met each of the conditions required for immediate recognition under our revenue recognition policy.

We have also received various payments under our alliance agreement and related stock purchase agreement with GlaxoSmithKline.

- GlaxoSmithKline made an initial payment to us of $20.0 million and purchased 1,275,502 shares of our common stock for an aggregate purchase price of $15.0 million, which resulted in an aggregate deemed premium of $3.5 million based on the closing price of our common stock on the trading day immediately preceding the date that the alliance was announced. In July 2007, we commenced recognizing the initial payment and deemed premium as revenue on a straight-line basis over the estimated period of our research and early development performance obligations under the agreement.
- In December 2007, we initiated a Phase 1 clinical trial of a product candidate that had been in development for pain, triggering a $6.0 million milestone payment to us from GlaxoSmithKline. We determined the milestone payment did not meet all of the conditions required for immediate revenue recognition. Specifically, based on the status of development of the applicable product candidate as of the inception of the agreement, we determined that achievement of the milestone event was reasonably assured. Consequently, we recorded the $6.0 million payment as deferred revenue and, in December 2007, commenced recognizing such amount on a straight-line basis over the estimated period of our research and early development performance obligations under the agreement.

- We received cumulative payments of $4.0 million from GlaxoSmithKline upon achievement of milestone events under the alliance agreement since inception of the agreement. We recognized the full amount of each payment as revenue upon achievement of the milestone event because the event met each of the conditions required for immediate recognition under our revenue recognition policy.

As a result of our receipt in late February 2011 of notice of termination of the alliance agreement, we expect to recognize into revenue in the first quarter of 2011 $18.4 million in deferred amounts received under the alliance agreement and remaining to be recognized as of December 31, 2010.

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 $4.9 million for the year ended December 31, 2010, $2.5 million for the year ended December 31, 2009 and $2.1 million for the year ended December 31, 2008. As of December 31, 2010, we had $11.0 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, 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 primarily 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 the April 2010 amendment to our cognitive disorders agreement with AstraZeneca, partially offset by the achievement for 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 alliance agreement and $1.1 million in license fees derived from the cognitive disorders agreement as a result of the expiration of the term of the preclinical research collaboration in January 2010.

The increase in grant revenue 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 resulted from the completion of the preclinical research collaboration under the cognitive disorders agreement with AstraZeneca.

In future periods, we are eligible to receive additional license fees and milestone payments under our agreements with AstraZeneca. The amount of license fees and milestone fees will depend on the timing and achievement of the discovery, development, regulatory and commercial milestone events and whether AstraZeneca exercises its right to license TC-5619. It is uncertain whether we will achieve any particular milestone event in 2011, in any future period or at all. We expect that the amount of our milestone-based revenue may vary from period to period.

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 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 ongoing 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 and was primarily due to a significantly higher fair value calculated for stock options granted during 2010 as compared to the fair value calculated for prior stock option grants;
- 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
- a $1.5 million upfront payment that we made to Cornerstone Therapeutics Inc. during 2010 under an exclusive license agreement.

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

We expect our research and development expenses for the year ending December 31, 2011 to increase, with the largest component anticipated to result from our obligation under our TC-5214 agreement with AstraZeneca to fund a portion of the costs of the initial development program for TC-5214.

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 fair value calculated for stock options granted during 2010 as compared to the fair value calculated for prior stock option grants.

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 the $10.0 million milestone payment received under our cognitive disorders agreement with AstraZeneca based on the achievement of the objective in the completed Phase 2 clinical trial of AZD3480 in adults with ADHD.

Cost of Product Sales

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

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

Interest Income and Interest Expense

	Year ended December 31,		
	2010	2009	Change
		(in thousands)	
Interest income	$1,463	$1,050	$ 413
Interest expense	153	217	(64)

Interest income for the year ended December 31, 2010 increased by $413,000 as compared to the year ended December 31, 2009. The increase was primarily attributable to significantly increased cash and investment balances, partially offset by lower short-term interest rates.

Interest expense for the year ended December 31, 2010 decreased by $64,000 as compared to the year ended December 31, 2009. The decrease was attributable to lower average interest rates and principal balances under loan facilities used to finance equipment, furnishings, software and other fixed assets.

Years ended December 31, 2009 and December 31, 2008

Net Operating Revenues

	Year ended December 31, 2009	2008	Change
		(in thousands)	
Operating revenues:			
Collaboration research and development	$ 5,246	$ 8,967	$(3,721)
Milestones and license fees from collaborations	18,934	10,179	8,755
Product sales, net	473	718	(245)
Grant revenue	409	221	188
Net operating revenues	$25,062	$20,085	$ 4,977

Net operating revenues for the year ended December 31, 2009 increased by $5.0 million as compared to the year ended December 31, 2008. The higher net operating revenues were primarily attributable to an increase of $8.8 million in milestones and license fees from collaborations, partially offset by a decrease of $3.7 million in collaboration research and development revenue. The increase in milestones and license fees from collaborations was principally attributable to the $10.0 million payment received under our cognitive disorders agreement with AstraZeneca based on the achievement of the objective in the completed Phase 2 clinical trial of AZD3480 in adults with ADHD and recognition of $398,000 of the upfront payment received under our TC-5214 agreement with AstraZeneca. These increases were partially offset by a decrease of $1.0 million in payments received based on the achievement of preclinical milestone events under our cognitive disorders agreement with AstraZeneca and our alliance agreement with GlaxoSmithKline and our recognition of less deferred license fee revenue for 2009 as a result of an extension of the estimated remaining development period for AZD3480 and an extension of the estimated period of our research and development obligations for TC-5619.

The decrease in collaboration research and development revenue for the year ended December 31, 2009 reflected reduced services rendered by us in our preclinical research collaboration with AstraZeneca as a result of progress that had previously been made toward meeting the objectives of the research plan. All of our collaboration research and development revenue for 2009 and 2008 was derived from our preclinical research collaboration with AstraZeneca. The preclinical research collaboration expired in January 2010.

Net product sales for the year ended December 31, 2009 decreased by $245,000 as compared to the year ended December 31, 2008 primarily as a result of our discontinuation of Inversine effective as of September 30, 2009. Grant revenue for the year ended December 31, 2009 increased by $188,000 as compared to the year ended December 31, 2008. The higher grant revenue was primarily due to recognition of $147,000 of the amounts awarded by MJFF.

Research and Development Expenses

	Year ended December 31, 2009	2008	Change
		(in thousands)	
Research and development expenses	$40,179	$40,981	$ (802)

Research and development expenses for the year ended December 31, 2009 decreased by $802,000 as compared to the year ended December 31, 2008. The lower research and development expenses were primarily attributable to a decrease of $908,000 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

$10.3 million for 2009, from $11.2 million for 2008. This decrease in third-party research and development costs for our clinical-stage product candidates was partially offset by an increase of $310,000 in costs incurred for third-party research and development services in connection with our preclinical programs.

The costs that we incurred for the years ended December 31, 2009 and 2008 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,		
	2009	2008	Change
		(in thousands)	
TC-5214	$ 5,527	$ 4,826	$ 701
TC-5619	2,585	3,151	(566)
TC-6987	1,752	78	1,674
TC-6499	210	2,291	(2,081)
AZD3480	217	322	(105)
AZD1446	—	—	—
	$10,291	$10,668	$ (377)

The table above does not include costs incurred for TC-2216, a compound that we are not currently progressing. For the years ended December 31, 2009 and 2008, we incurred $11,000 and $549,000, respectively, in expenses for third-party research and development services in connection with TC-2216.

General and Administrative Expenses

	Year ended December 31,		
	2009	2008	Change
		(in thousands)	
General and administrative expenses	$8,167	$6,499	$1,668

General and administrative expenses for the year ended December 31, 2009 increased by $1.7 million as compared to the year ended December 31, 2008. The higher general and administrative expenses were principally attributable to increased employee compensation and related expenses, primarily as a result of special bonuses paid to employees in December 2009, and increased legal and professional fees associated with our TC-5214 agreement with AstraZeneca.

License Fees

	Year ended December 31,		
	2009	2008	Change
		(in thousands)	
License fees and royalties	$16,350	—	$16,350

License fees for the year ended December 31, 2009 increased by $16.4 million as compared to the year ended December 31, 2008. 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 the $10.0 million milestone payment received under our cognitive disorders agreement with AstraZeneca.

Cost of Product Sales

	Year ended December 31, 2009	2008	Change
		(in thousands)	
Cost of product sales	$691	$749	$ (58)

Our cost of product sales are those costs related directly to the sale of Inversine. Cost of product sales for the year ended December 31, 2009 decreased by $58,000 as compared to the year ended December 31, 2008. The decrease was primarily attributable to our discontinuation of Inversine effective as of September 30, 2009.

Interest Income and Interest Expense

	Year ended December 31, 2009	2008	Change
		(in thousands)	
Interest income	$1,050	$2,734	$(1,684)
Interest expense	217	251	(34)

Interest income for the year ended December 31, 2009 decreased by $1.7 million as compared to the year ended December 31, 2008. The decrease was primarily attributable to lower short-term interest rates.

Interest expense for the year ended December 31, 2009 decreased by $34,000 as compared to the year ended December 31, 2008. The decrease was attributable to lower average principal balances under loan facilities used to finance equipment, furnishings, software and other fixed assets.

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 under collaborations and alliances, including upfront fees received, payments received for research and development services and payments received upon achievement of milestone events, equipment and building lease incentive financing, government grants and interest income. We discontinued our only approved product, Inversine, effective as of September 30, 2009. The net contribution from Inversine sales has not historically been a significant source of cash.

Our cash, cash equivalents and investments were $252.5 million as of December 31, 2010 and $111.1 million as of December 31, 2009. As of December 31, 2010, we had $147.3 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, which we do not expect to use to fund our short-term liquidity requirements, was invested as of December 31, 2010 in U.S. Treasury notes and bonds, U.S. and state agency-backed certificates, corporate debt securities that are rated at least A quality or equivalent and certificates of deposit.

Strategic Alliances and Collaborations

In May 2010, we received an $11.0 million payment from AstraZeneca in connection with a separate amendment to our cognitive disorders agreement with AstraZeneca to modify the terms applicable to TC-5619. In July 2009, we received a $10.0 million payment from AstraZeneca as a result of the achievement of the objective in the completed Phase 2 trial of AZD3480 in adults with ADHD, a milestone event under an amendment to our cognitive disorders agreement. From 2008 through 2010, we received cumulative payments of

$2.6 million from AstraZeneca upon achievement of milestone events under our cognitive disorders agreement related to the development of AZD1446 and other product candidates arising under the preclinical research collaboration conducted under the agreement. As of December 31, 2010, we had received $56.1 million in aggregate upfront fees and milestone payments under our cognitive disorders agreement with AstraZeneca and had recognized an additional $26.5 million in collaboration research and development revenue for research services that we provided in the preclinical research collaboration.

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 related stock purchase agreement with GlaxoSmithKline. As of December 31, 2010, we had received $45.0 million in aggregate payments from GlaxoSmithKline under the agreements. We received notice of termination of the product development and commercialization agreement from GlaxoSmithKline in late February 2011, and the agreement will no longer be 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, AZD1446, and, if AstraZeneca licenses TC-5619, TC-5619. There is no assurance that we will achieve any particular milestone event in 2011, in any future period or at all.

Stock Offerings

In October 2009 and January 2008, we completed public offerings of our common stock. The October 2009 offering consisted of 2.2 million shares at a price of $21.00 per share and, after deducting underwriting discounts and commissions and offering expenses payable by us, our net proceeds from the offering were $44.4 million. The January 2008 offering consisted of 4.4 million shares at a price of $7.07 per share and, after deducting underwriting discounts and commissions and offering expenses payable by us, our net proceeds from the offering were $29.1 million. Taken together with our initial public offering in April 2006, we have derived aggregate net proceeds of $114.3 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.

Loan Financing

In July 2010, we entered into a loan agreement with a bank that provides aggregate borrowing capacity of $4.0 million to be provided in up to three individual term loans that we may take 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 this loan facility at a fixed interest rate of 3.4% per annum. We were obligated only to pay interest through the remainder of 2010. Beginning January 1, 2011 and continuing through the maturity date of December 1, 2014, the loan is repayable in equal monthly installments of $28,000. We granted to the bank a first priority security interest in the assets acquired with the proceeds of the loan. Any future loan under the facility would, at our discretion on a loan-by-loan basis, bear interest at either a variable rate equal to the thirty-day LIBOR plus 2.15%, adjusted monthly on the first day of each month, or a fixed rate

equal to the bank's fixed rate cost of funds index corresponding to the term of the loan plus 2.15%. Any loan that we take during the first half of 2011 would be interest only through June 30, 2011 and then would be re-payable in equal monthly installments of principal and interest over the next 48 months.

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., or RJRT. We borrowed $4.8 million upon entering into the loan agreement and borrowed the remaining $489,000 in September 2008. Pursuant to the loan agreement, we granted a first priority security interest in favor of the bank in the assets acquired with the proceeds of the loan facility. The March 2008 loan bears interest at a fixed rate of 5.231% per annum and is repayable in equal monthly installments of $112,000 beginning April 1, 2008 and continuing through the maturity date of March 1, 2012. We used $1.7 million of the proceeds from the March 2008 loan to pay and satisfy in full the principal and interest outstanding on two of the tranches under the loan facility with RJRT and granted a first priority security interest in favor of the bank in assets previously acquired with the proceeds of those tranches. The September 2008 loan bears interest at a fixed rate of 6.131% per annum and is repayable in equal monthly installments of $11,000 beginning October 1, 2008 and continuing through the maturity date of September 1, 2012. As of December 31, 2010, the outstanding principal balance under the loan facility was $1.8 million. There is no additional borrowing capacity remaining available to us under the loan agreement.

In April 2002, we received a $500,000 loan from the City of Winston-Salem. Under the terms of the loan, there was no interest accrual or payment due until the fifth anniversary of the loan. Following expiration of the five-year grace period in April 2007, the outstanding principal balance of the loan 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 $135,000 that remained outstanding under the loan.

Cash Flows

	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	

	Year ended December 31,		
	2009	2008	Change
		(in thousands)	
Net cash used in operating activities	$(24,271)	$(28,261)	$ 3,990
Net cash provided by (used in) investing activities	9,800	(5,519)	15,319
Net cash provided by financing activities	47,178	31,579	15,599
Net increase (decrease) in cash and cash equivalents	$ 32,707	$ (2,201)	

Net cash provided by operating activities for the year ended December 31, 2010 was $138.3 million and net cash used in operating activities for the year ended December 31, 2009 was $24.3 million, a difference of $162.6 million.

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
- $1.3 million in interest income.

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 an exclusive worldwide 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, 2011 to increase, with the largest component anticipated to result from our obligation under our TC-5214 agreement with AstraZeneca to fund a portion of the costs of the initial development program for TC-5214.

For 2009, net cash used in operating activities was principally the result of aggregate payments of $44.2 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, and was partially offset by our receipt of:

- the $10.0 million payment from AstraZeneca in July 2009;
- $5.5 million in payments for research services under our preclinical research collaboration with AstraZeneca;
- $2.5 million in aggregate payments from GlaxoSmithKline upon achievement of milestone events under our alliance agreement; and
- $1.0 million in interest income.

Net cash used in operating activities for the year ended December 31, 2009 of $24.3 million decreased by $4.0 million as compared to net cash used in operating activities for the year ended December 31, 2008 of $28.3 million.

For 2008, net cash used in operating activities was principally the result of aggregate payments of $46.3 million made 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, and was partially offset by our receipt of:

- $11.1 million in payments for research services under our preclinical research collaboration with AstraZeneca;
- $2.7 million in interest income;
- $2.2 million in aggregate payments upon achievement of milestone events under our cognitive disorders agreement with AstraZeneca related to the development of product candidates arising under the preclinical research collaboration; and
- $1.5 million in aggregate payments from GlaxoSmithKline upon achievement of milestone events under our alliance agreement.

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. Net cash provided by investing activities for the year ended December 31, 2009 changed by $15.3 million as compared to net cash used in operating activities of $5.5 million for the year ended December 31, 2008. 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 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. 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. Our net purchases of investments in marketable securities for 2008 were $3.5 million. Additionally, we purchased $3.3 million of property and equipment during 2010, an increase of $3.1 million from $200,000 during 2009. The $200,000 of property and equipment purchases during 2009 reflected a decrease of $1.9 million from $2.1 million for 2008. Purchases of property and equipment for 2010 were primarily to expand our internal research and development capacity.

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 of tax deductions for stock-based compensation in excess of expense recorded for stock options under GAAP of $3.5 million for the year ended 2010 and a decrease in net borrowings under our loan facilities of $1.0 million. Net cash provided by financing activities for the year ended December 31, 2009 increased by $15.6 as compared to the year ended December 31, 2008. Cash provided by financing activities for the year ended December 31, 2008 reflected proceeds of $29.1 million from a common stock offering in January 2008 and net borrowings under our loan facilities of $2.2 million.

Funding Requirements

As of December 31, 2010, we had an accumulated deficit of $218.4 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 and GlaxoSmithKline, 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 and for 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 development costs for TC-5214 payable by us;
- whether AstraZeneca exercises its right to license TC-5619;
- the scope, progress, duration, results and cost of clinical trials, as well as non-clinical studies and assessments, of our other product candidates;
- the impact of the termination of our alliance agreement with GlaxoSmithKline;

- 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;
- whether we establish strategic alliances, collaborations and licensing or other arrangements on terms favorable to us;
- the costs, timing and outcomes of regulatory reviews or other regulatory actions;
- the number and characteristics of product candidates that we pursue;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending patents and other intellectual property rights;
- the costs of manufacturing-related services for our product candidates in clinical and late preclinical development;
- the rate of technological advancements for the indications that we target;
- the costs to satisfy our obligations under existing and potential future alliances and collaborations;
- the timing, receipt and amount of sales or royalties, if any, from our potential products; and
- the extent and scope of our general and administrative expenses.

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 at least through the end of 2013, 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 for product development.

To the extent our capital resources are insufficient to meet future capital requirements, we may need to finance future cash needs through alliances, collaborations or licensing or other arrangements, public or private equity or debt offerings or other financings. The global credit and financial markets continue to be negatively impacted by the recessionary environment. This, coupled with other factors, may limit our access to additional equity or debt financing in the future on acceptable terms or at all. Also, additional strategic alliances, collaborations or licensing or other arrangements may not be available on acceptable terms or at all. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate our research and development programs or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently. Additionally, any future equity funding may dilute the ownership of our stockholders.

We cannot accurately determine the completion dates and related costs of our research and development programs due to inherent uncertainties in outcomes of clinical trials and regulatory approvals of our product candidates. We cannot be certain that we will be able to successfully complete our research and development projects or establish strategic alliances, collaborations or licensing or other arrangements for our product candidates. Our failure, or the failure of any of our 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, 2010:

Contractual Obligation	Payments Due by Period				
	Total	Less Than 1 Year	1 - 3 Years	3 - 5 Years	More Than 5 Years
			(in thousands)		
Long-term debt obligations	$ 3,215	$ 1,812	$1,095	$308	$ —
Operating lease obligations	4,076	2,531	1,518	27	—
Purchase obligations	22,222	21,642	517	49	14
	$29,513	$ 25,985	$3,130	$384	$ 14

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, 2010 and exclude payments on amounts available under loan facilities at December 31, 2010.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Recent Accounting Pronouncements

In April 2010, the Financial Accounting Standards Board, or FASB, issued Accounting Standards Update No. 2010-17, *Milestone Method of Revenue Recognition*, or ASU 2010-17. ASU 2010-17 defines a milestone event and permits an entity to make an accounting policy election to recognize a payment that is contingent upon achievement of a substantive milestone in its entirety in the period in which the milestone is achieved. ASU 2010-17 is effective for fiscal years beginning on or after June 15, 2010, and for interim periods within those years, and may be applied prospectively to milestones achieved after the adoption date or retrospectively for all periods presented. Early adoption is permitted. We do not expect ASU 2010-17 to have a material impact on our financial results.

In October 2009, the FASB issued Accounting Standards Update No. 2009-13, *Revenue Recognition (Topic 605): Multiple-Deliverable Revenue Arrangements—a consensus of the FASB Emerging Issues Task Force*, or ASU 2009-13. ASU 2009-13 addresses the units of accounting for arrangements involving multiple deliverables and how arrangement consideration should be allocated to the separate units of accounting, when applicable. ASU 2009-13 eliminates the criterion in prior accounting guidance that objective and reliable evidence of the fair value of any undelivered items must exist for the delivered items to be considered a separate unit or separate units of accounting. ASU 2009-13 is effective for financial statements issued for fiscal years beginning after June 15, 2010 and can be applied either prospectively or retrospectively for all periods presented. We do not plan to apply ASU 2009-13 retrospectively and, therefore, do not expect ASU 2009-13 to impact the accounting treatment for our current strategic alliance and collaboration agreements. The impact of ASU 2009-13 on the accounting treatment for any future strategic alliance or collaboration agreement, or for any amendment to a current agreement, is not yet determinable.

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

The primary objective of our investment activities is 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, 2010, we had cash, cash equivalents and investments in marketable securities of $252.5 million. Our investments 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 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, 2010 would not have a material impact on the total fair value of our portfolio.

We contract for the conduct of some of our clinical trials and other research and development and manufacturing activities with contract research organizations, clinical trial sites and contract manufacturers in Europe and India. We may be subject to exposure to fluctuations in foreign currency exchange rates in connection with these agreements. If the average Euro/U.S. dollar or Indian Rupee/U.S. dollar exchange rate were to strengthen or weaken by 10% against the corresponding exchange rate as of December 31, 2010, 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, 2010 and 2009, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2010. 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, 2010 and 2009, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2010, 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, 2010, 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 11, 2011 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Raleigh, North Carolina
March 11, 2011

TARGACEPT, INC.

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

	December 31, 2010	December 31, 2009
ASSETS		
Current assets:		
Cash and cash equivalents	$ 165,854	$ 83,909
Investments in marketable securities—short term	48,168	27,157
Receivables from collaborations	838	201,801
Prepaid expenses	3,219	1,562
Total current assets	218,079	314,429
Investments in marketable securities—long term	38,487	—
Property and equipment, net	6,072	4,783
Intangible assets	149	167
Total assets	$ 262,787	$ 319,379
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 4,721	$ 1,275
License fee payable	—	16,000
Accrued expenses	10,516	5,267
Current portion of long-term debt	1,710	1,442
Current portion of deferred revenue	81,710	77,243
Total current liabilities	98,657	101,227
Long-term debt, net of current portion	1,349	1,966
Deferred revenue, net of current portion	70,934	147,195
Total liabilities	170,940	250,388
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.001 par value, 100,000,000 shares authorized ; 28,870,691 and 28,226,829 shares issued and outstanding at December 31, 2010 and December 31 2009, respectively	29	28
Preferred stock, $0.001 par value, 5,000,000 shares authorized; 0 shares issued and outstanding at December 31, 2010 and 2009	—	—
Capital in excess of par value	309,994	298,263
Accumulated other comprehensive income	225	—
Accumulated deficit	(218,401)	(229,300)
Total stockholders' equity	91,847	68,991
Total liabilities and stockholders' equity	$ 262,787	$ 319,379

See accompanying notes.

TARGACEPT, INC.

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

	Year ended December 31,		
	2010	2009	2008
Operating revenues:			
Milestones and license fees from collaborations	$ 83,380	$ 18,934	$ 10,179
Collaboration research and development	—	5,246	8,967
Product sales, net	—	473	718
Grant revenue	2,333	409	221
Net operating revenues	85,713	25,062	20,085
Operating expenses:			
Research and development (including stock-based compensation of $2,768, $1,353 and $1,130 in 2010, 2009 and 2008, respectively)	64,546	40,179	40,981
General and administrative (including stock-based compensation of $2,169, $1,101 and $935 in 2010, 2009 and 2008, respectively)	8,052	8,167	6,499
License fees	—	16,350	—
Cost of product sales	—	691	749
Total operating expenses	72,598	65,387	48,229
Income (loss) from operations	13,115	(40,325)	(28,144)
Other income (expense):			
Interest income	1,463	1,050	2,734
Interest expense	(153)	(217)	(251)
Total other income (expense)	1,310	833	2,483
Income (loss) before income taxes	14,425	(39,492)	(25,661)
Income tax (expense) benefit	(3,526)	88	—
Net income (loss)	$ 10,899	$ (39,404)	$ (25,661)
Basic net income (loss) per share	$ 0.38	$ (1.54)	$ (1.04)
Diluted net income (loss) per share	$ 0.36	$ (1.54)	$ (1.04)
Weighted average common shares outstanding—basic	28,543,408	25,636,419	24,664,169
Weighted average common shares outstanding—diluted	30,150,324	25,636,419	24,664,169

See accompanying notes.

TARGACEPT, INC.

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

	Common Stock		Capital in Excess of Par Value	Accumulated Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balances at December 31, 2007	20,503,419	$ 20	$215,799	$ —	$ (164,235)	$ 51,584
Issuance of common stock related to exercise of stock options	90,954	—	271	—	—	271
Stock-based compensation	—	—	2,065	—	—	2,065
Net proceeds from public stock offering	4,370,000	5	29,109	—	—	29,114
Net loss and comprehensive loss	—	—	—	—	(25,661)	(25,661)
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

See accompanying notes.

TARGACEPT, INC.

STATEMENTS OF CASH FLOWS
(in thousands)

	Year ended December 31,		
	2010	2009	2008
Operating activities			
Net income (loss)	$ 10,899	$(39,404)	$ (25,661)
Adjustments to reconcile net income (loss) to net cash provided by (used in) operating activities:			
Recognition of deferred revenue	(83,767)	(6,383)	(6,479)
Amortization of premium on marketable securities, net	416	—	—
Depreciation and amortization	1,997	1,835	1,800
Stock-based compensation expense	4,937	2,454	2,065
Impairment of intangible asset	—	—	220
Excess tax benefits from stock-based compensation	(3,503)	(41)	—
Changes in operating assets and liabilities:			
Receivables from collaborations(1)	200,963	272	2,125
Prepaid expenses, inventories and accrued interest receivable	(1,815)	(28)	(413)
Accounts payable, license fees payable and accrued expenses	(3,802)	16,551	(1,918)
Deferred revenue(1)	11,973	473	—
Net cash provided by (used in) operating activities	138,298	(24,271)	(28,261)
Investing activities			
Purchase of investments in marketable securities	(144,012)	(31,000)	(104,800)
Proceeds from sale of investments in marketable securities	84,481	41,000	101,334
Purchase of property and equipment	(3,311)	(200)	(2,053)
Proceeds from sale of property and equipment	43	—	—
Net cash (used in) provided by investing activities	(62,799)	9,800	(5,519)
Financing activities			
Proceeds from issuance of long-term debt	1,228	—	5,300
Principal payments on long-term debt	(1,577)	(1,390)	(3,106)
Proceeds from issuance of common stock, net	3,292	48,527	29,385
Excess tax benefits from stock-based compensation	3,503	41	—
Net cash provided by financing activities	6,446	47,178	31,579
Net increase (decrease) in cash and cash equivalents	81,945	32,707	(2,201)
Cash and cash equivalents at beginning of year	83,909	51,202	53,403
Cash and cash equivalents at end of year	$ 165,854	$ 83,909	$ 51,202

(1) 2009 amount does not include a $200,000 non-cash item related to the Company's December 2009 collaboration and license agreement with AstraZeneca AB (see Note 12).

See accompanying notes.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS
DECEMBER 31, 2010

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 and Reclassifications

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

Certain reclassifications have been made to the financial statements for the years ended December 31, 2009 and 2008 to conform to the presentation in the financial statements for the year ended December 31, 2010. These reclassifications had no impact on previously reported net loss or stockholders' equity.

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 expected 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 agency-backed certificates and 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 the classification as of each balance sheet date. All marketable securities owned during 2010 and 2009 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 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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

2. Summary of Significant Accounting Policies—(continued)

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, 2010 and 2009 are related to the Company's collaboration agreement with AstraZeneca AB entered into in December 2009.

During 2010, 2009, and 2008, the Company recognized revenue of $83,380,000, $24,180,000, and $19,146,000, respectively, or 97%, 96% and 95% 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 each of the years ended December 31, 2009 and 2008 includes materials and manufacturing costs, applied by the weighted average method, FDA fees and other fees associated with the manufacture and selling of Inversine. As a result of the discontinuation 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 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 and 2008, cost of product sales included of shipping and handling costs of $183,000 and $204,000, respectively.

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

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.

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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

2. Summary of Significant Accounting Policies—(continued)

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, 2010 and 2009, the Company had deposits in excess of federally insured limits of $160,932,000 and $110,159,000, 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 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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

2. Summary of Significant Accounting Policies—(continued)

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, a revenue recognition policy must be determined for each unit. If the arrangement constitutes a single unit of accounting, the revenue recognition policy must be determined for the entire arrangement.

Collaboration research and development revenue is earned and recognized as research is performed and related expenses are incurred. Non-refundable upfront fees, which may include, 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 milestones and license fees 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 over the estimated development period for the applicable licensed product candidate(s).

Revenue for non-refundable payments based on the achievement of collaboration milestones is recognized as revenue when the milestone events are achieved if all of the following conditions are met: (1) achievement of the milestone event was not reasonably assured at the inception of the arrangement; (2) substantive effort is involved to achieve the milestone event; and (3) the amount of the milestone payment appears reasonable in relation to the effort expended, the other milestone payments in the arrangement and the related risk associated with achievement of the milestone event. If any of these conditions is not met, the milestone payment is deferred and recognized on a straight-line basis over 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 is recognized when goods are shipped, at which point title has passed, net of allowances for returns and discounts. Grant payments received prior to the Company's performance of work required by the terms of the award are recorded as deferred revenue and recognized as grant revenue as the Company performs the work and incurs reimbursable costs in accordance with the objectives of the award.

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 these 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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

2. Summary of Significant Accounting Policies—(continued)

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 (Loss) Per Share

The Company computes net income (loss) per share in accordance with ASC Topic 260, *Earnings Per Share*, or ASC 260. Under the provisions of ASC 260, basic net income (loss) per share, or Basic EPS, is computed by dividing net income (loss) by the weighted average number of common shares outstanding. Diluted net income (loss) per share, or Diluted EPS, is computed by dividing net income (loss) by the weighted average number of common shares and 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,		
	2010	2009	2008
Basic:			
Net income (loss)	$ 10,899	$ (39,404)	$ (25,661)
Weighted average common shares—basic	28,543,408	25,636,419	24,664,169
Basic EPS	$ 0.38	$ (1.54)	$ (1.04)
Diluted:			
Net income (loss)	$ 10,899	$ (39,404)	$ (25,661)
Weighted average common shares—basic	28,543,408	25,636,419	24,664,169
Common share equivalents	1,606,916	—	—
Weighted average common shares—diluted	30,150,324	25,636,419	24,664,169
Diluted EPS	$ 0.36	$ (1.54)	$ (1.04)

Common share equivalents consist of the incremental common shares issuable upon the exercise of stock options. For each of the years ended December 31, 2009 and 2008, the Company excluded all common share equivalents from the calculation of Diluted EPS because their effect was anti-dilutive. As a result, Diluted EPS is identical to Basic EPS for those years. For each of the years ended December 31, 2009 and 2008, shares subject to outstanding stock options may have been included in the calculation of common share equivalents using the treasury stock method if the Company had been in a net income position. Shares subject to outstanding stock options that were anti-dilutive and consequently not included in the calculation of common share equivalents totaled 850,683, 3,648,268, and 3,123,249 for the years ended December 31, 2010, 2009, and 2008, respectively, calculated on a weighted-average basis.

Public Offerings of Common Stock

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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

2. Summary of Significant Accounting Policies—(continued)

On October 13, 2009, the Company completed a public offering of 2,200,000 shares of its common stock. The offering was priced to the public at $21.00 per share. The Company's net proceeds from the offering, after deducting underwriters' discounts and commissions and offering expenses payable 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.

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 November 28, 2007 and further amended effective June 10, 2009, 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 recognized $3,503,000 and $41,000 in excess tax deductions for the years ended December 31, 2010 and 2009, respectively. 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 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.

Non-refundable Advance Payments

The Company defers and capitalizes non-refundable advance payments for goods or services to be received in the future for use in research and development activities. The Company then charges the advance payments to expense ratably as the goods are delivered or the services are rendered in accordance with ASC Subtopic 730-20, *Research and Development Arrangements*, or ASC 730-20. If the Company's expectations change such that it does not expect it will need the goods to be delivered or the services to be rendered, it will charge the remaining balance of capitalized non-refundable advance payments to expense.

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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

2. Summary of Significant Accounting Policies—(continued)

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 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 of ASC 820 are based on both observable and unobservable inputs. Observable inputs reflect readily obtainable data from independent sources, and unobservable inputs reflect the Company's market assumptions. ASC 820 classifies these inputs 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.

The following tables present the Company's investments in marketable securities that are measured at fair value on a recurring basis as of December 31, 2010 and 2009, respectively:

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. government and 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	$102,651	$ —	$ —

December 31, 2009	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
		(in thousands)	
Certificates of deposit	$27,000	$ —	$ —
Accrued interest	157	—	—
Total cash equivalents and marketable securities	$27,157	$ —	$ —

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

2. Summary of Significant Accounting Policies—(continued)

The Company valued non-financial assets as of December 31, 2008, such as intangible assets measured at fair value, for an impairment assessment using other accounting standards in accordance with Section 15, *Scope and Scope Exceptions*, of ASC 820, Subtopic 10, *Overall* (see Note 5).

Comprehensive Income (Loss)

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

	Year Ended December 31,		
	2010	2009	2008
		(in thousands)	
Net income (loss)	$10,899	$(39,404)	$(25,661)
Unrealized gain on marketable securities, net	225	—	—
Comprehensive income (loss)	$11,124	$(39,404)	$(25,661)

Recent Accounting Pronouncements

In April 2010, the FASB issued Accounting Standards Update No. 2010-17, *Milestone Method of Revenue Recognition*, or ASU 2010-17. ASU 2010-17 defines a milestone event and permits an entity to make an accounting policy election to recognize a payment that is contingent upon achievement of a substantive milestone in its entirety in the period in which the milestone is achieved. ASU 2010-17 is effective for fiscal years beginning on or after June 15, 2010, and for interim periods within those years, and may be applied prospectively to milestones achieved after the adoption date or retrospectively for all periods presented. Early adoption is permitted. The Company does not expect ASU 2010-17 to have a material impact on its financial results.

In October 2009, the FASB issued Accounting Standards Update No. 2009-13, *Revenue Recognition (Topic 605): Multiple-Deliverable Revenue Arrangements—a consensus of the FASB Emerging Issues Task Force*, or ASU 2009-13. ASU 2009-13 addresses the units of accounting for arrangements involving multiple deliverables and how arrangement consideration should be allocated to the separate units of accounting, when applicable. ASU 2009-13 eliminates the criterion in prior accounting guidance that objective and reliable evidence of the fair value of any undelivered items must exist for the delivered items to be considered a separate unit or separate units of accounting. ASU 2009-13 is effective for financial statements issued for fiscal years beginning after June 15, 2010 and can be applied either prospectively or retrospectively for all periods presented. The Company does not plan to apply ASU 2009-13 retrospectively and, therefore, does not expect ASU 2009-13 to impact the accounting treatment for its current strategic alliance and collaboration agreements. The impact of ASU 2009-13 on the accounting treatment for any future strategic alliance or collaboration agreement, or for any amendment to a current agreement, is not yet determinable.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

3. Investments in Marketable Securities

The following is a reconciliation of amortized cost to fair value of available-for-sale marketable securities held at December 31, 2010:

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. government and 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. government and 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. government and 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, 2010, the Company held investments in marketable securities with unrealized gains of $254,000 and unrealized losses of $29,000. 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, 2010, the Company's investments in marketable securities including those classified on its balance sheet as cash equivalents, reach maturity between January 12, 2011 and November 15, 2013, with a weighted average maturity date of approximately October 31, 2011.

As of December 31, 2009, the Company's investments in marketable securities consisted of certificates of deposit of $27,000,000 and accrued interest of $157,000 for which amortized cost approximated fair value.

4. Property and Equipment

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

	December 31, 2010	December 31, 2009
	(in thousands)	
Laboratory equipment	$ 12,133	$ 10,371
Office furniture and fixtures	4,640	3,328
Leasehold improvements	1,175	1,133
	17,948	14,832
Less: accumulated depreciation	(11,876)	(10,049)
Property and equipment, net	$ 6,072	$ 4,783

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2009

4. Property and Equipment—(continued)

The Company recorded $1,979,000, $1,818,000, and $1,767,000 of depreciation expense for the years ended December 31, 2010, 2009 and 2008, respectively.

5. Intangible Assets

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

	December 31,	
	2010	2009
	(in thousands)	
Patents	$ 296	$ 296
Less: accumulated amortization	(147)	(129)
Total	$ 149	$ 167

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 2002 assignment by Layton Bioscience also included rights related to the Inversine trademark and product technology, an intangible asset that had an original value to the Company of $346,000. During the fourth quarter of 2008, as part of its processes for preparation of its financial statements, the Company performed an impairment analysis of its intangible assets. As of the date of the analysis, the Company had recognized a net loss on sales of Inversine in each of 2008 and 2007 and did not expect to recognize net income from sales of Inversine in future periods. The history of losses on sales of Inversine and the forecast for future periods indicated the carrying value of the Inversine trademark and product technology intangible asset may not have been recoverable. Using a discounted cash flow model that is based on estimated future net product sales and cost of product sales and considers assumptions such as, among other things, estimated future product sales volumes and estimated future sales price increases, the Company estimated the fair value of the Inversine trademark and product technology intangible asset and determined that it had no fair value. As a result, the Company recorded an impairment charge for the full amount of the unamortized balance of the Inversine trademark and product technology intangible asset as of the valuation date, or $220,000, to research and development expense in the fourth quarter of 2008.

The impairment charge had no effect on the Company's prospective amortization of $17,000 each year of the licensed patent rights intangible asset 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,	
	2010	2009
	(in thousands)	
Clinical trial and preclinical study costs	$ 8,326	$2,551
Employee compensation	2,032	2,447
Other	158	269
Total	$10,516	$5,267

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

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 that the Company may take at any time 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. 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. Any future borrowing under the loan agreement would bear interest, at the Company's discretion on a loan-by-loan basis, at either a variable rate equal to the thirty-day LIBOR plus 2.15%, adjusted monthly on the first day of each month, or a fixed rate equal to the bank's fixed rate cost of funds index corresponding to the term of the loan plus 2.15%. Also, any future borrowing would be interest only through June 30, 2011 and then would be re-payable in equal monthly installments of principal and interest over the next 48 months. 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 facility.

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 borrowing bears interest at a fixed rate of 5.231% per annum and is repayable in equal monthly installments of $112,000 beginning April 1, 2008 through the maturity date of March 1, 2012. The Company used $1,679,000 of the proceeds from the March 2008 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 $156,000, $223,000 and $244,000 in interest under notes payable during the years ended December 31, 2010, 2009 and 2008, respectively. Maturities of long-term debt were as follows at December 31, 2010 (in thousands):

2011	$1,710
2012	728
2013	319
2014 and thereafter	302
	$3,059

8. Income Taxes

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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2009

8. Income Taxes—(continued)

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.

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 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. For the year ended December 31, 2008, there was no net income tax expense (benefit) for federal or state income taxes because the Company incurred net operating losses. 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,		
	2010	2009	2008
		(in thousands)	
Current:			
Federal	$ 3,086	$ (96)	$ —
State	440	8	—
Net current income tax expense (benefit)	3,526	(88)	—
Deferred:			
Federal	(1,519)	13,230	9,462
State	1,321	2,951	1,112
Valuation allowance	198	(16,181)	(10,574)
Net deferred income tax expense (benefit)	—	—	—
Net income tax expense (benefit)	$ 3,526	$ (88)	$ —

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

	Year Ended December 31,		
	2010	2009	2008
Expected federal income tax benefit/expense at statutory rate	35%	35%	34%
Increase (decrease) resulting from:			
Research and development credits	(12)	5	4
Stock-based compensation	4	(1)	(1)
State income tax expense, net of federal benefit	3	4	4
Qualifying Therapeutic Drug Project grant	(3)	—	—
Change in unrecognized tax benefit reserves	(3)	—	—
Change in valuation allowance	(1)	(41)	(41)
Other	1	(2)	—
	24%	— %	— %

At December 31, 2010, 2009 and 2008, the Company had net operating loss carryforwards for federal income tax purposes of $39,011,000, $152,839,000 and $113,648,000, respectively, and for state income tax

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2009

8. Income Taxes—(continued)

purposes of $76,178,000, $135,789,000 and $113,493,000, respectively. At December 31, 2010, 2009 and 2008, the Company had research and development income tax credits for federal income tax purposes of $9,556,000, $7,340,000 and $6,118,000, respectively. The Company had research and development income tax credits for state income tax purposes of $1,021,000 and $595,000 at December 31, 2010 and 2009, respectively. The federal net operating loss carryforwards begin to expire in 2021. The state net operating loss carryforwards begin to expire in 2016. 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, 2010, the valuation allowance decreased $198,000. For the years ended December 31, 2009 and 2008, the valuation allowance increased $16,181,000 and $10,574,000, respectively.

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

	December 31,	
	2010	2009
	(in thousands)	
Deferred tax assets:		
Collaboration revenue	$ 55,857	$ 9,296
Research and development tax credit	8,443	6,346
Net operating loss carryforward	7,463	50,750
Patents	2,125	1,704
Stock-based compensation	1,903	1,317
Accrued royalties	—	6,068
Other	35	—
Total gross deferred tax assets	75,826	75,481
Valuation allowance	(75,114)	(75,311)
Net deferred tax asset	712	170
Deferred tax liabilities		
Equipment and other	(712)	(170)
Net deferred tax asset	$ —	$ —

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2009

8. Income Taxes—(continued)

For the year ended December 31, 2009, stock option exercises resulted in $5,714,000 in excess tax deductions. The benefit of these excess tax deductions had not begun to be realized as of December 31, 2010 because the Company has incurred cumulative net operating losses. Accordingly, the tax benefit will not be recognized as an increase to capital in excess of par value until the excess deductions reduce income taxes payable.

The Company follows the provisions 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, 2008	$ 942
Additions based on tax positions related to the current year	278
Balance at December 31, 2008	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

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 2011. 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, 2010, 2009 or 2008.

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. The Company's 2009, 2008, 2007 and 2006 North Carolina income tax returns are under examination.

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, 2010, the number of shares authorized for issuance under the Plans was 7,282,078, of which 2,261,896 shares remained available for grant.

Awards may be made with respect to the 2006 Plan, or may have been made with respect to both Plans, to participants under the Plans in the form of incentive and nonqualified stock options, restricted stock, stock

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2009

9. Stock-Based Incentive Plans—(continued)

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 based on the calculated historical volatility of twelve to sixteen benchmark companies in the Company's industry that have been identified as comparable public entities. The expected term for stock options granted during 2010, 2009 and 2008 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,		
	2010	2009	2008
Dividend yield	—	—	—
Risk-free interest rate	2.9%	2.0%	3.4%
Volatility	0.7	0.7	0.7
Expected term	6.27 years	6.72 years	6.43 years

A summary of option activity and changes during each of the years ended December 31, 2010, 2009 and 2008 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, 2007	3,125,161	$ 5.11		
Granted	106,485	6.71		
Forfeited	(21,595)	6.73		
Exercised	(90,954)	2.98		
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	7.11 years	$ 50,931
Vested and exercisableat December 31, 2010	1,933,244	$ 7.38	6.20 years	$ 36,971

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2009

9. Stock-Based Incentive Plans—(continued)

The weighted average grant date fair value of options granted during the years ended December 31, 2010, 2009, and 2008 was $13.46, $2.03, and $4.38, respectively. The total intrinsic value of options exercised during the years ended December 31, 2010, 2009, and 2008 was $11,527,000, $16,833,000, and $489,000, respectively.

A summary of the status of non-vested stock options granted under the 2006 Plan as of December 31, 2010 and changes during the year ended December 31, 2010 appears below:

	Shares Subject to Options	Weighted Average Grant-Date Fair Value Per Share
Non-vested at January 1, 2010	936,326	$ 3.14
Granted	941,532	13.46
Vested	(690,166)	6.37
Forfeited	(21,321)	11.43
Non-vested at December 31, 2010	1,166,371	$ 9.41

As of December 31, 2010, there was $10,972,000 of total unrecognized compensation expense related to non-vested stock-based compensation arrangements granted under the Plans, before considering estimated forfeitures. That cost is expected to be recorded over a weighted average period of 2.62 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, 2010, 2009, and 2008 was $4,396,000, $2,338,000 and $2,217,000, respectively.

The Company had 3,099,615 and 2,823,812 shares of common stock reserved for future issuance upon the exercise of outstanding stock options at December 31, 2010 and 2009, respectively.

10. Commitments and Contingencies

Office Lease

On March 1, 2002, the Company entered into an agreement with Wake Forest University Health Sciences to lease an office and research facility in Winston-Salem, North Carolina with an initial term that extended through July 31, 2007. The lease contained a renewal option for up to one additional five-year term, with a 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.

Rent expense incurred by the Company under the office lease and other operating leases was $2,003,000 for the year ended December 31, 2010 and $2,148,000 for each of the years ended December 31, 2009 and 2008.

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

2011	$2,531
2012	1,489
2013	29
2014 and thereafter	27
	$4,076

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2009

10. Commitments and Contingencies—(continued)

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 $487,000, $666,000, and $558,000 to the plan for the years ended December 31, 2010, 2009 and 2008, respectively. The Company matched employee contributions to the plan, on a per employee basis, up to 4% of each employee's wages for the year ended December 31, 2010. During 2009 and 2008 the Company matched employee contributions to the plan, on a per employee basis, up to 6% of each employee's wages.

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 known as AZD3480 (TC-1734) as a treatment for specified conditions characterized by cognitive impairment, including 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 development, regulatory, first commercial sale and first detail milestone events.

AstraZeneca paid the Company an initial fee of $10,000,000 in February 2006. Based on the 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 five-year development period for AZD3480. In July 2009, based on feedback received from AstraZeneca regarding its development plans for AZD3480 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 as revenue on a straight-line basis over the remaining estimated development period. The Company recognized $683,000, $1,934,000, and $2,250,000 of the initial fee as revenue for the years ended December 31, 2010, 2009, and 2008, respectively.

Under the agreement, the Company is also eligible to receive (1) additional payments of up to $103,000,000 if development, regulatory, and first commercial sale milestone events for AZD3480 are achieved only for

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

12. Strategic Alliance and Collaboration Agreements—(continued)

ADHD, (2) other payments if development, regulatory, first commercial sale and first detail milestone events for AZD3480 are achieved for any other target indication under the agreement and (3) if regulatory approval is achieved for AZD3480 for any particular indication, stepped double-digit royalties on any sales of AZD3480 for that indication or any other indication. 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.

The Company is exploring the practicability of conducting an additional clinical trial of AZD3480 in Alzheimer's disease. In September 2010, the Company and AstraZeneca amended the agreement to enable the Company potentially to conduct such a trial and to provide for respective roles and responsibilities and associated financial terms. Under the amendment, the Company received $500,000 from AstraZeneca in October 2010 and is eligible to receive additional payments of up to $5,700,000 in the aggregate.

With respect to AZD1446, the most advanced product candidate that arose out of the parties' preclinical research collaboration described below, the Company is also eligible to receive payments of up to $73,000,000, if development, regulatory, first commercial sale and first detail milestone events for AZD1446 are achieved for a single indication under the agreement, and, if regulatory approval is achieved for AZD1446 for any particular indication, stepped royalties on any sales of AZD1446 for that indication or any other indication.

The Company would recognize any revenue based on the achievement of any milestone event under the agreement upon achievement of the milestone event if the Company determines that the revenue satisfies the requirements for immediate recognition under its revenue recognition policy (see Note 2).

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 year ended December 31, 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 and $8,921,000 for the years ended December 31, 2009 and 2008, respectively. The Company recognized additional collaboration research and development revenue of $46,000 for the year ended December 31, 2008 for clinical trial material purchased by AstraZeneca from the Company and other research and development costs reimbursable under the collaboration.

In October 2007, the Company provided notice under 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 is recognizing the $2,000,000 payment as revenue on a straight-line basis over the estimated period of the Company's research and development obligations for TC-5619. Accordingly, the Company recognized $278,000, $596,000 and $923,000 of the payment as revenue for the years ended December 31, 2010, 2009 and 2008, respectively.

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 is recognizing it as revenue on a straight-line basis over the estimated period of the Company's research and development obligations for TC-5619. The Company recognized $6,286,000 of the payment as revenue for the year ended December 31, 2010.

As part of the expanded TC-5619 development program, the Company had two Phase 2 clinical proof of concept trials ongoing as of December 31, 2010, one in cognitive dysfunction in schizophrenia, or CDS, and one in adults with ADHD. The Company is also conducting specified clinical and non-clinical studies to support the potential advancement of TC-5619 into Phase 2 clinical development for Alzheimer's disease. Under the agreement, AstraZeneca has an option for an exclusive license to TC-5619 for various cognitive disorders. If TC-5619 has been licensed by AstraZeneca or remains subject to AstraZeneca's license option, any future Phase 2 clinical development for Alzheimer's disease will be funded by AstraZeneca.

In January 2011, the Company announced positive top-line results from the CDS trial. If AstraZeneca exercises its option, it would pay the Company an exercise fee of $30,000,000 and assume responsibility for and fund all future development (except for completion of the Company's ongoing studies) and commercialization for TC-5619. In that event, the Company would be eligible to receive additional payments of up to $212,000,000, if development, regulatory, first commercial sale and first detail milestone events for TC-5619 are achieved in three indications, and stepped double-digit royalties on any future TC-5619 product sales for any indication. If AstraZeneca does not exercise its option, the Company would retain all of its rights in TC-5619.

The Company has also received payments under the agreement that it recognized in full as revenue upon achievement of the corresponding milestone event 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 December 2009 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 $82,620,000 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 cumulative payments of up to an additional $540,000,000 if specified development, regulatory and first commercial sale milestone events for TC-5214 are achieved, cumulative payments of up to an additional $500,000,000 if specified sales related milestone events for TC-5214 are achieved and 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

12. Strategic Alliance and Collaboration Agreements—(continued)

substantive performance obligations under the agreement, or approximately 33 months. The Company recognized $72,565,000 and $398,000 of the upfront payment as revenue for the years ended December 31, 2010 and 2009, respectively. The Company would recognize as revenue the full amount of each payment received based on the achievement of milestone events under the agreement upon its achievement if the Company determines that the revenue satisfies the requirements for immediate recognition under its revenue recognition policy (see Note 2).

The Company and AstraZeneca have jointly designed a program for the global development of TC-5214. The initial program includes 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 the initial 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 initial 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 initial 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 initial 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 initial 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 initial program for the year ended December 31, 2010 was $10,771,000. AstraZeneca’s allocable portion of the initial program costs paid by the Company for the year ended December 31, 2010 was $2,023,000, which 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 global commercialization of TC-5214. 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 Company’s projected share of the costs of the initial development program for TC-5214, as well as royalties on

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

12. Strategic Alliance and Collaboration Agreements—(continued)

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

Under the 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 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 is recognizing both amounts into revenue on a straight-line basis over the estimated nine-year period of the Company's research and early development obligations under 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, 2009, and 2008.

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, achievement of this milestone was reasonably assured within the meaning of the Company's revenue recognition policy. Accordingly, the Company recorded the payment as deferred revenue and is recognizing it into revenue on a straight-line basis over the estimated period of the Company's research and early development obligations under the agreement. The Company recognized $692,000 of the payment as revenue for each of the years ended December 31, 2010, 2009 and 2008.

Beyond the $6,000,000 payment discussed above, the Company has received an aggregate of $4,000,000 in payments from GlaxoSmithKline for achievement of various milestone events under the agreement related to progress in the Company's preclinical programs, including $2,500,000 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).

13. Subsequent Event

In late February 2011, the Company received notice of termination of its product development and commercialization agreement from GlaxoSmithKline. By the terms of the agreement, the termination becomes effective in late May 2011. As a result of the termination, the Company expects to recognize into revenue in the

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS—(continued)
DECEMBER 31, 2010

13. Subsequent Event —(continued)

first quarter of 2011 $18,421,000 in deferred amounts received under the agreement and remaining to be recognized as of December 31, 2010. The Company recognized $3,305,000 of the deferred amounts received under the agreement for each of 2010, 2009 and 2008.

14. Selected Quarterly Financial Data (unaudited)

	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	$ 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

	2009 Quarter			
	First	Second	Third	Fourth
	(in thousands, except share and per share amounts)			
Net operating revenues	$ 6,141	$ 2,830	$ 12,663	$ 3,428
(Loss) income from operations	(5,052)	(9,855)	1,204	(26,622)
Income tax benefit	73	—	10	5
Net (loss) income	(4,677)	(9,654)	1,334	(26,407)
Basic net (loss) income per share(1)(2)	$ (0.19)	$ (0.39)	$ 0.05	$ (0.96)
Diluted net (loss) income per share	$ (0.19)	$ (0.39)	$ 0.05	$ (0.96)
Weighted average common shares outstanding—basic(2)	24,964,909	24,966,347	25,126,823	27,465,714
Weighted average common shares outstanding—diluted(2)	24,964,909	24,966,347	26,943,535	27,465,714

(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 fourth quarter of 2010 and for the first, second and fourth quarters of 2009 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, 2010 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, 2010, 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, 2010. 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, 2010, 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, 2010, 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, 2010 and 2009, and the related statements of operations, stockholders' equity and cash flows for each of the three years in the period ended December 31, 2010 and our report dated March 11, 2011 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Raleigh, North Carolina
March 11, 2011

(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, 2010 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 2011 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 or NASDAQ listing standards, we intend to post on our website any amendment to the code of business conduct and ethics, or any grant of a waiver from a provision of the code of business conduct and ethics, that requires disclosure under applicable law, the rules of the SEC or NASDAQ listing standards.

Item 11. Executive Compensation.

Information called for by this Item may be found in our definitive Proxy Statement in connection with our 2011 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 2011 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 2011 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 2011 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 92.

(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 11, 2011

Targacept, Inc.

By: /S/ J. DONALD DEBETHIZY
J. Donald deBethizy
Chief Executive Officer and President

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

Signature	Title	Date
/S/ J. DONALD DEBETHIZY **J. Donald deBethizy**	Chief Executive Officer, President and Director (principal executive officer)	March 11, 2011
/S/ ALAN A. MUSSO **Alan A. Musso**	Senior Vice President, Chief Financial Officer and Treasurer (principal financial officer and principal accounting officer)	March 11, 2011
/S/ MARK SKALETSKY **Mark Skaletsky**	Chairman of the Board of Directors	March 11, 2011
/S/ M. JAMES BARRETT **M. James Barrett**	Director	March 11, 2011
/S/ CHARLES A. BLIXT **Charles A. Blixt**	Director	March 11, 2011
/S/ JULIA R. BROWN **Julia R. Brown**	Director	March 11, 2011
/S/ G. STEVEN BURRILL **G. Steven Burrill**	Director	March 11, 2011
/S/ ERROL B. DE SOUZA **Errol B. De Souza**	Director	March 11, 2011
/S/ ALAN W. DUNTON **Alan W. Dunton**	Director	March 11, 2011
/S/ JOHN P. RICHARD **John P. Richard**	Director	March 11, 2011
/S/ RALPH SNYDERMAN **Ralph Snyderman**	Director	March 11, 2011

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 (incorporated by reference to Exhibit 10.2(d) to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2006)
10.2(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
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)

Exhibit Number	Description
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))
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 (incorporated by reference to Exhibit 10.20 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2006)
10.16+	Product Development and Commercialization Agreement, dated July 27, 2007, by and between the Company, on the one hand, and SmithKline Beecham Corporation, doing business as GlaxoSmithKline, and Glaxo Group Limited, on the other hand (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2007)
10.17+	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)
10.18^	Exclusive License Agreement, effective August 3, 2010, between the Company and Cornerstone Therapeutics Inc.
10.19*	Description of Annual Cash Incentive Program
10.20*	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)

Exhibit Number	Description
23.1	Consent of Ernst & Young LLP
24.1	Power of Attorney (included on signature page)
31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1	Certification of the Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

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

^ Portions of this Exhibit have been omitted and filed separately with the Securities and Exchange Commission as part of an application for confidential treatment pursuant to the Exchange Act.

* Denotes management compensation plan or contract

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

TARGACEPT, INC.

2006 STOCK INCENTIVE PLAN

(As Amended and Restated Through March 9, 2011)

TARGACEPT, INC.
2006 STOCK INCENTIVE PLAN
(As Amended and Restated Through March 9, 2011)

1. Definitions

In addition to other terms defined herein, the following terms shall have the meanings given below:

(a) Administrator means the Board, and, upon its delegation of all or part of its authority to administer the Plan to the Committee, the Committee.

(b) Affiliate means any Parent or Subsidiary of the Corporation, and also includes any other business entity which is controlled by, under common control with or controls the Corporation; provided, however, that the term "Affiliate" shall be construed in a manner in accordance with the registration provisions of applicable federal securities laws.

(c) Annual Option means an Option granted on an annual basis to a Nonemployee Director of the Corporation as provided in Section 8.

(d) Award means, individually or collectively, a grant under the Plan of an Option (including an Incentive Option, Nonqualified Option or a Director Option); a Stock Appreciation Right (including a Related SAR or a Freestanding SAR); a Restricted Award (including a Restricted Stock Award or a Restricted Unit Award); a Performance Award (including a Performance Share Award or a Performance Unit Award); a Phantom Stock Award; a Dividend Equivalent Award; or any other award granted under the Plan.

(e) Award Agreement means an agreement (which may be in written or electronic form, in the Administrator's discretion, and which includes any amendment or supplement thereto) between the Corporation and a Participant specifying the terms, conditions and restrictions of an Award granted to the Participant. An Agreement may also state such other terms, conditions and restrictions, including but not limited to terms, conditions and restrictions applicable to shares or any other benefit underlying an Award, as may be established by the Administrator.

(f) Board or Board of Directors means the Board of Directors of the Corporation.

(g) Cause shall mean, unless the Administrator determines otherwise, a Participant's termination of employment or service resulting from the Participant's (i) termination for "cause" as defined under the Participant's employment, consulting or other agreement with the Corporation or an Affiliate, if any, or (ii) if the Participant has not entered into any such employment, consulting or other agreement (or if any such agreement does not address the effect of a "cause" termination), then the Participant's termination shall be for "Cause" if termination results due to the Participant's (A) dishonesty; (B) refusal to perform his duties for the Corporation; (C) engaging in fraudulent conduct; or (D) engaging in any conduct that could be materially damaging to the Corporation without a reasonable good faith belief that such conduct was in the best interest of the Corporation. The determination of "Cause" shall be made by the Administrator and its determination shall be final and conclusive.

(h) Change in Control:

(i) *General*: Except as may be otherwise provided in an individual Award Agreement or as may be otherwise required in order to comply with Code Section 409A, a Change in Control shall be deemed to have occurred on the earliest of the following dates:

(A) The date any entity or person shall have become the beneficial owner of, or shall have obtained voting control over, thirty percent (30%) or more of the outstanding Common Stock of the Corporation;

(B) With respect to Awards granted before March 9, 2011, the date of stockholder approval of, and, with respect to Awards granted on or after March 9, 2011, the date of the consummation of: (A) a merger, consolidation, reorganization or similar business transaction of the Corporation with or into another corporation or other business entity (each, a "corporation"), in which the Corporation is not the continuing or surviving entity or pursuant to which any shares of Common Stock of the Corporation would be converted into cash, securities or other property of another entity, other than a transaction of the Corporation in which holders of Common Stock immediately prior to the transaction continue to own at least 50% of the outstanding Common Stock, or if the Corporation is not the surviving entity, the common stock (or other voting securities) of the surviving entity immediately after the transaction as immediately before (provided, however, that, solely with respect to Awards granted prior to March 9, 2011, if consummation of such transaction is subject to the approval of federal, state or other regulatory authorities, then, unless the Administrator determines otherwise, a "Change in Control" shall not be deemed to occur until the later of the date of stockholder approval of such transaction or the date of final regulatory clearance or approval of such transaction); or (B) the sale or other disposition of all or substantially all of the assets of the Corporation; or

(C) The date there shall have been a change in a majority of the Board of Directors of the Corporation within a 12-month period unless the nomination for election by the Corporation's stockholders of each new Director was approved by the vote of two-thirds of the members of the Board (or a committee of the Board, if nominations are approved by a Board committee rather than the Board) then still in office who were in office at the beginning of the 12-month period.

(For the purposes herein, the term "person" shall mean any individual, corporation, partnership, group, association or other person, as such term is defined in Section 13(d)(3) or Section 14(d)(2) of the Exchange Act, other than the Corporation, a subsidiary of the Corporation or any employee benefit plan(s) sponsored or maintained by the Corporation or any subsidiary thereof, and the term "beneficial owner" shall have the meaning given the term in Rule 13d-3 under the Exchange Act.)

(D) The Administrator shall have full and final authority, in its discretion, to determine whether a Change in Control of the Corporation has occurred pursuant to the above definition, the date of the occurrence of such Change in Control and any incidental matters relating thereto.

(ii) *Definition Applicable to Awards subject to Code Section 409A*: Notwithstanding the preceding provisions of Section 1(h)(i), in the event that any Awards granted under the Plan

are deemed to be deferred compensation subject to the provisions of Code Section 409A, then distributions related to such Awards may be permitted, in the Administrator's discretion, upon the occurrence of one or more of the following events (as they are defined and interpreted under Code Section 409A): (A) a change in the ownership of the Corporation, (B) a change in effective control of the Corporation, or (C) a change in the ownership of a substantial portion of the assets of the Corporation.

(i) Code means the Internal Revenue Code of 1986, as amended. Any reference herein to a specific Code section shall be deemed to include all related regulations or other guidance with respect to such Code section.

(j) Committee means the Compensation Committee of the Board appointed to administer the Plan.

(k) Common Stock means the common stock of Targacept, Inc., $0.001 par value.

(l) Corporation means Targacept, Inc., a Delaware corporation, together with any successor thereto.

(m) Covered Employee shall have the meaning given the term in Section 162(m) of the Code.

(n) Director means a member of the Board or of the board of directors of an Affiliate.

(o) Director Option means an Option granted to a Nonemployee Director of the Corporation as provided in Section 8. Director Options may be Initial Options or Annual Options as provided in Section 8.

(p) Disability shall, except as may be otherwise determined by the Administrator (taking into account any Code Section 409A considerations), have the meaning given in any employment agreement, consulting agreement or other similar agreement, if any, to which a Participant is a party, or, if there is no such agreement (or if any such agreement does not address the effect of termination due to disability), "Disability" shall mean the inability to engage in any substantial gainful activity by reason of any medically determinable physical or mental impairment which can be expected to result in death, or which has lasted or can be expected to last for a continuous period of not less than 12 months. The Administrator shall have discretion to determine if a termination due to Disability has occurred.

(q) Displacement shall, as applied to any Participant, be as defined in any employment agreement, consulting agreement or other similar agreement, if any, to which the Participant is a party, or, if there is no such agreement (or if any such agreement does not address the effect of a termination due to displacement), "Displacement" shall mean the termination of the Participant's employment or service due to the elimination of the Participant's job or position without fault on the part of the Participant (as determined by the Administrator).

(r) Dividend Equivalent Award means a right granted to a Participant pursuant to Section 13 to receive the equivalent value (in cash or shares of Common Stock) of dividends paid on Common Stock.

(s) Effective Date means the effective date of the Plan, as provided in Section 4.

(t) Employee means any person who is an employee of the Corporation or any Affiliate (including entities which become Affiliates after the Effective Date of the Plan). For this purpose, an individual shall be considered to be an Employee only if there exists between the individual and the Corporation or an Affiliate the legal and bona fide relationship of employer and employee (taking into account any Code Section 409A considerations); provided, however, that, with respect to Incentive Options, "Employee" means any person who is considered an employee of the Corporation or any Parent or Subsidiary for purposes of Treas. Reg. Section 1.421-1(h) (or any successor provision related thereto).

(u) Exchange Act means the Securities Exchange Act of 1934, as amended.

(v) Fair Market Value per share of the Common Stock shall be established in good faith by the Administrator and, unless otherwise determined by the Administrator, the Fair Market Value shall be determined in accordance with the following provisions: (A) if the shares of Common Stock are listed for trading on the New York Stock Exchange, the American Stock Exchange or the Nasdaq Stock Market, the Fair Market Value shall be the closing sales price per share of the shares on the New York Stock Exchange, the American Stock Exchange or the Nasdaq Stock Market (as applicable) on the date an Option is granted or other determination is made (such date of determination being referred to herein as a "valuation date"), or, if there is no transaction on such date, then on the trading date nearest preceding the valuation date for which closing price information is available, and, provided further, if the shares are not listed for trading on the New York Stock Exchange, the American Stock Exchange or the Nasdaq Stock Market, the Fair Market Value shall be the average between the highest bid and lowest asked prices for such stock on the date of grant or other valuation date as reported on the Nasdaq OTC Bulletin Board Service or by the National Quotation Bureau, Incorporated or a comparable service; or (B) if the shares of Common Stock are not listed or reported in any of the foregoing, then the Fair Market Value shall be determined by the Administrator based on such valuation measures or other factors as it deems appropriate. Notwithstanding the foregoing, (i) with respect to the grant of Incentive Options, the Fair Market Value shall be determined by the Administrator in accordance with the applicable provisions of Section 20.2031-2 of the Federal Estate Tax Regulations, or in any other manner consistent with the Code Section 422; and (ii) Fair Market Value shall be determined in accordance with Code Section 409A to the extent required.

(w) Freestanding SAR means an SAR that is granted without relation to an Option, as provided in Section 9.

(x) Incentive Option means an Option that is designated by the Administrator as an Incentive Option pursuant to Section 7 and intended to meet the requirements of incentive stock options under Code Section 422.

(y) Independent Contractor means an independent contractor, consultant or advisor providing services to the Corporation or an Affiliate.

(z) Initial Option means an Option granted to a Nonemployee Director of the Corporation upon initial election or appointment to the Board, as provided in Section 8.

(aa) Nonemployee Director means a Director of the Board who is not an Employee of the Corporation or an Affiliate and who is eligible to receive a Director Option pursuant to Section 8.

(bb) Nonqualified Option means an Option granted under Section 7 or Section 8 that is not intended to qualify as an incentive stock option under Code Section 422.

(cc) Option means a stock option granted under Section 7 or Section 8 that entitles the holder to purchase from the Corporation a stated number of shares of Common Stock at the price set forth in an Award Agreement.

(dd) Option Period means the term of an Option, as provided in Section 7(d) and Section 8(f).

(ee) Option Price means the price at which an Option may be exercised, as provided in Section 7(b) and Section 8(e).

(ff) Parent means a "parent corporation," whether now or hereafter existing, as defined in Section 424(e) of the Code.

(gg) Participant means an individual employed by, or providing services to, the Corporation or an Affiliate who satisfies the requirements of Section 6 and is selected by the Administrator to receive an Award under the Plan.

(hh) Performance Award means a Performance Share Award and/or a Performance Unit Award, as provided in Section 11.

(ii) Performance Measures mean one or more performance factors which may be established by the Administrator with respect to an Award. Performance factors may be based on such corporate, business unit or division and/or individual performance factors and criteria as the Administrator in its discretion may deem appropriate; provided, however, that, such performance factors shall be limited to one or more of the following (as determined by the Administrator in its discretion): (i) cash flow; (ii) return on equity; (iii) return on assets; (iv) earnings per share; (v) achievement of clinical development or regulatory milestones; (vi) operations expense efficiency milestones; (vii) consolidated earnings before or after taxes (including earnings before interest, taxes, depreciation and amortization); (viii) net income; (ix) operating income; (x) book value per share; (xi) return on investment; (xii) return on capital; (xiii) improvements in capital structure; (xiv) expense management; (xv) profitability of an identifiable business unit or product; (xvi) maintenance or improvement of profit margins; (xvii) stock price or total stockholder return; (xviii) market share; (xix) revenues or sales; (xx) costs; (xxi) working capital; (xxii) economic wealth created; (xxiii) strategic business criteria; (xxiv) efficiency ratio(s); (xxv) achievement of division, group, function or corporate financial, strategic or operational goals; and (xxvi) comparisons with stock market indices or performances of metrics of peer companies. To the extent that Section 162(m) of the Code is applicable, the Administrator shall, within the time and in the manner prescribed by Section 162(m) of the Code, define in an objective fashion the manner of calculating the Performance Measures it selects to use for Participants during any specific performance period. Such performance factors may be adjusted or modified due to extraordinary items, transactions, events or developments, or in recognition of, or in anticipation of, any other unusual or nonrecurring events affecting the Corporation or the financial statements of the Corporation, or in response to, or in anticipation of, changes in applicable laws, regulations, accounting principles or business conditions, in each case as determined by the Administrator.

(jj) Performance Share means an Award granted under Section 11, in an amount determined by the Administrator and specified in an Award Agreement, stated with reference to a specified number of shares of Common Stock, that entitles the holder to receive shares of Common Stock, a cash payment or a combination of Common Stock and cash (as determined by the Administrator), subject to the terms of the Plan and the terms and conditions established by the Administrator.

(kk) Performance Unit means an Award granted under Section 11, in an amount determined by the Administrator and specified in an Award Agreement, that entitles the holder to receive Shares of Common Stock, a cash payment or a combination of Common Stock and cash (as determined by the Administrator), subject to the terms of the Plan and the terms and conditions established by the Administrator.

(ll) Phantom Stock Award means an Award granted under Section 12, entitling a Participant to a payment in cash, shares of Common Stock or a combination of cash and Common Stock (as determined by the Administrator), following the completion of the applicable vesting period and compliance with the terms of the Plan and other terms and conditions established by the Administrator. The unit value of a Phantom Stock Award shall be based on the Fair Market Value of a share of Common Stock.

(mm) Plan means the Targacept, Inc. 2006 Stock Incentive Plan, as amended and restated through March 9, 2011, and as it may be hereafter amended and/or restated.

(nn) Prior Plan or Prior Plans means the 2000 Equity Incentive Plan of Targacept, Inc., as amended, and any other employee stock incentive plan maintained by the Corporation prior to the Effective Date of the Plan.

(oo) Public Offering Date means the date on which the Underwriting Agreement between the Corporation and the managing underwriters of the Corporation's initial public offering of its Common Stock was executed and delivered.

(pp) Related SAR means an SAR granted under Section 9 that is granted in relation to a particular Option and that can be exercised only upon the surrender to the Corporation, unexercised, of that portion of the Option to which the SAR relates.

(qq) Restricted Award means a Restricted Stock Award and/or a Restricted Stock Unit Award, as provided in Section 10.

(rr) Restricted Stock Award means shares of Common Stock awarded to a Participant under Section 10. Shares of Common Stock subject to a Restricted Stock Award shall cease to be restricted when, in accordance with the terms of the Plan and the terms and conditions established by the Administrator, the shares vest and become transferable and free of substantial risks of forfeiture.

(ss) Restricted Stock Unit means a Restricted Award granted to a Participant pursuant to Section 10 which is settled (i) by the delivery of one share of Common Stock for each Restricted Stock Unit, (ii) in cash in an amount equal to the Fair Market Value of one share of Common Stock for each Restricted Stock Unit, or (iii) in a combination of cash and Shares equal to the Fair Market Value of one share of Common Stock for each Restricted Stock Unit, as determined by the Administrator. A Restricted Stock Unit Award represents the promise of the Corporation to deliver shares, cash or a combination thereof, as applicable, at the end of the Restriction Period, subject to compliance with the terms of the Plan and the terms and conditions established by the Administrator.

(tt) Retirement shall, as applied to any Participant, be as defined in any employment agreement, consulting agreement or other similar agreement, if any, to which the Participant is a party, or, if there is no such agreement (or if any such agreement does address the effect of termination due to retirement), "Retirement" shall mean retirement in accordance with the retirement policies and

procedures established by the Corporation, as determined by the Administrator (taking into account any Code Section 409A considerations).

(uu) SAR means a stock appreciation right granted under Section 9 entitling the Participant to receive, with respect to each share of Common Stock encompassed by the exercise of such SAR, the excess of the Fair Market Value on the date of exercise over the SAR base price, subject to the terms of the Plan and any other terms and conditions established by the Administrator. References to "SARs" include both Related SARs and Freestanding SARs, unless the context requires otherwise.

(vv) Securities Act means the Securities Act of 1933, as amended.

(ww) Subsidiary means a "subsidiary corporation," whether now or hereafter existing, as defined in Section 424(f) of the Code.

(xx) Termination Date means the date of termination of a Participant's employment or service for any reason, as determined by the Administrator in its discretion.

2. Purpose

The purpose of the Plan is to encourage and enable selected Employees, Directors and Independent Contractors of the Corporation and its Affiliates to acquire or to increase their holdings of Common Stock of the Corporation and other proprietary interests in the Corporation in order to promote a closer identification of their interests with those of the Corporation and its stockholders, thereby further stimulating their efforts to enhance the efficiency, soundness, growth and stockholder value of the Corporation. This purpose will be carried out through the granting of Awards to selected Employees, Independent Contractors and Directors, including the granting to selected Participants of Options in the form of Incentive Stock Options and Nonqualified Options; SARs in the form of Related SARs and Freestanding SARs; Restricted Awards in the form of Restricted Stock Awards and Restricted Stock Units; Performance Awards in the form of Performance Shares and Performance Units; Phantom Stock Awards; Director Options in the form of Initial Options and Annual Options; and/or Dividend Equivalent Awards.

3. Administration of the Plan

(a) The Plan shall be administered by the Board of Directors of the Corporation or, upon its delegation, by the Committee. Unless the Board determines otherwise, the Committee shall be comprised solely of two or more "non-employee directors," as such term is defined in Rule 16b-3 under the Exchange Act, or as may otherwise be permitted under Rule 16b-3. Further, to the extent required by Section 162(m) of the Code, the Plan shall be administered by a committee comprised of two or more "outside directors" (as such term is defined in Section 162(m)) or as may otherwise be permitted under Section 162(m). For the purposes of the Plan, the term "Administrator" shall refer to the Board and, upon its delegation to the Committee of all or part of its authority to administer the Plan, to the Committee. Notwithstanding the foregoing, the Board shall have sole authority to grant discretionary Awards (that is, Awards other than Director Options) to Directors who are not employees of the Corporation or its Affiliates.

(b) Subject to the provisions of the Plan, the Administrator shall have full and final authority in its discretion to take any action with respect to the Plan including, without limitation, the authority (i) to determine all matters relating to Awards, including selection of individuals to be granted Awards, the types of Awards, the number of shares of the Common Stock, if any, subject to an Award, and all terms,

conditions, restrictions and limitations of an Award; (ii) to prescribe the form or forms of Award Agreements evidencing any Awards granted under the Plan; (iii) to establish, amend and rescind rules and regulations for the administration of the Plan; and (iv) to construe and interpret the Plan, Awards and Award Agreements made under the Plan, to interpret rules and regulations for administering the Plan and to make all other determinations deemed necessary or advisable for administering the Plan. In addition, (i) the Administrator shall have the authority, in its sole discretion, to accelerate the date that any Award which was not otherwise exercisable, vested or earned shall become exercisable, vested or earned in whole or in part without any obligation to accelerate such date with respect to any other Award granted to any recipient; and (ii) the Administrator also may in its sole discretion modify or extend the terms and conditions for exercise, vesting or earning of an Award (in each case, taking into account any Code Section 409A considerations). The Administrator may determine that a Participant's rights, payments and/or benefits with respect to an Award (including but not limited to any shares issued or issuable and/or cash paid or payable with respect to an Award) shall be subject to reduction, cancellation, forfeiture or recoupment upon the occurrence of certain specified events, in addition to any otherwise applicable vesting or performance conditions of an Award. Such events may include, but shall not be limited to, termination of employment or service for cause, violation of policies of the Corporation or an Affiliate, breach of non-solicitation, noncompetition, confidentiality or other restrictive covenants that may apply to the Participant, or other conduct by the Participant that is determined by the Administrator to be detrimental to the business or reputation of the Corporation or any Affiliate. In addition, the Administrator shall have the authority and discretion to establish terms and conditions of Awards (including but not limited to the establishment of subplans) as the Administrator determines to be necessary or appropriate to conform to the applicable requirements or practices of jurisdictions outside of the United States. In addition to action by meeting in accordance with applicable laws, any action of the Administrator with respect to the Plan may be taken by a written instrument signed by all of the members of the Board or Committee, as appropriate, and any such action so taken by written consent shall be as fully effective as if it had been taken by a majority of the members at a meeting duly held and called. No member of the Board or Committee, as applicable, shall be liable while acting as Administrator for any action or determination made in good faith with respect to the Plan, an Award or an Award Agreement. The members of the Board or Committee, as applicable, shall be entitled to indemnification and reimbursement in the manner provided in the Corporation's certificate of incorporation and bylaws and/or under applicable law.

(c) Notwithstanding the other provisions of Section 3, the Administrator may delegate to one or more officers of the Corporation the authority to grant Awards, and to make any or all of the determinations reserved for the Administrator in the Plan and summarized in Section 3(b) with respect to such Awards (subject to any restrictions imposed by applicable laws, rules and regulations and such terms and conditions as may be established by the Administrator); provided, however, that, to the extent required by Section 16 of the Exchange Act or Section 162(m) of the Code, the Participant, at the time of said grant or other determination, (i) is not deemed to be an officer or director of the Corporation within the meaning of Section 16 of the Exchange Act; and (ii) is not deemed to be a Covered Employee as defined under Section 162(m) of the Code. To the extent that the Administrator has delegated authority to grant Awards pursuant to this Section 3(c) to one or more officers of the Corporation, references to the Administrator shall include references to such officer or officers, subject, however, to the requirements of the Plan, Rule 16b-3, Section 162(m) of the Code and other applicable laws, rules and regulations.

4. Effective Date

The Effective Date of the Plan shall be the day prior to the Public Offering Date. The Plan was amended effective June 14, 2007, amended and restated effective November 28, 2007, amended effective June 10, 2009, and amended and restated effective March 9, 2011. Awards may be granted under the

Plan on and after the Effective Date, but not after the date that is the tenth anniversary less one day after the Effective Date. Awards that are outstanding at the end of the Plan term (or such earlier termination date as may be established by the Board pursuant to Section 15(a)) shall continue in accordance with their terms, unless otherwise provided in the Plan or an Award Agreement.

5. Shares of Stock Subject to the Plan; Award Limitations

(a) *Shares of Stock Subject to the Plan*: Subject to adjustments as provided in Section 5(d), the aggregate number of shares of Common Stock that may be issued pursuant to Awards granted under the Plan shall not exceed the sum of (i) 5,620,000 shares, plus (ii) no more than 30,968 shares of Common Stock remaining available for issuance as of the Effective Date of the Plan under any Prior Plan, plus (iii) no more than 1,631,110 shares of Common Stock if and to the extent that any of such shares are subject to an award granted under a Prior Plan, which award was or is forfeited, cancelled, terminated, expires or lapses for any reason without the issuance of shares pursuant to the award. Shares delivered under the Plan shall be authorized but unissued shares, treasury shares or shares purchased on the open market or by private purchase. The Corporation hereby reserves sufficient authorized shares of Common Stock to meet the grant of Awards hereunder.

(b) *Award Limitation*s: Notwithstanding any provision in the Plan to the contrary, the following limitations shall apply to Awards granted under the Plan, in each case subject to adjustments pursuant to Section 5(d):

(i) The maximum number of shares of Common Stock that may be issued under the Plan pursuant to the grant of Incentive Options shall not exceed 7,282,078 shares, or such lesser number of shares as may be available under the Plan pursuant to Section 5(a) herein;

(ii) In any calendar year, no Participant may be granted Options and SARs that are not related to an Option for more than 500,000 shares of Common Stock;

(iii) No Participant may be granted Awards in any calendar year for more than 500,000 shares of Common Stock; and

(iv) No Participant may be paid more than $1,000,000 with respect to any cash-settled award or awards which were granted during any single calendar year.

(For purposes of Section 5(b)(ii) and (iii), an Option and Related SAR shall be treated as a single Award.)

(c) *Shares Not Subject to Limitations*: The following will not be applied to the share limitations of Section 5(a) above: (i) dividends, including dividends paid in shares, or dividend equivalents paid in cash in connection with outstanding Awards; (ii) Awards which by their terms are settled in cash rather than the issuance of shares; and (iii) any shares subject to an Award under the Plan which Award is forfeited, cancelled, terminated, expires or lapses for any reason or any shares subject to an Award which shares are repurchased or reacquired by the Corporation.

(d) *Adjustments*: If there is any change in the outstanding shares of Common Stock because of a merger, consolidation or reorganization involving the Corporation or an Affiliate, or if the Board of Directors of the Corporation declares a stock dividend, stock split distributable in shares of Common Stock, reverse stock split, combination or reclassification of the Common Stock, or if there is a similar change in the capital stock structure of the Corporation or an Affiliate affecting the Common Stock, the

number of shares of Common Stock reserved for issuance under the Plan shall be correspondingly adjusted, and the Administrator shall make such adjustments to Awards and to any provisions of this Plan as the Administrator deems equitable to prevent dilution or enlargement of Awards or as may be otherwise advisable.

6. Eligibility

An Award may be granted only to an individual who satisfies all of the following eligibility requirements on the date the Award is granted:

(a) The individual is either (i) an Employee, (ii) a Director, or (iii) an Independent Contractor.

(b) With respect to the grant of Incentive Options, the individual is otherwise eligible to participate under Section 6, is an Employee of the Corporation or a Parent or Subsidiary and does not own, immediately before the time that the Incentive Option is granted, stock possessing more than 10% of the total combined voting power of all classes of stock of the Corporation or a Parent or Subsidiary. Notwithstanding the foregoing, an Employee who owns more than 10% of the total combined voting power of the Corporation or a Parent or Subsidiary may be granted an Incentive Option if the Option Price is at least 110% of the Fair Market Value of the Common Stock, and the Option Period does not exceed five years. For this purpose, an individual will be deemed to own stock which is attributable to him under Section 424(d) of the Code.

(c) With respect to the grant of substitute awards or assumption of awards in connection with a merger, consolidation, acquisition, reorganization or similar business combination involving the Corporation or an Affiliate, the recipient is otherwise eligible to receive the Award and the terms of the award are consistent with the Plan and applicable laws, rules and regulations (including, to the extent deemed applicable, the federal securities laws registration provisions, Code Section 409A and Code Section 424(a)).

(d) The individual, being otherwise eligible under this Section 6, is selected by the Administrator as an individual to whom an Award shall be granted (as defined above, a “Participant”).

7. Options

(a) *Grant of Options*: Subject to the limitations of the Plan, the Administrator may in its sole and absolute discretion grant Options to such eligible individuals in such numbers, subject to such terms and conditions, and at such times as the Administrator shall determine. Both Incentive Options and Nonqualified Options may be granted under the Plan, as determined by the Administrator; provided, however, that Incentive Options may only be granted to Employees of the Corporation or a Parent or Subsidiary. To the extent that an Option is designated as an Incentive Option but does not qualify as such under Section 422 of the Code, the Option (or portion thereof) shall be treated as a Nonqualified Option. An Option may be granted with or without a Related SAR.

(b) *Option Price*: The Option Price shall be established by the Administrator and stated in the Award Agreement evidencing the grant of the Option; provided, that (i) the Option Price of an Incentive Option shall be no less than 100% of the Fair Market Value per share of the Common Stock as determined on the date the Option is granted (or 110% of the Fair Market Value with respect to Incentive Options granted to an Employee who owns stock possessing more than 10% of the total voting power of all classes of stock of the Corporation or a Parent or Subsidiary, as provided in Section 6(b)); (ii) the

Option Price of a Nonqualified Option shall be no less than 85% of the Fair Market Value per share of the Common Stock on the date the Option is granted; and (iii) in no event shall the Option Price per share of any Option be less than the par value per share of the Common Stock. Notwithstanding the foregoing, the Administrator may in its discretion authorize the grant of substitute or assumed options of an acquired entity with an Option Price not equal to at least 100% of the Fair Market Value of the stock on the date of grant if the terms of such substitution or assumption otherwise comply, to the extent deemed applicable, with Code Section 409A and Code Section 424(a).

(c) *Date of Grant*: An Option shall be considered to be granted on the date that the Administrator acts to grant the Option or on such other date as may be established by the Administrator in accordance with applicable laws.

(d) *Option Period and Limitations on the Right to Exercise Options*:

(i) The Option Period shall be determined by the Administrator at the time the Option is granted and shall be stated in the Award Agreement. With respect to Incentive Options, the Option Period shall not extend more than 10 years from the date on which the Option is granted (or five years with respect to Incentive Options granted to an Employee who owns stock possessing more than 10% of the total combined voting power of all classes of stock of the Corporation or a Parent or Subsidiary, as provided in Section 6(b)). Any Option or portion thereof not exercised before expiration of the Option Period shall terminate. The period or periods during which, and conditions pursuant to which, an Option may vest and become exercisable shall be determined by the Administrator in its discretion, subject to the terms of the Plan.

(ii) An Option may be exercised by giving written notice to the Corporation in form acceptable to the Administrator at such place and subject to such conditions as may be established by the Administrator or its designee. Such notice shall specify the number of shares to be purchased pursuant to an Option and the aggregate purchase price to be paid therefor and shall be accompanied by payment of such purchase price. The total number of shares that may be acquired upon exercise of an Option shall be rounded down to the nearest whole share. Unless an Award Agreement provides otherwise, such payment shall be in the form of cash or cash equivalent; provided that, where permitted by the Administrator and applicable laws, rules and regulations (and subject to such terms and conditions as may be established by the Administrator), payment may also be made:

(A) By delivery (by either actual delivery or attestation) of shares of Common Stock owned by the Participant for such time period, if any, as may be determined by the Administrator and otherwise acceptable to the Administrator;

(B) By shares of Common Stock withheld upon exercise;

(C) With respect only to purchases upon exercise of an Option after a public market for the Common Stock exists, by delivery of written notice of exercise to the Corporation and delivery to a broker of written notice of exercise and irrevocable instructions to promptly deliver to the Corporation the amount of sale or loan proceeds to pay the Option Price;

(D) By such other payment methods as may be approved by the Administrator and which are acceptable under applicable law; or

(E) By any combination of the foregoing methods.

Shares tendered or withheld in payment on the exercise of an Option shall be valued at their Fair Market Value on the date of exercise. For the purposes of the Plan, a "public market" for the Common Stock shall be deemed to exist (i) upon consummation of a firm commitment underwritten public offering of the Common Stock pursuant to an effective registration statement under the Securities Act, or (ii) if the Administrator otherwise determines that there is an established public market for the Common Stock.

(iii) Unless the Administrator determines otherwise, no Option granted to a Participant who was an Employee at the time of grant shall be exercised unless the Participant is, at the time of exercise, an Employee as described in Section 6(a), and has been an Employee continuously since the date the Option was granted, subject to the following:

(A) The employment relationship of a Participant shall be treated as continuing intact for any period that the Participant is on military or sick leave or other bona fide leave of absence, provided that the period of such leave does not exceed 90 days, or, if longer, as long as the Participant's right to reemployment is guaranteed either by statute or by contract. The employment relationship of a Participant shall also be treated as continuing intact while the Participant is not in active service because of Disability. The Administrator shall have sole authority to determine whether a Participant is disabled under the Plan and, if applicable, the Participant's Termination Date.

(B) Unless the Administrator determines otherwise (taking into account any Code Section 409A considerations), if the employment of a Participant is terminated because of Disability or death, the Option may be exercised only to the extent vested and exercisable on the Participant's Termination Date, except that the Administrator may in its sole discretion (taking into account any Code Section 409A considerations) accelerate the date for exercising all or any part of the Option which was not otherwise vested and exercisable on the Termination Date. The Option must be exercised, if at all, prior to the first to occur of the following, whichever shall be applicable: (X) the close of the one-year period following the Termination Date (or such other period stated in the Award Agreement); or (Y) the close of the Option Period. In the event of the Participant's death, such Option shall be exercisable by such person or persons as shall have acquired the right to exercise the Option by will or by the laws of intestate succession.

(C) Unless the Administrator determines otherwise (taking into account any Code Section 409A considerations), if the employment of the Participant is terminated for any reason other than Disability, death or for "Cause," his Option may be exercised to the extent vested and exercisable on his Termination Date, except that the Administrator may in its sole discretion (taking into account any Code Section 409A considerations) accelerate the date for exercising all or any part of the Option which was not otherwise vested and exercisable on the Termination Date. The Option must be exercised, if at all, prior to the first to occur of the following, whichever shall be applicable: (X) the close of the period of three months next succeeding the Termination Date (or such other period stated in the Award Agreement); or (Y) the close of the Option Period. If the Participant dies following such termination of employment and prior to the earlier of the dates specified in (X) or (Y) of this subparagraph (C), the Participant shall be treated as having died while employed under subparagraph (B) (treating for this purpose the Participant's

date of termination of employment as the Termination Date). In the event of the Participant's death, such Option shall be exercisable by such person or persons as shall have acquired the right to exercise the Option by will or by the laws of intestate succession.

(D) Unless the Administrator determines otherwise (taking into account any Code Section 409A considerations), if the employment of the Participant is terminated for "Cause," his Option shall lapse and no longer be exercisable as of his Termination Date, as determined by the Administrator.

(E) Notwithstanding the foregoing, the Administrator may, in its sole discretion (taking into account any Code Section 409A considerations), accelerate the date for exercising all or any part of an Option which was not otherwise vested and exercisable on the Termination Date, extend the period during which an Option may be exercised, modify the terms and conditions to exercise, or any combination of the foregoing.

(iv) Unless the Administrator determines otherwise (taking into account any Code Section 409A considerations), an Option granted to a Participant who was a Director but who was not an Employee at the time of grant may be exercised only to the extent vested and exercisable on the Participant's Termination Date (unless the termination was for Cause), and must be exercised, if at all, prior to the first to occur of the following, as applicable: (X) the close of the period of six months next succeeding the Termination Date (or such other period stated in the Award Agreement); or (Y) the close of the Option Period. If the services of a Participant are terminated for Cause, his Option shall lapse and no longer be exercisable as of his Termination Date, as determined by the Administrator. Notwithstanding the foregoing, the Administrator may in its sole discretion (taking into account any Code Section 409A considerations), accelerate the date for exercising all or any part of an Option which was not otherwise exercisable on the Termination Date, extend the period during which an Option may be exercised, modify the other terms and conditions to exercise, or any combination of the foregoing.

(v) Unless the Administrator determines otherwise (taking into account any Code Section 409A considerations), an Option granted to a Participant who was an Independent Contractor at the time of grant (and who does not thereafter become an Employee, in which case he shall be subject to the provisions of Section 7(d)(iii)) may be exercised only to the extent vested and exercisable on the Participant's Termination Date (unless the termination was for Cause), and must be exercised, if at all, prior to the first to occur of the following, as applicable: (X) the close of the period of three months next succeeding the Termination Date (or such other period stated in the Award Agreement); or (Y) the close of the Option Period. If the services of a Participant are terminated for Cause, his Option shall lapse and no longer be exercisable as of his Termination Date, as determined by the Administrator. Notwithstanding the foregoing, the Administrator may in its sole discretion (taking into account any Code Section 409A considerations), accelerate the date for exercising all or any part of an Option which was not otherwise exercisable on the Termination Date, extend the period during which an Option may be exercised, modify the other terms and conditions to exercise, or any combination of the foregoing.

(e) *Notice of Disposition*: If shares of Common Stock acquired upon exercise of an Incentive Option are disposed of within two years following the date of grant or one year following the transfer of such shares to a Participant upon exercise, the Participant shall, promptly following such disposition,

notify the Corporation in writing of the date and terms of such disposition and provide such other information regarding the disposition as the Administrator may reasonably require.

(f) *Limitation on Incentive Options*: In no event shall there first become exercisable by an Employee in any one calendar year Incentive Options granted by the Corporation or any Parent or Subsidiary with respect to shares having an aggregate Fair Market Value (determined at the time an Incentive Option is granted) greater than $100,000. To the extent that any Incentive Options are first exercisable by a Participant in excess of such limitation, the excess shall be considered a Nonqualified Option.

(g) *Nontransferability*: Incentive Options shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession or, in the Administrator's discretion, as may otherwise be permitted in accordance with Treas. Reg. Section 1.421-1(b)(2) or any successor provision thereto. Nonqualified Options shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, except as may be permitted by the Administrator in a manner consistent with the registration provisions of the Securities Act. An Option shall be exercisable during the Participant's lifetime only by him, by his guardian or legal representative or by a transferee in a transfer permitted by this Section 7(g). The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

8. Director Options

(a) *General*: Each Nonemployee Director who is otherwise eligible under this Section 8 shall be granted a Director Option or Director Options as provided in Section 8. Director Options shall be designated as Nonqualified Options. Director Options shall be subject to the other terms and conditions of the Plan except as otherwise provided in Section 8.

(b) *Eligibility*: A Director Option may be granted only to an individual who is a Nonemployee Director of the Corporation on the date the Director Option is granted. A Nonemployee Director may also be eligible for other Awards (including but not limited to Options granted pursuant to Section 7), subject to the terms of the Plan and the Administrator's discretion.

(c) *Grant of Initial Options Upon Initial Election or Appointment to the Board*: Each Nonemployee Director who is first elected or appointed to the Board after the Public Offering Date shall receive an Initial Option to purchase 25,000 shares of Common Stock. The date of grant of such an Initial Option shall be the fifth business day after the date of the annual meeting of stockholders as to those Nonemployee Directors who are first elected at an annual meeting of stockholders and the fifth business day after the date of election or appointment to the Board as to those Nonemployee Directors who are first elected or appointed to the Board other than at an annual meeting of stockholders. In addition, a Nonemployee Director who serves as chairman of the Board shall also receive an Initial Option for 10,000 shares when first elected or appointed as chairman. The date of grant of such Initial Option shall be the fifth business day after the date on which the Director is first elected or appointed as chairman of the Board.

(d) *Grant of Annual Options*: Each Nonemployee Director also shall be granted, on an annual basis commencing with the 2007 annual meeting of stockholders, a Director Option to purchase 7,500 shares of Common Stock (or, a Director Option for 12,500 shares, in the case of the chairman of the Board), provided that the Nonemployee Director continues to serve as a member of the Board as of the date of grant. The date of grant of such an Annual Option shall be the fifth business day after the date of the annual or other stockholders meeting at which directors are elected. For the avoidance of

doubt, a Nonemployee Director elected for the first time to the Board at an annual meeting of stockholders shall only receive an Initial Option in connection with such election, and shall not receive an Annual Option on the fifth business day following such meeting as well.

(e) *Option Price*: The price per share of Common Stock at which a Director Option may be exercised shall be 100% of the Fair Market Value per share of the Common Stock on the date the Option is granted.

(f) *Option Period and Limitations on the Right to Exercise Options*:

(i) The Option Period of a Director Option shall be 10 years from the date of grant. Initial Options shall become exercisable as provided in Section 8(f)(i)(A), and Annual Options shall become exercisable as provided in Section 8(f)(i)(B). To the extent that all or part of an Option becomes exercisable but is not exercised, such Option shall accumulate and be exercisable by the Director in whole or in part at any time before the expiration of the Option Period. The total number of shares that may be acquired upon the exercise of an Initial Option or Annual Option shall be rounded down to the nearest whole share. Any Director Option or portion thereof not exercised before expiration of the Option Period shall terminate.

(A) Initial Options. An Initial Option shall vest and become exercisable with respect to one-third of the shares subject to the Option on the earlier of (w) the first anniversary of the date of grant or (x) the business day immediately preceding the date of the Corporation's annual meeting of stockholders that occurs in the calendar year immediately following the calendar year in which the date of grant occurs, provided that the Nonemployee Director remains in service on such earlier date. An Initial Option shall vest and become exercisable with respect to the remaining two-thirds of the shares subject to the Option in pro rata quarterly installments over the second and third years following the date of grant so that an Initial Option will be vested and exercisable in full on the earlier of (y) the third anniversary of the date of grant or (z) the business day immediately preceding the date of the Corporation's annual meeting of stockholders that occurs in the third calendar year following the calendar year in which the date of grant occurs, provided that the Nonemployee Director remains in service as a Director during such periods.

(B) Annual Options. An Annual Option granted shall vest and become exercisable on the earlier of (i) the first anniversary of the date of grant or (ii) the business day immediately preceding the date of the Corporation's annual meeting of stockholders that occurs in the calendar year immediately following the calendar year in which the date of grant occurs, provided that the Nonemployee Director remains in service as a Director on such earlier date.

(ii) Unless the Administrator determines otherwise (taking into account any Code Section 409A considerations), a Director Option granted to a Nonemployee Director at the time of grant may be exercised only to the extent vested and exercisable on the Nonemployee Director's Termination Date (unless the termination was for Cause), and must be exercised, if at all, prior to the first to occur of the following, as applicable: (X) the close of the period of six months next succeeding the Termination Date (or such other period stated in the Award Agreement); or (Y) the close of the Option Period. If the services of a Nonemployee Director are terminated for Cause, his Director Option shall lapse and no longer be exercisable as of his Termination Date, as determined by the Administrator.

(iii) A Director Option shall be exercised by giving written notice to the Administrator or its designee at such time and place as the Administrator shall direct. Such notice shall specify the number of shares to be purchased pursuant to the Director Option and the aggregate purchase price to be paid therefor, and shall be accompanied by the payment of such purchase price. Payment shall be made in accordance with Section 7(d)(ii).

(g) *Nontransferability*: A Director Option shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, except as may be permitted by the Administrator in a manner consistent with the registration provisions of the Securities Act. Except as may be permitted by the preceding sentence, a Director Option shall be exercisable during the Nonemployee Director's lifetime only by him or by his guardian or legal representative. The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

9. Stock Appreciation Rights

(a) *Grant of SARs*: Subject to the limitations of the Plan, the Administrator may in its sole and absolute discretion grant SARs to such eligible individuals, in such numbers, upon such terms and at such times as the Administrator shall determine. SARs may be granted to the holder of an Option (a "Related Option") with respect to all or a portion of the shares of Common Stock subject to the Related Option (a "Related SAR") or may be granted separately to an eligible individual (a "Freestanding SAR"). The base price per share of an SAR shall be no less than 100% of the Fair Market Value per share of the Common Stock on the date the SAR is granted. Notwithstanding the foregoing, the Administrator may in its discretion authorize the grant of substitute or assumed SARs of an acquired entity with a base price per share not equal to at least 100% of the Fair Market Value of the stock on the date of grant, if the terms of such substitution or assumption otherwise comply, to the extent deemed applicable, with Code Section 409A and Code Section 424(a).

(b) *Related SARs*: A Related SAR may be granted either concurrently with the grant of the Related Option or (if the Related Option is a Nonqualified Option) at any time thereafter prior to the complete exercise, termination, expiration or cancellation of such Related Option; provided, however, that Related SARs must be granted in accordance with Code Section 409A. The base price of a Related SAR shall be equal to the Option Price of the Related Option. Related SARs shall be exercisable only at the time and to the extent that the Related Option is exercisable (and may be subject to such additional limitations on exercisability as the Administrator may provide in the agreement), and in no event after the complete termination or full exercise of the Related Option. Notwithstanding the foregoing, a Related SAR that is related to an Incentive Option may be exercised only to the extent that the Related Option is exercisable and only when the Fair Market Value exceeds the Option Price of the Related Option. Upon the exercise of a Related SAR granted in connection with a Related Option, the Option shall be canceled to the extent of the number of shares as to which the SAR is exercised, and upon the exercise of a Related Option, the Related SAR shall be canceled to the extent of the number of shares as to which the Related Option is exercised or surrendered.

(c) *Freestanding SARs*: An SAR may be granted without relationship to an Option (as defined above, a "Freestanding SAR") and, in such case, will be exercisable upon such terms and subject to such conditions as may be determined by the Administrator, subject to the terms of the Plan.

(d) *Exercise of SARs*:

(i) Subject to the terms of the Plan, SARs shall be vested and exercisable in whole or in part upon such terms and conditions as may be established by the Administrator and stated in the applicable Award Agreement. The period during which an SAR may be exercisable shall not exceed 10 years from the date of grant or, in the case of Related SARs, such shorter Option Period as may apply to the Related Option. Any SAR or portion thereof not exercised before expiration of the period established by the Administrator shall terminate.

(ii) SARs may be exercised by giving written notice to the Corporation in form acceptable to the Administrator at such place and subject to such terms and conditions as may be established by the Administrator or its designee. Unless the Administrator determines otherwise, the date of exercise of an SAR shall mean the date on which the Corporation shall have received proper notice from the Participant of the exercise of such SAR.

(iii) Each Participant's Award Agreement shall set forth the extent to which the Participant shall have the right to exercise an SAR following termination of the Participant's employment or service with the Corporation. Such provisions shall be determined in the sole discretion of the Administrator, need not be uniform among all SARs issued pursuant to this Section 9, and may reflect distinctions based on the reasons for termination of employment. Notwithstanding the foregoing, unless the Administrator determines otherwise, no SAR may be exercised unless the Participant is, at the time of exercise, an eligible Participant, as described in Section 6, and has been a Participant continuously since the date the SAR was granted, subject to the provisions of Sections 7(d)(iii), (iv) and (v).

(e) *Payment Upon Exercise*: Subject to the limitations of the Plan, upon the exercise of an SAR, a Participant shall be entitled to receive payment from the Corporation in an amount determined by multiplying (i) the difference between the Fair Market Value of a share of Common Stock on the date of exercise of the SAR over the base price of the SAR by (ii) the number of shares of Common Stock with respect to which the SAR is being exercised. Notwithstanding the foregoing, the Administrator in its discretion may limit in any manner the amount payable with respect to an SAR. The consideration payable upon exercise of an SAR shall be paid in cash, shares of Common Stock (valued at Fair Market Value on the date of exercise of the SAR) or a combination of cash and shares of Common Stock, as determined by the Administrator.

(f) *Nontransferability*: Unless the Administrator determines otherwise, (i) SARs shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, and (ii) SARs may be exercised during the Participant's lifetime only by him or by his guardian or legal representative. The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

10. Restricted Awards

(a) *Grant of Restricted Awards*: Subject to the limitations of the Plan, the Administrator may in its sole and absolute discretion grant Restricted Awards to such individuals for such numbers of shares of Common Stock, upon such terms and at such times as the Administrator shall determine. Such Restricted Awards may be in the form of Restricted Stock Awards and/or Restricted Stock Units that are subject to certain conditions, which conditions must be met in order for the Restricted Award to vest and be earned (in whole or in part) and no longer subject to forfeiture. Restricted Stock Awards shall be payable in shares of Common Stock. Restricted Stock Units shall be payable in cash or shares of

Common Stock, or partly in cash and partly in shares of Common Stock, in accordance with the terms of the Plan and the discretion of the Administrator. The Administrator shall determine the nature, length and starting date of the period, if any, during which a Restricted Award may be earned (the "Restriction Period"), and shall determine the conditions which must be met in order for a Restricted Award to be granted or to vest or be earned (in whole or in part), which conditions may include, but are not limited to, payment of a stipulated purchase price, attainment of performance objectives, continued service or employment for a certain period of time (or a combination of attainment of performance objectives and continued service), Retirement, Displacement, Disability, death, or any combination of such conditions. Notwithstanding the foregoing, Restricted Awards that vest based solely on continued service or the passage of time shall be subject to a minimum Restriction Period of one year (except in the case of (i) Restricted Awards assumed or substituted in connection with mergers, acquisitions or other business transactions, (ii) Restricted Awards granted in connection with the recruitment or hiring of a Participant, and/or (iii) Restricted Awards granted pursuant to any incentive compensation or bonus program established by the Corporation). In the case of Restricted Awards based upon performance criteria, or a combination of performance criteria and continued service, the Administrator shall determine the Performance Measures applicable to such Restricted Awards (subject to Section 1(ii)).

(b) *Vesting of Restricted Awards*: Subject to the terms of the Plan (and taking into account any Code Section 409A considerations), the Administrator shall have sole authority to determine whether and to what degree Restricted Awards have vested and been earned and are payable and to establish and interpret the terms and conditions of Restricted Awards. The Administrator may (taking into account any Code Section 409A considerations) accelerate the date that any Restricted Award granted to a Participant shall be deemed to be vested or earned in whole or in part, without any obligation to accelerate such date with respect to other Restricted Awards granted to any Participant.

(c) *Forfeiture of Restricted Awards*: Unless the Administrator determines otherwise (taking into account any Code Section 409A considerations), if the employment or service of a Participant shall be terminated for any reason and all or any part of a Restricted Award has not vested or been earned pursuant to the terms of the Plan and the individual Award, such Award, to the extent not then vested or earned, shall be forfeited immediately upon such termination and the Participant shall have no further rights with respect thereto.

(d) *Dividend and Voting Rights; Share Certificates*: The Administrator shall have sole discretion to determine whether a Participant shall have dividend rights, voting rights or other rights as a stockholder with respect to shares subject to a Restricted Award which has not yet vested or been earned. If the Administrator so determines, a certificate or certificates for shares of Common Stock subject to a Restricted Award may be issued in the name of the Participant as soon as practicable after the Award has been granted; provided, however, that, notwithstanding the foregoing, the Administrator shall have the right to retain custody of certificates evidencing the shares subject to a Restricted Award and to require the Participant to deliver to the Corporation a stock power, endorsed in blank, with respect to such Award, until such time as the Restricted Award vests (or is forfeited) and is no longer subject to a substantial risk of forfeiture.

(e) *Nontransferability*: Unless the Administrator determines otherwise, Restricted Awards that have not vested shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, and the recipient of a Restricted Award shall not sell, transfer, assign, pledge or otherwise encumber shares subject to the Award until the Restriction Period has expired and until all conditions to vesting have been met. The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

11. Performance Awards

(a) *Grant of Performance Awards*: Subject to the terms of the Plan, the Administrator may in its discretion grant Performance Awards to such eligible individuals upon such terms and conditions and at such times as the Administrator shall determine. Performance Awards may be in the form of Performance Shares and/or Performance Units. An Award of a Performance Share is a grant of a right to receive shares of Common Stock, the cash value thereof, or a combination thereof (as determined in the Administrator's discretion), which is contingent upon the achievement of performance or other objectives during a specified period and which has a value on the date of grant equal to the Fair Market Value of a share of Common Stock. An Award of a Performance Unit is a grant of a right to receive shares of Common Stock, a designated dollar value amount of Common Stock or a combination thereof (as determined in the Administrator's discretion) which is contingent upon the achievement of performance or other objectives during a specified period, and which has an initial value determined in a dollar amount established by the Administrator at the time of grant. Subject to Section 5(b), the Administrator shall have complete discretion in determining the number of Performance Units and/or Performance Shares granted to any Participant. The Administrator shall determine the nature, length and starting date of the period during which a Performance Award may be earned (the "Performance Period"), and shall determine the conditions which must be met in order for a Performance Award to be granted or to vest or be earned (in whole or in part), which conditions may include but are not limited to specified performance objectives, continued service or employment for a certain period of time, or a combination of such conditions. Subject to Section 1(ii), the Administrator shall determine the Performance Measures to be used in valuing Performance Awards.

(b) *Earning of Performance Awards*: Subject to the terms of the Plan (and taking into account any Code Section 409A considerations), the Administrator shall have sole authority to determine whether and to what degree Performance Awards have been earned and are payable and to interpret the terms and conditions of Performance Awards and the provisions of Section 11. The Administrator, in its sole and absolute discretion, may (taking into account any Code Section 409A considerations) accelerate the date that any Performance Award granted to a Participant shall be deemed to be earned in whole or in part, without any obligation to accelerate such date with respect to other Awards granted to any Participant.

(c) *Form of Payment*: Payment of the amount to which a Participant shall be entitled upon earning a Performance Award shall be made in cash, shares of Common Stock, or a combination of cash and shares of Common Stock, as determined by the Administrator in its sole discretion. Payment may be made in a lump sum or in installments upon such terms as may be established by the Administrator.

(d) *Forfeiture of Performance Awards*: Unless the Administrator determines otherwise (taking into account any Code Section 409A considerations), if the employment or service of a Participant shall terminate for any reason and the Participant has not earned all or part of a Performance Award pursuant to the terms of the Plan and individual Award, such Award, to the extent not then earned, shall be forfeited immediately upon such termination and the Participant shall have no further rights with respect thereto.

(e) *Nontransferability:* Unless the Administrator determines otherwise, Performance Awards that have not been earned shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, and the recipient of a Performance Award shall not sell, transfer, assign, pledge or otherwise encumber any shares subject to the Award until the Performance Period has expired and until the conditions to earning the Award have been met. The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

12. Phantom Stock Awards

(a) *Grant of Phantom Stock Awards*: Subject to the terms of the Plan, the Administrator may in its discretion grant Phantom Stock Awards to such eligible individuals, in such numbers, upon such terms and at such times as the Administrator shall determine. A Phantom Stock Award is an Award to a Participant of a number of hypothetical share units with respect to shares of Common Stock, with a value per unit based on the Fair Market Value of a share of Common Stock.

(b) *Vesting of Phantom Stock Awards*: Subject to the terms of the Plan (and taking into account any Code Section 409A considerations), the Administrator shall have sole authority to determine whether and to what degree Phantom Stock Awards have vested and are payable and to interpret the terms and conditions of Phantom Stock Awards.

(c) *Forfeiture of Phantom Stock Awards*: Unless the Administrator determines otherwise (taking into account any under Code Section 409A considerations), if the employment or service of a Participant shall be terminated for any reason and all or any part of a Phantom Stock Award has not vested and become payable pursuant to the terms of the Plan and the individual Award, such Award, to the extent not then vested or earned, shall be forfeited immediately upon such termination and the Participant shall have no further rights with respect thereto.

(d) *Payment of Phantom Stock Awards*: Upon vesting of all or a part of a Phantom Stock Award and satisfaction of such other terms and conditions as may be established by the Administrator, the Participant shall be entitled to a payment of an amount equal to the Fair Market Value of one share of Common Stock with respect to each such Phantom Stock unit which has vested and is payable. Payment may be made, in the discretion of the Administrator, in cash or in shares of Common Stock valued at their Fair Market Value on the applicable vesting date or dates (or other date or dates determined by the Administrator), or in a combination thereof. The Administrator may, however, establish a limitation on the amount payable in respect of each share of Phantom Stock. Payment may be made in a lump sum or upon such terms as may be established by the Administrator.

(e) *Nontransferability*: Unless the Administrator determines otherwise, (i) Phantom Stock Awards that have not vested shall not be transferable (including by sale, assignment, pledge or hypothecation) other than by will or the laws of intestate succession, (ii) Phantom Stock Awards may be exercised during the Participant's lifetime only by him or by his guardian or legal representative, and (iii) shares of Common Stock (if any) subject to a Phantom Stock Award may not be sold, transferred, assigned, pledged or otherwise encumbered until the Phantom Stock Award has vested and all other conditions established by the Administrator have been met. The designation of a beneficiary in accordance with Section 19(g) does not constitute a transfer.

13. Dividends and Dividend Equivalents

The Administrator may, in its sole discretion, provide that the Awards granted under the Plan earn dividends or dividend equivalents; provided, however, that dividends and dividend equivalents, if any, on unearned or unvested awards shall not be paid (even if accrued) unless and until the underlying Award (or portion thereof) has vested and/or been earned. Any crediting of dividends or dividend equivalents may be subject to such additional restrictions and conditions as the Administrator may establish, including reinvestment in additional shares of Common Stock or share equivalents. Notwithstanding the other provisions herein, any dividends or dividend equivalent rights related to an Award shall be structured in a manner so as to avoid causing the Award and related dividends or

dividend equivalent rights to be subject to Code Section 409A or shall otherwise be structured so that the Award and the dividends or dividend equivalents are in compliance with Code Section 409A.

14. No Right or Obligation of Continued Employment or Service

Neither the Plan, the grant of an Award nor any other action related to the Plan shall confer upon the Participant any right to continue in the employment or service of the Corporation or an Affiliate as an Employee, Director or Independent Contractor or to interfere in any way with the right of the Corporation or an Affiliate to terminate the Participant's employment or service at any time.

15. Amendment and Termination of the Plan

(a) *Amendment and Termination of Plan*: The Plan may be amended, altered and/or terminated at any time by the Board; provided, that (i) approval of an amendment to the Plan by the stockholders of the Corporation shall be required to the extent, if any, that stockholder approval of such amendment is required by applicable law, rule or regulation; and (ii) except for adjustments made pursuant to Section 5(d), (A) the Option Price for any outstanding Option or base price of any outstanding SAR may not be decreased after the date of grant and (B) as of any particular date, no outstanding Option or SAR that has an Option Price or base price above Fair Market Value on such date may be surrendered to the Corporation as consideration for the grant of a new Option or SAR with a lower Option Price or base price than the original Option or SAR, as the case may be, or for another equity award, in each case (clauses (A) and (B)) without stockholder approval.

(b) *Amendment and Termination of Awards*: The Administrator may amend, alter or terminate any Award granted under the Plan, prospectively or retroactively, but such amendment, alteration or termination of an Award shall not, without the consent of the recipient of an outstanding Award, materially adversely affect the rights of the recipient with respect to the Award.

(c) *Unilateral Authority of Administrator to Modify Plan and Awards*: Notwithstanding Section 15(a) and Section 15(b) herein, the following provisions shall apply:

(i) The Administrator shall have unilateral authority to amend the Plan and any Award (without Participant consent and without stockholder approval, unless such stockholder approval is required by applicable laws, rules or regulations) to the extent necessary to comply with applicable laws, rules or regulations or changes to applicable laws, rules or regulations (including but not limited to Code Section 409A, Code Section 422 and federal securities laws).

(ii) The Administrator shall have unilateral authority to make adjustments to the terms and conditions of Awards in recognition of unusual or nonrecurring events affecting the Corporation or any Affiliate, or the financial statements of the Corporation or any Affiliate, or of changes in accounting principles, if the Administrator determines that such adjustments are appropriate in order to prevent dilution or enlargement of the benefits or potential benefits intended to be made available under the Plan or necessary or appropriate to comply with applicable accounting principles.

16. Restrictions on Awards and Shares

The Corporation may impose such restrictions on Awards, shares and any other benefits underlying Awards hereunder as it may deem advisable, including without limitation restrictions under the federal securities laws, the requirements of any stock exchange or similar organization and any blue

sky, state or foreign securities laws applicable to such securities. Notwithstanding any other Plan provision to the contrary, the Corporation shall not be obligated to issue, deliver or transfer shares of Common Stock under the Plan, make any other distribution of benefits under the Plan, or take any other action, unless such delivery, distribution or action is in compliance with all applicable laws, rules and regulations (including but not limited to the requirements of the Securities Act). The Corporation may cause a restrictive legend to be placed on any certificate issued pursuant to an Award hereunder in such form as may be prescribed from time to time by applicable laws and regulations or as may be advised by legal counsel.

17. Change in Control

The Administrator shall (taking into account any Code Section 409A considerations) have sole discretion to determine the effect, if any, on an Award, including but not limited to the vesting, earning and/or exercisability of an Award, in the event of a Change in Control. Without limiting the effect of the foregoing, in the event of a Change in Control, the Administrator's discretion shall include, but shall not be limited to, the discretion to determine that an Award shall vest, be earned or become exercisable in whole or in part, shall be assumed or substituted for another award, shall be cancelled without the payment of consideration, shall be cancelled in exchange for a cash payment or other consideration, and/or that other actions (or no action) shall be taken with respect to the Award. The Administrator also has discretion to determine that acceleration or any other effect of a Change in Control on an Award shall be subject to both the occurrence of a Change in Control event and termination of employment or service of the Participant. Any such determination of the Administrator may be, but shall not be required to be, stated in an individual Award Agreement.

18. Compliance with Code Section 409A

(a) *General*: Notwithstanding any other provision in the Plan or an Award to the contrary, if and to the extent that Code Section 409A is deemed to apply to the Plan or any Award granted under the Plan, it is the general intention of the Corporation that the Plan and all such Awards shall, to the extent practicable, comply with Code Section 409A, and the Plan and any such Award shall, to the extent practicable, be construed in accordance therewith. Deferrals of shares or any other benefits distributable pursuant to an Award otherwise exempt from Code Section 409A in a manner that would cause Code Section 409A to apply shall not be permitted unless such deferrals are in compliance with Code Section 409A. Without in any way limiting the effect of the foregoing, (i) in the event that exemption from or compliance with Code Section 409A requires that any special terms, provisions or conditions be included in the Plan or any Award, then such terms, provisions and conditions shall, to the extent practicable, be deemed to be made a part of the Plan or Award, as applicable; and (ii) terms used in the Plan or an Award Agreement shall be construed in accordance with Code Section 409A if and to the extent required. Further, in the event that the Plan or any Award shall be deemed not to comply with Code Section 409A, then neither the Corporation, the Administrator nor its or their designees or agents shall be liable to any Participant or other person for actions, decisions or determinations made in good faith.

(b) *Specific Terms Applicable to Awards Subject to Code Section 409A*: Without limiting the effect of Section 18(a), above, and notwithstanding any other provision in the Plan to the contrary, the following provisions shall, to the extent required under Code Section 409A, apply with respect to Awards deemed to involve the deferral of compensation under Code Section 409A:

(i) Distributions: Distributions may be made with respect to Awards subject to Code Section 409A not earlier than upon the occurrence of one or more of the following events: (A) separation from service; (B) disability; (C) death; (D) a specified time or pursuant to a fixed

schedule; (E) a change in the ownership or effective control of the Corporation, or in the ownership of a substantial portion of the assets of the Corporation; or (F) the occurrence of an unforeseeable emergency. Each of the preceding distribution events shall be defined and interpreted in accordance with Code Section 409A.

(ii) Specified Employees: With respect to Participants who are "specified employees" (as defined in Code Section 409A), a distribution due to separation from service may not be made before the date that is six months after the date of separation from service (or, if earlier, the date of death of the Participant), except as may be otherwise permitted pursuant to Code Section 409A. The aggregate amount of payments the Participant would have received but for the application of this section shall be paid during the seventh month following separation from service; all remaining payments shall be made in their ordinary course or as may be otherwise permitted under Code Section 409A.

(iii) No Acceleration: Acceleration of the time or schedule of any payment under the Plan that is subject to Code Section 409A (or that would become subject to Code Section 409A as a result of such acceleration) is prohibited, except that, to the extent permitted by the Administrator, acceleration of the time and/or form of a payment, where such accelerations do not violate Code Section 409A, may be allowed.

(iv) Short-Term Deferrals: If and to the extent deemed necessary to comply with short-term deferral exemption under Code Section 409A, shares of Common Stock, cash payments or other benefits subject to an Award shall, upon vesting and/or earning of the Award, be issued and distributed to the Participant (or his beneficiary) no later than the later of (a) the 15th day of the third month following the end of the Participant's first taxable year in which the amount is no longer subject to a substantial risk of forfeiture, or (b) the 15th day of the third month following the end of the Company's first taxable year in which the amount is no longer subject to a substantial risk of forfeiture, or shall otherwise be made in accordance with Code Section 409A.

(v) Deferral Elections:

(A) In the sole discretion of the Administrator, a Participant may be permitted to make an election as to the time or form of any distribution from an Award, provided that, except as specified in (B), (C) and (D) below, such election is made and becomes irrevocable not later than the close of the taxable year preceding the taxable year in which the services for which the Award is granted are to be performed, or at such other time or times as may be permitted under Code Section 409A. Notwithstanding the foregoing, a Participant may cancel a deferral election upon (X) a hardship distribution pursuant to Code Section 401(k), or (Y) upon application for a distribution under section 18(b)(i)(F) (unforeseeable emergency).

(B) In the case of the first year in which the Participant becomes eligible to participate in the Plan, the election described in (A) may be made with respect to services to be performed after the election within 30 days after the date the Participant becomes eligible to participate in the Plan.

(C) In the case of any performance-based compensation (as that term is defined in Code Section 409A), where such compensation is based on services

performed over a period of at least 12 months, the election described in (A) may be made no later than six months before the end of the period.

(D) In the case of any Award subject to a substantial risk of forfeiture (as defined in Code Section 409A), the election described in (A) may be made within 30 days of the date the Participant first obtains a legally binding right to the Award, provided that the Award requires the Participant to perform at least 12 months of service after such election is made.

(vi) Changes to Elections: To the extent that the Administrator, in its sole discretion, permits a subsequent election to delay a payment or change the form of payment that has been specified under (A), (B), (C) or (D) above, the following provisions shall apply:

(A) Such election may not take effect until 12 months after the date on which the election is made;

(B) Where the payment is to be made for reasons other than death, disability or unforeseeable emergency, as those terms are defined in Section 18(b)(i), above, the first payment with respect to which such election is made must be deferred for a period of not less than five years from the date such payment would otherwise have been made; and

(C) Any election related to a payment based upon a specified term or pursuant to a fixed schedule, as such terms are defined in Section 18(b)(i), above, may not be made less than 12 months prior to the date of the first scheduled payment hereunder.

Notwithstanding anything else in this Section 18(b)(vi) to the contrary and consistent with Code Section 409A, (i) the Administrator may elect, or may allow the Participant to elect, on or before December 31, 2007, the time or form of payment of amounts subject to Code Section 409A, provided that any such election occurring in 2007 shall apply only to amounts that are not otherwise payable in 2007 and does not cause an amount to be paid in 2007 that would not otherwise be payable in that year; and (ii) the Administrator may elect, or may allow the Participant to elect, on or before December 31, 2008, the time or form of payment of amounts subject to Code Section 409A, provided that any such election occurring in 2008 shall apply only to amounts that are not otherwise payable in 2008 and does not cause an amount to be paid in 2008 that would not otherwise be payable in that year.

(vii) Termination of Awards Subject to Code Section 409A. As permitted by the Administrator in its sole discretion, and in accordance with Code Section 409A, the Corporation may terminate an Award that is subject to Code Section 409A and distribute benefits to Participants.

19. General Provisions

(a) *Stockholder Rights*: Except as otherwise determined by the Administrator (and subject to the provisions of Section 10(d) regarding Restricted Awards), a Participant and his legal representative, legatees or distributees shall not be deemed to be the holder of any shares subject to an Award and shall not have any rights of a stockholder unless and until certificates for such shares have been issued and delivered to him or them under the Plan. A certificate or certificates for shares of

Common Stock acquired upon exercise of an Option or SAR shall be promptly issued in the name of the Participant (or his beneficiary) and distributed to the Participant (or his beneficiary) as soon as practicable following receipt of notice of exercise and, with respect to Options, payment of the Option Price (except as may otherwise be determined by the Corporation in the event of payment of the Option Price pursuant to Section 7(d)(ii)(C)). Except as otherwise provided in Section 10(d) regarding Restricted Awards, a certificate for any shares of Common Stock issuable pursuant to a Restricted Award, Performance Award or Phantom Stock Award shall be promptly issued in the name of the Participant (or his beneficiary) and distributed to the Participant (or his beneficiary) after the Award (or portion thereof) has vested or been earned.

(b) *Withholding*: The Corporation shall withhold all required local, state, federal, foreign and other taxes and any other amount required to be withheld by any governmental authority or law from any amount payable in cash with respect to an Award. Prior to the delivery or transfer of any certificate for shares or any other benefit conferred under the Plan, the Corporation shall require any recipient of an Award to pay to the Corporation in cash the amount of any tax or other amount required by any governmental authority to be withheld and paid over by the Corporation to such authority for the account of such recipient. Notwithstanding the foregoing, the Administrator may establish procedures to permit a recipient to satisfy such obligation in whole or in part, and any local, state, federal, foreign or other income tax obligations relating to such an Award, by electing (the "election") to have the Corporation withhold shares of Common Stock from the shares to which the recipient is entitled. The number of shares to be withheld shall have a Fair Market Value as of the date that the amount of tax to be withheld is determined as nearly equal as possible to (but not exceeding) the amount of such obligations being satisfied. Each election must be made in writing to the Administrator in accordance with election procedures established by the Administrator.

(c) *Section 16(b) Compliance*: To the extent that any Participants in the Plan are subject to Section 16(b) of the Exchange Act, it is the general intention of the Corporation that transactions under the Plan shall comply with Rule 16b-3 under the Exchange Act and that the Plan shall be construed in favor of such Plan transactions meeting the requirements of Rule 16b-3 or any successor rules thereto. Notwithstanding anything in the Plan to the contrary, the Administrator, in its sole and absolute discretion, may bifurcate the Plan so as to restrict, limit or condition the use of any provision of the Plan to Participants who are officers or directors subject to Section 16 of the Exchange Act without so restricting, limiting or conditioning the Plan with respect to other Participants.

(d) *Code Section 162(m) Performance-Based Compensation*. To the extent to which Section 162(m) of the Code is applicable, the Corporation intends that compensation paid under the Plan to Covered Employees will, to the extent practicable, constitute "qualified performance-based compensation" within the meaning of Section 162(m), unless otherwise determined by the Administrator. Accordingly, Awards granted to Covered Employees which are intended to qualify for the performance-based exception under Code Section 162(m) shall be deemed to include any such additional terms, conditions, limitations and provisions as are necessary to comply with the performance-based compensation exemption of Section 162(m), unless the Administrator, in its discretion, determines otherwise.

(e) *Unfunded Plan; No Effect on Other Plans*:

(i) The Plan shall be unfunded, and the Corporation shall not be required to create a trust or segregate any assets that may at any time be represented by Awards under the Plan. The Plan shall not establish any fiduciary relationship between the Corporation and any Participant or other person. Neither a Participant nor any other person shall, by reason of the Plan, acquire any

right in or title to any assets, funds or property of the Corporation or any Affiliate, including, without limitation, any specific funds, assets or other property which the Corporation or any Affiliate, in their discretion, may set aside in anticipation of a liability under the Plan. A Participant shall have only a contractual right to the Common Stock or other amounts, if any, payable under the Plan, unsecured by any assets of the Corporation or any Affiliate. Nothing contained in the Plan shall constitute a guarantee that the assets of such entities shall be sufficient to pay any benefits to any person.

(ii) The amount of any compensation deemed to be received by a Participant pursuant to an Award shall not constitute compensation with respect to which any other employee benefits of such Participant are determined, including, without limitation, benefits under any bonus, pension, profit sharing, life insurance or salary continuation plan, except as otherwise specifically provided by the terms of such plan or as may be determined by the Administrator.

(iii) The adoption of the Plan shall not affect any other stock incentive or other compensation plans in effect for the Corporation or any Affiliate, nor shall the Plan preclude the Corporation from establishing any other forms of stock incentive or other compensation for employees or service providers of the Corporation or any Affiliate.

(f) *Applicable Law*: The Plan shall be governed by and construed in accordance with the laws of the State of Delaware, without regard to the conflict of laws provisions of any state, and in accordance with applicable federal laws of the United States.

(g) *Beneficiary Designation*: The Administrator may permit a Participant to designate in writing a person or persons as beneficiary, which beneficiary shall be entitled to receive settlement of Awards (if any) to which the Participant is otherwise entitled in the event of death. In the absence of such designation by a Participant, and in the event of the Participant's death, the estate of the Participant shall be treated as beneficiary for purposes of the Plan, unless the Administrator determines otherwise. The Administrator shall have sole discretion to approve and interpret the form or forms of such beneficiary designation. A beneficiary, legal guardian, legal representative or other person claiming any rights pursuant to the Plan is subject to all terms and conditions of the Plan and any Award Agreement applicable to the Participant, except to the extent that the Plan and/or Award Agreement provide otherwise, and to any additional restrictions deemed necessary or appropriate by the Administrator.

(h) *Gender and Number*: Except where otherwise indicated by the context, words in any gender shall include any other gender, words in the singular shall include the plural and words in the plural shall include the singular.

(i) *Severability*: If any provision of the Plan shall be held illegal or invalid for any reason, such illegality or invalidity shall not affect the remaining parts of the Plan, and the Plan shall be construed and enforced as if the illegal or invalid provision had not been included.

(j) *Rules of Construction*: Headings are given to the sections of this Plan solely as a convenience to facilitate reference. The reference to any statute, regulation or other provision of law shall be construed to refer to any amendment to or successor of such provision of law.

(k) *Successors and Assigns*: The Plan shall be binding upon the Corporation, its successors and assigns, and Participants, their executors, administrators and permitted transferees and beneficiaries.

(l) *Right of Offset*: Notwithstanding any other provision of the Plan or an Award Agreement, the Corporation may reduce the amount of any payment or benefit otherwise payable to or on behalf of a Participant by the amount of any obligation of the Participant to the Corporation that is or becomes due and payable.

(m) *Effect of Changes in Status*: Unless otherwise provided in an Award Agreement or determined by the Administrator, an Award shall not be affected by any change in the terms, conditions or status of the Participant's employment or service, provided that the Participant continues to be in the employ of, or in service to, the Corporation or an Affiliate. Without limiting the foregoing, the Administrator has sole discretion to determine (taking into account any Code Section 409A considerations), at the time of grant of an Award or at any time thereafter, the effect, if any, on Awards granted to a Participant if the Participant's status as an Employee, Director or Independent Contractor changes, including but not limited to a change from full-time to part-time, or vice versa, or if other similar changes in the nature or scope of the Participant's employment or service occur.

(n) *Fractional Shares:* Except as otherwise provided by the Plan or the Administrator, (i) the total number of shares issuable pursuant to the exercise, vesting or earning of an Award shall be rounded under general rounding principles to the nearest whole share (except where rounding down is required in order to preserve intended tax treatment or otherwise required by applicable law, rule or regulation), (ii) no fractional shares shall be issued, and (iii) no consideration shall be paid for any such fractional shares.

[Signature page to follow]

IN WITNESS WHEREOF, this Targacept, Inc. 2006 Stock Incentive Plan, as amended and restated through March 9, 2011, is, by the authority of the Board of Directors of the Corporation, executed in behalf of the Corporation, effective as of the 9th day of March, 2011.

TARGACEPT, INC.

By: /s/ J. Donald deBethizy
Name: J. Donald deBethizy
Title: President and CEO

ATTEST:

/s/ Peter A. Zorn
Peter A. Zorn
Secretary

[Corporate Seal]

Exhibit 10.18

[********] 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 promulgated under the Securities Exchange Act of 1934, as amended.

EXCLUSIVE LICENSE AGREEMENT

BETWEEN

CORNERSTONE THERAPEUTICS INC.

AND

TARGACEPT, INC.

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EXCLUSIVE LICENSE AGREEMENT

This Exclusive License Agreement (this "Agreement"), effective as of the date of signature of the last Party to sign below (the "Effective Date"), is between Cornerstone Therapeutics Inc., a Delaware corporation that was formerly known as Critical Therapeutics, Inc. ("Cornerstone"), and Targacept, Inc., a Delaware corporation ("Targacept"). Cornerstone and Targacept are sometimes hereinafter referred to each as a "Party" and collectively as the "Parties."

WHEREAS, Cornerstone has been engaged in the development of certain Technology (as defined below) and owns and otherwise controls certain patent rights and know-how with respect thereto;

WHEREAS, Targacept desires to acquire exclusive rights under the Licensed Intellectual Property (as defined below) to exploit Licensed Products (as defined below), as well as certain other rights as described herein; and

WHEREAS, the Parties desire to enter into an agreement pursuant to which Cornerstone will grant such rights to Targacept.

NOW, THEREFORE, in consideration of the mutual covenants contained herein and for other good and valuable consideration, the receipt and sufficiency of which are hereby acknowledged, the Parties hereby agree as follows:

Section 1. Definitions.

1.1 Defined Terms. In addition to the terms defined elsewhere in this Agreement and listed in Section 1.2, for purposes of this Agreement, the following words and phrases and their correlatives shall have the meanings set forth below:

"Affiliate" of an entity means any other entity which (directly or indirectly) is controlled by, controls or is under common control with such first entity. For the purposes of this definition, the term "control" (including, with correlative meanings, the terms "controlled by" and "under common control with") as used with respect to an entity means (i) in the case of a corporate entity, ownership (direct or, if sufficient to direct voting in the election of directors, indirect) of voting securities entitled to cast at least fifty percent (50%) of the votes in the election of directors or (ii) in the case of a non-corporate entity, direct or indirect ownership of at least fifty percent (50%) of the equity interests with the power to direct the management and policies of such entity, provided that if local law restricts foreign ownership, control shall be established by direct or indirect ownership of the maximum ownership percentage that may, under such local law, be owned by foreign interests.

"Annual Net Sales" means aggregate worldwide Net Sales of Licensed Products during any Calendar Year.

"**[********]** Patents" means all "Limited Right Patent Rights" as defined in the Feinstein License.

"Calendar Quarter" means a consecutive 3-month period beginning on January 1, April 1, July 1 or October 1.

"Calendar Year" means a consecutive 12-month period beginning on January 1 and ending on December 31.

"Confidential Information" shall have the meaning assigned such term in the Confidentiality Agreement.

"Confidentiality Agreement" means the Confidential Disclosure Agreement dated May 14, 2007 between Cornerstone and Targacept.

"Controlled," when used in reference to (i) Patent Rights or other intellectual property rights means the legal authority or right of a Person to grant a license or sublicense or covenant not to sue with respect to such Patent Rights or other intellectual property rights to another Person or (ii) Technology or tangible materials means to disclose or provide such Technology or tangible materials to such other Person, in each case by ownership, license, sublicense, contract or otherwise, without breaching the terms of any agreement with a Third Party.

"Cornerstone Compounds" means, collectively, CTI-**[********]**, CTI-**[********]** and all Other Cornerstone Compounds.

"Cornerstone Exemplified Compound Library" means the written list of exemplified pharmaceutical agents identified by chemical formula and structure and acknowledged to be the Cornerstone Exemplified Compound Library by the Parties as of the Effective Date.

"CTI-[********]" means the pharmacological agent identified as such in the Cornerstone Exemplified Compound Library, together with any salt form, polymorph, crystalline form, hydrate, solvate or formulation of such pharmacological agent or any salt form of any of the foregoing.

"CTI-[********]" means the pharmacological agent identified as such in the Cornerstone Exemplified Compound Library, together with any salt form, polymorph, crystalline form, hydrate, solvate or formulation of such pharmacological agent or any salt form of any of the foregoing.

"Excluded Field" means **[********]** by any means other than by **[********]** by a pharmacological agent of the activity of a cholinergic receptor (including the neuronal nicotinic alpha-7 (acetylcholine) receptor); provided that **[********]** via a **[********]** resulting solely from use of **[********]** is included in the Excluded Field. Exemplary **[********]** within the Excluded Field include **[********]** (such as **[********]**, or as produced by any other **[********]**.

"Excluded Field Patents" means (i) all "Feinstein Patent Rights" as defined in the Feinstein License and (ii) all other Patent Rights licensed as of the Effective Date or during the

term of this Agreement to Cornerstone under the Feinstein License, if any, in each case (clauses (i) and (ii)) with respect to each individual "Feinstein Patent Right" or other Patent Right, but only if and for so long as such "Feinstein Patent Right" or other Patent Right applies solely to the Excluded Field (it being understood that, if and at such time as an Excluded Field Patent ceases to apply solely to the Excluded Field, such Excluded Field Patent shall automatically and without further action by either Party become a Licensed Patent and either a Mixed Patent or a Field Patent, as the case may be).

"Excluded Product" means any product in the Excluded Field; provided that, if and at such time as Cornerstone makes, has made, uses, sells, offers to sell, imports or otherwise exploits, or seeks to grant, or grants to any Third Party a right or license under the Licensed Intellectual Property to make, have made, use, sell, offer to sell, import or otherwise exploit, any product that **[********]** where both (i) such **[********]** or **[********]** is covered by a Valid Claim included in the Licensed Patents and (ii) such **[********]**, then such product shall cease to be an Excluded Product.

"Feinstein" means the Feinstein Institute for Medical Research, formerly known as North Shore—Long Island Jewish Research Institute, a New York not-for-profit corporation.

"Feinstein License" means that certain Sponsored Research and License Agreement, effective as of January 1, 2003, between Cornerstone and Feinstein, as modified or amended by (i) that certain Letter Agreement dated February 3, 2004 (and effective February 10, 2004), (ii) that certain Amendment No. 1 dated September 18, 2006, (iii) that certain Amendment No. 2 dated January 8, 2007, (iv) that certain Amendment No. 3 dated June 29, 2007, (v) that certain Letter Agreement effective September 26, 2007, (vi) that certain Amendment No. 4 dated August 3, 2010, (vii) that certain Amendment No. 5 dated August 3, 2010 and (viii) that certain Amendment No. 6 dated August 3, 2010, and as may further be amended, restated, waived or changed in a manner that does not constitute a breach of this Agreement.

"Feinstein Licensed Know-How" means all "Feinstein Technology" as defined in the Feinstein License.

"Feinstein Licensed Patents" means (i) all "Feinstein Patent Rights" as defined in the Feinstein License and (ii) all other Patent Rights licensed as of the Effective Date or during the term of this Agreement to Cornerstone under the Feinstein License, if any, in each case (clauses (i) and (ii)) excluding Excluded Field Patents.

"Field" means any or all uses, except (i) the Excluded Field and (ii) the **[********]**.

"Field Patents" means all Licensed Patents that are not Mixed Patents or **[********]** Patents.

"GAAP" means generally accepted accounting principles in the United States.

"Generic Equivalent" means, with respect to each Licensed Product or Targacept Returned Product, a product that contains the same active ingredient (including, for clarity, any ester or salt of the active ingredient) as such Licensed Product or Targacept Returned Product.

"Generic Erosion" means, with respect to each Licensed Product or Targacept Returned Product and each country, the date a Generic Equivalent with respect to such Licensed Product or Targacept Returned Product becomes available for sale in such country; provided that, for purposes of this definition, availability for sale in any country in Europe shall be deemed to be availability for sale in all countries in Europe.

"License" means, collectively, the licenses and covenants not to sue granted to Targacept pursuant to Section 2.1.

"Licensed Intellectual Property" means all (i) Licensed Know-How and (ii) Licensed Patents.

"Licensed Know-How" means (i) the Feinstein Licensed Know-How and (ii) all Technology (other than the Feinstein Licensed Know-How and the Licensed Patents) Controlled by Cornerstone or any of its Affiliates as of the Effective Date or during the term of this Agreement that, solely in the case of this clause (ii), is necessary or reasonably useful to make, use, sell, offer to sell, import or otherwise exploit any product in the Primary Field.

"Licensed Patents" means (i) the Feinstein Licensed Patents and (ii) all Patent Rights (other than the Feinstein Licensed Patents) Controlled by Cornerstone or any of its Affiliates as of the Effective Date or during the term of this Agreement that, solely in the case of this clause (ii), are necessary or reasonably useful to make, use, sell, offer to sell, import or otherwise exploit any product in the Primary Field. For clarity, all Patent Rights that issue from, or claim priority to, any of the Licensed Patents as of the Effective Date shall also be Licensed Patents.

"Licensed Product" means each pharmaceutical or medicinal item, substance or formulation that is comprised of or contains a pharmacological agent or other compound and that, absent the licenses granted hereunder, would infringe one or more Valid Claims of the Licensed Patents in the country in which it is made, used or sold; provided that (i) Excluded Products are not Licensed Products and (ii) with respect to any particular country, a Licensed Product shall continue to be a Licensed Product notwithstanding the expiration of the Royalty Term for such Licensed Product in such country. "Licensed Products" includes combination products/services discussed in the "Net Sales" definition.

"Licensee" means, with respect to each Licensed Product, Targacept and, with respect to each Targacept Returned Product, Cornerstone.

"Licensor" means, with respect to each Licensed Product, Cornerstone and, with respect to each Targacept Returned Product, Targacept.

"Major Country" means each of **[********]**.

"Mixed Patents" means, subject to Section 6.2 and the definition of Excluded Field Patents above, collectively, (i) those issued patents and pending patent applications included in the Licensed Patents that are identified as such on Exhibit A, (ii) provisionals, substitutions, divisionals, continuations, continuations-in-part, reissues, renewals, registrations, confirmations, re-examinations, extensions, supplementary protection certificates, term extensions (under patent or other law), certificates of invention and the like, of such issued patents or pending patent applications, as the case may be, and (iii) counterparts or equivalents of any of the foregoing in any country or jurisdiction in the world.

"Net Sales" means (i) with respect to each Licensed Product, the gross amount received by Targacept or its Affiliates or Sublicensees for bona fide sales of such Licensed Product to a Third Party (including any Third Party distributors for resale), and (ii) with respect to each Targacept Returned Product, the gross amount received by Cornerstone or its Affiliates or Sublicensees (or licensees) for bona fide sales of such Targacept Returned Product to a Third Party (including any Third Party distributors for resale), in each case, less the following amounts actually incurred, allowed, paid, accrued or specifically allocated in connection with such sales of such Licensed Product or Targacept Returned Product (as applicable) in accordance with GAAP (or, if applicable to the seller, International Financial Reporting Standards), applied in a consistent manner:

(a) amounts repaid or credits or allowances granted for spoiled or damaged Licensed Product or Targacept Returned Product (as applicable), returns, recalls or rejections of the Licensed Product or Targacept Returned Product (as applicable), and price adjustments;

(b) customary trade, quantity, and cash discounts (including chargebacks and allowances) and wholesaler allowances (as relates to "bundles" of products, all discounts, wholesaler allowances and the like shall be allocated among products on the basis on which such discounts, wholesaler allowances or the like were actually granted or, if such basis cannot be determined, in proportion to the respective list prices of such products);

(c) freight out, postage, shipping, insurance and other transportation charges to the extent included (but whether or not broken out) in the invoice price to a Third Party;

(d) legally allowed chargebacks, rebates and fees or similar payments actually granted to customers, including pharmacy benefit management companies, health maintenance organizations, managed care organizations, federal, state, local and other governments, their agencies and purchasers and reimbursers;

(e) taxes or duties levied on, absorbed or otherwise imposed on such sale or performance, including excise taxes, value-added taxes, sales taxes, customs duties, customs levies and import fees or other governmental charges otherwise imposed upon the billed amount, to the extent such amounts are not paid directly to the tax authority by the Third Party and Targacept or Cornerstone is not otherwise entitled to a credit or a refund for such taxes, duties or payments made.

(f) launch discounts, stocking fees and other discounts extended to wholesalers, distributors, chain drug stores and other Third Party organizations who distribute the Licensed Product to pharmacies;

(g) to the extent not included in clause (f) above, fees paid to Third Party distributors, brokers or agents (in each case, other than sales personnel, sales representatives and sales agents); and

(h) any amounts actually written off or specifically identified as uncollectible in accordance with GAAP.

Use of Licensed Product or Targacept Returned Product (as applicable) for **[********]** or **[********]** or **[********]** or **[********]** (but **[********]** for which **[********]**) shall not be considered in determining Net Sales. In the case of any sale of Licensed Product or Targacept Returned Product (as applicable) between a Party and its Affiliates or Sublicensees (or licensees) for resale, Net Sales shall be calculated as above only on the first arm's length sale thereafter to a Third Party.

A Net Sale shall be deemed to have been made upon the date such sale is so recorded in accordance with GAAP.

With respect to each Licensed Product or Targacept Returned Product, country and Calendar Quarter, in the event that such Licensed Product or Targacept Returned Product (as applicable) is sold in such country in such Calendar Quarter in the form of a combination product/service containing or using one or more articles, devices, components or methods that are not Licensed Products or Targacept Returned Products (as applicable) hereunder (each, a "Non-Product Component"), Net Sales of such combination product/service in such country in such Calendar Quarter shall be calculated as follows:

(1) First, Net Sales of such combination product/service in such country in such Calendar Quarter shall be determined as if such combination product/service were not a combination product/service (i.e., as provided above).

(2) Second, the amount calculated in clause (1) shall be multiplied by:

(A) if all such Licensed Products or Targacept Returned Products (as applicable) and Non-Product Components are sold/performed separately in such country in such Calendar Quarter, the fraction A/(A+B), where A is the average price in such country for such Calendar Quarter of the Licensed Product or Targacept Returned Product (as applicable) and B is the invoice price in such country for such Calendar Quarter of all Non-Product Components in such combination product/service;

(B) if any of such Non-Product Components is not sold/performed separately in such country in such Calendar Quarter, the fraction A/C, where A is the average price in such country for such Calendar Quarter of such Licensed Products or

Targacept Returned Products (as applicable) and C is the average price in such country for such Calendar Quarter of such combination product/service;

(C) if any of such Licensed Products or Targacept Returned Products is not sold/performed separately in such country in such Calendar Quarter, the fraction (C-B)/C, where B is the average price in such country for such Calendar Quarter of all such Non-Product Components in such combination product/service and C is the average price in such country for such Calendar Quarter of such combination product/service; or

(D) if the conditions in both clause (B) and clause (C) above apply, a market price for such Licensed Products or Targacept Returned Products (as applicable) and all such Non-Product Components shall be negotiated by the Parties in good faith based upon the costs, overhead and profit as are then incurred for such combination product/service, the apportionment of Net Sales as provided in clauses (A) to (C) above in other countries for such Calendar Quarter if available, and all other products, articles, devices, components or methods then being sold or performed by Targacept and having an ascertainable market price.

"Other Cornerstone Compound" means each pharmacological agent identified as such in the Cornerstone Exemplified Compound Library, together with any salt form, polymorph, crystalline form, hydrate, solvate or formulation of such pharmacological agent or any salt form of any of the foregoing.

"Patent Rights" means (i) issued patents and pending patent applications, (ii) provisionals, substitutions, divisionals, continuations, continuations-in-part, reissues, renewals, registrations, confirmations, re-examinations, extensions, supplementary protection certificates, term extensions (under patent or other law), certificates of invention and the like, of issued patents or pending patent applications, as the case may be, and (iii) counterparts or equivalents of any of the foregoing in any country or jurisdiction in the world.

"Person" means an individual, a partnership, a limited liability company, a corporation, an association, a joint stock company, a trust, a joint venture, an unincorporated organization and a governmental entity or any department, agency or political subdivision thereof.

"Phase I Clinical Trial" means a human clinical trial that is the first time a drug is given to humans at any dose, the principal purpose of which is a preliminary determination of safety of a drug in healthy individuals or patients, as contemplated by 21 C.F.R. §312.21(a), whether or not conducted in the United States.

"Phase II Clinical Trial" means a human clinical trial, with subjects with a particular disease or condition, for which a primary objective is a preliminary determination of the efficacy **[********]** of a drug for such disease or condition, as contemplated by 21 C.F.R. §312.21(b), whether or not conducted in the United States.

"Phase III Clinical Trial" means a human clinical trial, with subjects with a particular disease or condition, the principal purpose of which is to demonstrate clinically and statistically

the efficacy and safety of such drug for such disease or condition in order to obtain marketing approval of such drug for such disease or condition, as contemplated by 21 C.F.R. §312.21(c), whether or not conducted in the United States. For clarity, a Phase IIb clinical trial is not a Phase III Clinical Trial.

"Primary Field" means direct or indirect modulation or other affecting of the activity of any cholinergic receptor (including, for clarity, the neuronal nicotinic alpha-7 (acetylcholine) receptor) by a pharmacological agent for therapeutic, diagnostic or palliative use in humans.

"Proof of Concept" means, with respect to a Subject Compound, the achievement of **[********]** in a Phase II Clinical Trial of such Subject Compound **[********]** and that **[********]**. For clarity, a study designed to demonstrate Proof of Concept is intended only to **[********]** of a particular Subject Compound and is not intended to **[********]** or **[********]** or to otherwise **[********]**.

"Regulatory Approval" means all technical, medical and scientific licenses, registrations, authorizations and approvals (including approval of a New Drug Application, as defined in the U.S. Federal Food, Drug, and Cosmetic Act, as amended, and its supplements and amendments, pre- and post- approvals, and labeling approvals, as well as analogous marketing approval applications outside of the United States) of any Regulatory Authority, that are necessary or reasonably useful for the manufacture, distribution, marketing, promotion, offer for sale, use, storage, import, export or sale of a Licensed Product in a regulatory jurisdiction (including, with respect to the European Union or any country therein, approval of price and reimbursement).

"Regulatory Authority" means the U.S. Food and Drug Administration (or any successor agency) or any comparable regulatory or governmental agency or authority in the rest of the world with authority over the distribution, importation, exportation, manufacture, production, use, storage, transport, clinical testing, pricing or sale of pharmaceutical products.

"Restricted Field" means direct or indirect modulation or other affecting of any neuronal nicotinic (acetylcholine) receptor by a pharmacological agent for therapeutic, diagnostic or palliative use in humans.

"SetPoint" means SetPoint Medical Corporation (formerly known as Innovative Metabolics, Inc.), a Delaware corporation.

"SetPoint License" means that certain Exclusive License Agreement, dated January 29, 2007, between Cornerstone and SetPoint, as amended by (i) that certain First Amendment dated June 29, 2007, and (ii) that certain Second Amendment dated August 3, 2010, and as may further be amended, restated, waived or changed in a manner that does not constitute a breach of this Agreement.

"Subject Compound" means any Cornerstone Compound or Targacept Compound.

"Sublicensees" means any Person that receives, directly or indirectly through multiple tiers, a sublicense from a Party to intellectual property Controlled by such Party and licensed (or sublicensed) from the other Party under this Agreement.

"Targacept Compound" means a pharmacological agent (other than a Cornerstone Compound) that, absent the License granted hereunder, would infringe one or more Valid Claims of the Licensed Patents in the country in which it is made, used or sold.

"Technology" means know-how, trade secrets, materials, formulations, information, documents, studies, results, data (including preclinical, clinical and assay data), manufacturing processes and data, specifications, sourcing information, assays, and quality control and testing procedures, whether or not patented or patentable.

"Third Party" means any Person, other than Targacept or Cornerstone or their respective Affiliates.

"Valid Claim" means a claim of (i) an issued and unexpired patent, which claim has not been cancelled, revoked or held invalid or unenforceable by a court or other government agency of competent jurisdiction from which no appeal can be taken or is taken within the time allowed for appeal and has not been held or admitted to be invalid or unenforceable through re-examination or disclaimer, reissue, opposition procedure, nullity suit or otherwise, or (ii) a pending patent application that was filed in good faith, is being prosecuted with the good faith belief of potential issuance and has not been cancelled, withdrawn or abandoned without the possibility of appeal or re-filing.

1.2 Terms Defined Elsewhere in this Agreement. In addition to the terms defined in Section 1.1, the following terms shall have the respective meanings assigned thereto in the Sections indicated below:

Defined Term	Section
Agreement	Preamble
Claim	9.6(c)(i)
Commercially Reasonable Efforts	4.1(a)
Cornerstone	Preamble
Cornerstone Indemnitees	9.6(a)
Cornerstone Restricted Field	10.5(b)
Earlier Subject Compound	5.2(d)(v)
Effective Date	Preamble
Effective Extension Notice	4.1(b)(i)
Field Patent Action	6.5(b)(i)

Defined Term	Section
Infringement	6.5(a)
In-License Breach Notice	2.3(e)
Indemnitee	9.6(c)(i)
Indemnitor	9.6(c)(i)
Intellectual Property	10.4(a)
Inventions	9.1(e)
Inventors	9.1(o)
Later Subject Compound	5.2(d)(v)
Losses	9.6(a)
Material	3.2
Material Acceptance Date	4.1(b)(i)
Milestone Event	5.2(a)
Milestone Payment	5.2(a)
Mixed Patent Action	6.5(c)
Parties	Preamble
Party	Preamble
Patent Action	6.5(d)
Preclinical Milestone	4.1(b)(i)
Prime Rate	5.6(g)
Product Royalty Term	5.5(b)(ii)(B)
Requisite Assigned Rights	6.9
Royalty Term	5.5(b)(ii)(B)
Subject Rights	2.4(b)
Targacept	Preamble
Targacept Indemnitees	9.6(b)
Targacept Returned Product	10.5(b)
Third Party In-Licenses	2.3(c)(i)
WSJ Exchange Rate	5.6(d)

Section 2. License Grants by Cornerstone.

2.1 Exclusive License and Covenants Not to Sue.

(a) Effective as of the Effective Date, Cornerstone, for itself and on behalf of its Affiliates, hereby grants to Targacept and its Affiliates a perpetual and irrevocable (subject to the terms of this Agreement and the Feinstein License), worldwide, royalty-bearing, exclusive (even as to Cornerstone and its Affiliates, unless otherwise expressly provided hereunder) license or sublicense (as the case may be), with the right to further sublicense in accordance with Section 2.2, under the Licensed Intellectual Property to make, have made, use, have used, import, have imported, sell, have sold, offer to sell and otherwise exploit Licensed Products in the Field.

(b) Cornerstone, for itself and on behalf of its Affiliates and licensees, hereby covenants not to sue, or cause or support any other Person to sue, Targacept, any of its Affiliates or Sublicensees, or any of their respective manufacturers, suppliers, distributors or customers for using Licensed Intellectual Property to research, develop, commercialize or otherwise exploit products in the Field, which covenant not to sue shall apply to all acts or omissions that occur while the License remains in force.

(c) For clarity, with respect to the Feinstein Licensed Patents and Feinstein Licensed Know-How, the License shall grant to Targacept all rights granted to Cornerstone under the Feinstein License in the Field, and Targacept expressly acknowledges that Feinstein has retained rights under the Feinstein License for itself and the U.S. government as expressly set forth in Articles 3.3 and 3.2, respectively, of the Feinstein License and that the License is subject to such retention of rights.

2.2 Sublicenses.

(a) The License includes the right to grant sublicenses (through multiple tiers of sublicensees) by Targacept to its Affiliates and Third Parties, provided that (i) any such sublicense agreement shall be subject to and subordinate to this Agreement and (ii) Targacept shall remain responsible for the performance of its direct Sublicensees.

(b) Targacept shall provide to Cornerstone a copy of each agreement pursuant to which Targacept sublicenses its rights hereunder within thirty (30) days following execution of such agreement; provided that (i) Targacept shall have the right to redact financial information, to the extent not publicly announced, and other confidential information from such agreement; and (ii) such agreement shall, to the extent not otherwise made public, be Targacept's Confidential Information.

(c) Each sublicense granted to any Sublicensee shall terminate immediately upon the termination of the License, provided that any such sublicense shall not terminate, on a Sublicensee-by-Sublicensee basis, if (i) all outstanding amounts owed Licensor by Licensee hereunder with respect to such sublicense as of such purported termination date, if any, are paid in full within **[********]** days after such date (whether by Licensee, its Affiliates or such Sublicensee) and (ii) within **[********]** days after such purported termination date the Sublicensee agrees in writing to be bound directly to Licensor under a license agreement

substantially similar to this Agreement with respect to the rights sublicensed to such Sublicensee hereunder, substituting such Sublicensee for Licensee. Licensor and such Sublicensee shall promptly memorialize such direct license.

2.3 Feinstein License and Other Licenses.

(a) *Feinstein License*. Except and solely to the extent expressly provided in this Agreement, if at all, neither Targacept nor any of its Affiliates or Sublicensees assumes any obligations of Cornerstone under the Feinstein License.

(b) *SetPoint License*.

(i) Targacept acknowledges that, under the SetPoint License, Cornerstone has previously licensed to SetPoint the Excluded Field Patents, the Mixed Patents and certain Technology included in the Feinstein Licensed Know-How, in each case solely for use in the Excluded Field.

(ii) Neither Targacept nor any of its Affiliates or Sublicensees assumes any obligations of Cornerstone under the SetPoint License.

(c) *Maintenance of Third Party In-Licenses*.

(i) Cornerstone shall maintain in full force and effect the Feinstein License and all other Third-Party agreements, if any, whereby Targacept gains rights hereunder in or to any of the Licensed Intellectual Property (collectively, "Third Party In-Licenses"). Without limiting the generality of the foregoing, Cornerstone shall be solely responsible for complying, and shall comply, with all of Cornerstone's financial and non-financial obligations under each Third Party In-License and under the SetPoint License.

(ii) Cornerstone shall provide Targacept with notice within **[********]** business days after receipt (and in any event substantially before the end of any applicable cure period under the applicable agreement) of any written claim of breach of any Third Party In-License or the SetPoint License. Cornerstone shall provide Targacept with copies of all notices and other documents Cornerstone receives or sends pursuant to each Third Party In-License or the SetPoint License that affects or might reasonably be expected to affect Targacept's rights hereunder (including any termination notice). To the extent of any conflict between this Section 2.3(c)(ii) and Section 2.3(e), Section 2.3(e) shall control.

(d) *Amendment*. Without the prior written consent of Targacept, Cornerstone shall not (i) terminate, assign, amend, restate, waive or otherwise change any of the terms and conditions of the Feinstein License, any other Third Party In-License or the SetPoint License or (ii) enter into any other agreement or understanding with Feinstein or any other Third Party that is a party to a Third Party In-License or with SetPoint, in either case (clause (i) or (ii)) that affects or might reasonably be expected to affect Targacept's rights hereunder.

(e) *Step-In Rights*. Cornerstone shall notify Targacept in writing within **[*********]** business days following Cornerstone's receipt of any notice from Feinstein (or any other Third Party to a Third Party In-License) to Cornerstone alleging that Cornerstone has breached any of its obligations under the Feinstein License (or other Third Party In-License) (each, an "In-License Breach Notice"). Cornerstone shall keep Targacept informed on a regular and timely basis of all non-trivial discussions, communications and correspondence between Cornerstone and Feinstein (or such other Third Party) following Cornerstone's receipt of any In-License Breach Notice through such time as Feinstein or other Third Party to a Third Party In-License acknowledges (and so notifies Targacept in writing) either that there has been no breach or that any breach has been cured or resolved without effect or potential effect on Targacept's rights hereunder. In addition to the rights granted to Targacept in the Feinstein License or, if any, other Third Party In-Licenses, upon receipt of any In-License Breach Notice, Targacept shall have the right to make a proposal to Cornerstone setting out the terms whereby Targacept would undertake to effect a cure of any breach or default of Cornerstone described in the applicable In-License Breach Notice. Such proposal shall include any proposed amendments to the terms of this Agreement that would be required by Targacept in return for granting any such undertaking and effecting such a cure. If Cornerstone wishes to implement any proposal received under this Section 2.3(e), the Parties shall discuss and agree upon the final terms on which Targacept shall effect a cure of the relevant breach or default by Cornerstone, amend the terms of this Agreement as required to reflect such agreed terms and Targacept and Cornerstone shall undertake any agreed obligations so as to effect such cure. In any event, any amounts paid by Targacept to Feinstein or to any other Third Party pursuant to this Section 2.3(e) shall be creditable by Targacept toward amounts owed by Targacept to Cornerstone pursuant to this Agreement. Nothing in this Section 2.3(e) is intended reduce, limit, modify or otherwise affect Cornerstone's obligations pursuant to Section 2.3(c)(i).

(f) *Bankruptcy*. Solely in connection with Cornerstone's rights that arise at the time that a Third Party to a Third Party In-License seeks relief (or is subject to an involuntary petition seeking relief) under any bankruptcy, reorganization, or insolvency or similar laws, Cornerstone hereby irrevocably appoints Targacept (with full right of substitution), as Cornerstone's special attorney-in-fact to act, in the name of Cornerstone, to protect and preserve the rights granted to Targacept pursuant to the License (including seeking to preserve Cornerstone's and Targacept's rights under any such laws, including under the U.S. Bankruptcy Code, Title 11 of the U.S. Code). Cornerstone acknowledges and agrees that the foregoing special power of attorney is coupled with an interest and therefore (a) will survive any termination of this Agreement in which any rights granted to Targacept hereunder survive and (b) is irrevocable. Without limiting the generality of the foregoing, Cornerstone agrees that if any Third Party to any Third Party In-License seeks relief under any bankruptcy, reorganization, insolvency or similar laws, Cornerstone shall give Targacept prompt written notice thereof and Targacept shall have the right to exercise the foregoing special power of attorney to take all action necessary, at Targacept's reasonable expense, to preserve the rights granted to Targacept (via Cornerstone) hereunder. Should any Third Party In-License terminate, Cornerstone shall give Targacept prompt written notice and assist Targacept in all reasonable respects, at Targacept's reasonable expense, in obtaining all rights granted to Targacept hereunder with respect to such terminated agreement, including by having the Third Party licensor thereof treat Targacept as a direct licensee thereunder. For clarity, if Targacept is treated as a direct licensee thereunder, Targacept

agrees that it will remain liable to Cornerstone for the payments under Sections 5.2 and 5.3 as if such Third Party In-License had not terminated, except that Targacept shall be entitled to credit against the amounts otherwise payable by Targacept to Cornerstone under either or both of Sections 5.2 and 5.3 for all upfront, milestones, royalties and other amounts, however characterized, paid by Targacept directly to such Third Party.

(g) *Payments*. For clarity and notwithstanding anything to the contrary in this Agreement, Cornerstone shall be solely responsible for all amounts owed to any Third Party arising from the Feinstein License, all amounts owed to any Third Party arising from any other Third Party In-License and all amounts owed to any Third Party arising from the SetPoint License.

2.4 Other Restrictions; Limited Right of First Negotiation and Right of First Refusal.

(a) Cornerstone shall not enter into any agreement or otherwise take any actions or omit to take any actions in conflict with, or that would or might reasonably be expected to encumber or diminish, the License and the other rights granted to Targacept hereunder.

(b) In the event that the SetPoint License expires or terminates for any reason as to some or all of the "Licensed Know-How" and "Licensed Patents" (each as defined in the SetPoint License) licensed or sublicensed to SetPoint (together with any or all rights granted to Cornerstone pursuant to Section 9.6 of the SetPoint License, the "Subject Rights"), Cornerstone shall notify Targacept in writing of such expiration or termination, and Cornerstone shall not offer the Subject Rights for license, sublicense or other transfer to any Third Party without first offering such Subject Rights to Targacept in accordance with the terms of this Section 2.4(b). Targacept shall have the right within [*********] days following such notification to request in writing a license to some or all of such Subject Rights. Upon such request, Cornerstone and Targacept shall negotiate in good faith a license agreement pursuant to which Cornerstone would license or sublicense the Subject Rights to Targacept. If the parties are unable to reach agreement within [*********] days following such request or such longer period as agreed by the Parties in writing, then Cornerstone shall have the right to offer to license, sublicense or otherwise transfer such Subject Rights to a Third Party, provided that if Cornerstone receives a *bona fide* Third Party offer whereby such Third Party would obtain from Cornerstone a right or license to all or any portion of such Subject Rights on financial terms less favorable to Cornerstone than the most favorable financial terms previously proposed by Targacept to Cornerstone or by Cornerstone to Targacept, Cornerstone shall notify Targacept of all material terms of such offer in writing and Targacept shall thereupon have a right of first refusal to license such Subject Rights on the same terms set forth in the notice. Targacept may exercise its right of first refusal at any time within [*********] days after its receipt of the notice by written notice to Cornerstone, and, in such event, the Parties shall work diligently towards the execution of a definitive license agreement reflecting the terms in the notice and, to the extent not inconsistent, the terms hereof.

2.5 License Limitations. No licenses or other rights are granted by Cornerstone hereunder to use any trademark, trade name, trade dress or

service mark Controlled by Cornerstone or any of its Affiliates. All licenses and other rights are granted only as expressly provided in this Agreement, and no other licenses or other rights are or shall be created or granted hereunder by implication, estoppel or otherwise.

Section 3. Transfer of Licensed Know-How and Supply of CTI-**[********]** and CTI-[********].

3.1 Transfer of Licensed Know-How. Within **[********]** days after the Effective Date, Cornerstone shall provide to Targacept, at Targacept's reasonable expense, one (1) copy (in electronic form, if available) of all documents in Cornerstone's or any of its Affiliates' possession as of the Effective Date (including laboratory notebooks) to the extent that such documents describe or contain Licensed Know-How. Cornerstone shall promptly provide and transfer to Targacept all additional Licensed Know-How that may from time to time become available to Cornerstone.

3.2 Supply of CTI-**[********]** and CTI-**[********]**. Promptly following execution of this Agreement, Cornerstone shall supply to Targacept or its designee a one-time transfer of all quantities of CTI-**[********]** and CTI-**[********]** to the extent in Cornerstone's possession or Control on the Effective Date (collectively, the "Material"). Cornerstone hereby assigns all right, title and interest in and to the Material to Targacept free and clear of all liens and encumbrances as of the Effective Date, but the Material is otherwise conveyed 'as is, with all defects' to Targacept. Concurrently with the delivery of the Material, Cornerstone shall deliver to Targacept or its designee: (i) all records in Cornerstone's possession or control on the Effective Date relating to the manufacture of the Material, including manufacturing records, standard operating procedures, equipment log books, batch records, laboratory notebooks and all raw data relating to the manufacturing of the Material; and (ii) a certificate of analysis setting forth all tests conducted and the results thereof with respect to the Material. In addition, Cornerstone shall provide, or cause to be provided, to Targacept such other records and documentation in its possession or control relating to the Material as Targacept may reasonably request and, if requested by Targacept, Cornerstone shall use commercially reasonable efforts to cause the Third Party that manufactured the Material to perform, at Targacept's reasonable expense, release testing as required by applicable laws, regulations and ICH guidance documents for the delivery of the Material for use in GLP toxicology studies or human clinical trials.

Section 4. Development and Commercialization.

4.1 Commercially Reasonable Efforts.

(a) *General Level of Effort Required*. Targacept shall use Commercially Reasonable Efforts to develop at least one (1) Licensed Product in the Field to obtain approval from the applicable Regulatory Authority(ies) to market or sell such Licensed Product **[********]**; provided that, for clarity, Cornerstone expressly agrees that, with respect to the period beginning

on the Effective Date and ending **[********]** after the Material Acceptance Date, Targacept's compliance with Section 4.1(b)(i) shall also constitute compliance with this Section 4.1(a). For purposes of this Agreement, "Commercially Reasonable Efforts" means, with respect to Licensed Product, the carrying out of development activities using the efforts and resources that Targacept would typically devote to a product candidate of similar market potential or profit potential resulting from its own research efforts, based on conditions prevailing from time to time and taking into account issues of safety, tolerability and efficacy, product profile, intellectual property position, projected market exclusivity, the then current competitive environment for such product and target indication and the likely timing of such product's entry into the market, the regulatory environment and status of such product and target indication, and all other relevant scientific, medical, technical and commercial factors.

(b) *Specific Development Commitments; Cornerstone Acknowledgment*.

(i) Targacept shall use commercially reasonable efforts (taking into account cost and complexity) to procure or produce CTI-**[********]** or CTI-**[********]** in sufficient quantities and of sufficient quality to perform the toxicity studies described in either clause (A) or clause (B) of this Section 4.1(b)(i). Within **[********]** after the Material Acceptance Date, Targacept shall complete either (at Targacept's sole discretion) (A) a **[********]** toxicity study of the pharmacological agent identified as CTI-**[********]** in the Cornerstone Exemplified Compound Library and, only if such **[********]** study is successful (at Targacept's sole discretion), a **[********]** or **[********]** (at Targacept's sole discretion) toxicity study of the pharmacological agent identified as CTI-**[********]** in the Cornerstone Exemplified Compound Library or (B) a **[********]** or **[********]** (at Targacept's sole discretion) toxicity study of the pharmacological agent identified as CTI-**[********]** in the Cornerstone Exemplified Compound Library (the completion of either clause (A) or clause (B), the "Preclinical Milestone"). If Targacept realizes that it will be unable to meet the Preclinical Milestone by the required deadline, it may submit a written notice to Cornerstone at any time prior to such deadline and, if effective, thereby secure an automatic extension of **[********]** to such deadline; provided that, to be effective, such notice (an "Effective Extension Notice") must include **[********]** and Targacept's projected target date for completing the Preclinical Milestone. For purposes of this Section 4.1(b)(i), "Material Acceptance Date" shall mean the date, if any, on which Targacept reasonably determines that it has procured or produced either CTI-**[********]** or CTI-**[********]** in quantities and of quality sufficient to perform the applicable toxicity study(ies) as described in this Section 4.1(b)(i).

(ii) Termination of this Agreement pursuant to Section 10.2(a), if applicable, shall constitute Cornerstone's sole and exclusive remedy for Targacept's failure to complete the Preclinical Milestone in accordance with Section 4.1(b)(i).

(iii) Cornerstone acknowledges and agrees that the application of commercially reasonable efforts may not require Targacept to procure or produce CTI-**[********]** or CTI-**[********]** in sufficient quantities and of sufficient quality to perform the toxicity studies described in either Section 4.1(b)(i)(A) or Section 4.1(b)(i)(B) above.

4.2 Responsibilities and Costs. As between the Parties, following the Effective Date:

(a) except with respect to the Feinstein License and any other Third Party In-Licenses, Cornerstone shall have no responsibility for, or bear any of the costs of, the research, development or commercialization of Licensed Products (including manufacturing of materials required therefor);

(b) Targacept shall own all results of research, development and commercialization activities for each Licensed Product, including all Patent Rights, copyright, trade secret and other intellectual property rights and all Technology made, conceived, reduced to practice, authored or generated in connection with such activities; and

(c) all regulatory filings and Regulatory Approvals, if any, for each Licensed Product shall be obtained by, in the name of, and solely owned by Targacept; for clarity, Targacept shall solely own all data, materials and other information submitted in connection with such regulatory filings and Regulatory Approvals.

4.3 Progress Reports. Targacept will provide Cornerstone with a summary written progress report discussing the development, evaluation, testing and commercialization, as applicable, of Licensed Products at least once per Calendar Year, but, in any case, **[*********]** annual reports **[*********]**.

Section 5. Payments.

5.1 Initial Fees.

(a) *Initial License Fee*. As partial consideration for the License and Cornerstone's obligations under this Agreement, concurrently with the execution and delivery of this Agreement, Targacept shall pay to Cornerstone a non-refundable, non-creditable upfront fee equal to One Million Five Hundred Thousand U.S. dollars ($1,500,000) by wire transfer of immediately available funds to such bank account as Cornerstone may designate.

(b) *Reimbursement of Attorneys' Fees*. Upon execution of this Agreement by both Parties, Cornerstone shall pay to Targacept, in partial reimbursement of Targacept's attorneys' fees associated with the preparation and negotiation of this Agreement and other activities associated with the completion of the transactions contemplated hereby, [*********] by wire transfer of immediately available funds to such bank account as Targacept may designate.

5.2 Milestone Payments.

(a) As partial consideration for the License and Cornerstone's obligations under the terms of this Agreement, subject to Section 5.2(d), Targacept shall make the following non-refundable, non-creditable payments (each a "Milestone Payment") to Cornerstone upon the occurrence, after the Effective Date, of the events (each a "Milestone Event") below:

	Milestone Event	Licensed Product containing or comprised of*: A. CTI-[********]	B. CTI-[********]	C. Other Cornerstone Compound	D. Targacept Compound
1	Completion of the first **[********]** with **[********]** for **[********]**	$**[********]**	$**[********]**	$**[********]**	—
2	First **[********]** of the **[********]** in the **[********]**	$**[********]**	$**[********]**	$**[********]**	$[********]
3	First **[********]** of the **[********]** in the **[********]**	$**[********]**	$**[********]**	$**[********]**	$[********]
4	First **[********]**	$**[********]**	$**[********]**	$**[********]**	$[********]
5	First **[********]** of the **[********]** in the **[********]**	$**[********]**	$**[********]**	$**[********]**	$[********]
6	**[********]** of **[********]** in **[********]** for the **[********]**	$**[********]**	$**[********]**	$**[********]**	$[********]
7	**[********]** of **[********]** in **[********]** in **[********]** for the **[********]**	$**[********]**	$**[********]**	$**[********]**	$[********]
8	**[********]** of **[********]** in **[********]** for the **[********]**	$**[********]**	$**[********]**	$**[********]**	$[********]
9	First achievement of Aggregate Worldwide Net Sales of **[********]** in a Calendar Year	$**[********]**	$**[********]**	$**[********]**	$[********]
10	First achievement of Aggregate Worldwide Net Sales of **[********]** in a Calendar Year	$**[********]**	$**[********]**	$**[********]**	$[********]
11	First achievement of Aggregate Worldwide Net Sales of **[********]** in a Calendar Year	$**[********]**	$**[********]**	$**[********]**	$[********]

* Each Subject Compound may only be classified into one column.

(b) Targacept shall provide Cornerstone with prompt written notice upon each occurrence of a Milestone Event, but in no event will such notice be given to Cornerstone later than **[********]** days after Targacept becomes aware of the occurrence of any Milestone Event.

(c) Each Milestone Payment shall be due and payable within **[********]** days after the occurrence of the corresponding Milestone Event by wire transfer of immediately available funds to such bank account as Cornerstone may designate.

(d) Notwithstanding anything in this Agreement to the contrary, with respect to each Milestone Event, Targacept shall not be obligated to make a Milestone Payment:

(i) more than one (1) time in the aggregate for CTI-**[********]** and all Licensed Products that contain or comprise CTI-**[********]** (for clarity, each of the foregoing references to CTI-**[********]** includes, collectively, all salt forms, polymorphs, crystalline forms, hydrates, solvates and formulations of the pharmacological agent identified as CTI-**[********]** in the Cornerstone Exemplified Compound Library);

(ii) more than one (1) time in the aggregate for CTI-**[********]** and all Licensed Products that contain or comprise CTI-**[********]** (for clarity, each of the foregoing references to CTI-**[********]** includes, collectively, all salt forms, polymorphs, crystalline forms, hydrates, solvates and formulations of the pharmacological agent identified as CTI-**[********]** in the Cornerstone Exemplified Compound Library);

(iii) with respect to each Other Cornerstone Compound, more than one (1) time in the aggregate for such Other Cornerstone Compound and all Licensed Products that contain or comprise such Other Cornerstone Compound (for clarity, each of the foregoing references to an Other Cornerstone Compound includes, collectively, all salt forms, polymorphs, crystalline forms, hydrates, solvates and formulations of the pharmacological agent identified as such Other Cornerstone Compound in the Cornerstone Exemplified Compound Library);

(iv) with respect to each Targacept Compound, more than one (1) time in the aggregate for such Targacept Compound and all Licensed Products that contain or comprise such Targacept Compound (for clarity, each of the foregoing references to a Targacept Compound includes, collectively, all salt forms, polymorphs, crystalline forms, hydrates, solvates and formulations of such Targacept Compound); or

(v) with respect to the occurrence of Milestone Event **[********]** for any Subject Compound (the "Later Subject Compound"), if (A) a Milestone Payment **[********]** based on **[********]** and (B) following such payment, **[********]**, then the Milestone Payment **[********]** with respect to **[********]** by such **[********]** such Milestone Event **[********]** such Milestone Event **[********]**.

5.3 Royalties to be Paid by Targacept to Cornerstone. Subject to the terms and conditions of this Agreement, during the applicable Product Royalty Term, Targacept shall pay to Cornerstone royalties, at the applicable rate set forth in the table below, based upon Net Sales of each Licensed Product in the United States and Net Sales of each Licensed Product outside of the United States during each Calendar Quarter, if any.

	Licensed Product containing or comprised of*:			
	A. CTI-[********]	**B. CTI-[********]**	**C. Other Cornerstone Compound**	**D. Targacept Compound**
Net Sales in the United States	[********]%	[********]%	[********]%	[********]%
Net Sales outside of the United States	[********]%	[********]%	[********]%	[********]%

* Each Subject Compound may only be classified into one column.

5.4 Royalties to be Paid by Cornerstone to Targacept. Pursuant to Section 10.5(c) and subject to the terms and conditions of this Agreement, during the applicable Product Royalty Term, Cornerstone shall pay to Targacept royalties, at the applicable rate set forth in the table below, based upon Net Sales of each Targacept Returned Product in the United States and Net Sales of each Targacept Returned Product outside of the United States during each Calendar Quarter, if any.

	Targacept Returned Product containing or comprised of*:		
Net Sales	**A. CTI-[********]**	**B. CTI-[********]**	**C. Other Cornerstone Compound**
In the United States			
[********] Initiated Prior to Termination of Agreement^	**[********]**%	**[********]**%	**[********]**%
[********] Initiated Prior to Termination of Agreement^	**[********]**%	**[********]**%	**[********]**%
[********] Initiated Prior to Termination of Agreement^	**[********]**%	**[********]**%	**[********]**%
Outside of the United States			
[********] Initiated Prior to Termination of Agreement^	**[********]**%	**[********]**%	**[********]**%
[********] Initiated Prior to Termination of Agreement^	**[********]**%	**[********]**%	**[********]**%
[********] Initiated Prior to Termination of Agreement^	**[********]**%	**[********]**%	**[********]**%

* Each Subject Compound may only be classified into one column.

^ Includes a **[*********]** or **[*********]**, as the case may be, of CTI-**[*********]**, CTI-**[*********]** or an Other Cornerstone Compound, as the case may be, by Targacept or any Affiliate or Sublicensee thereof

5.5 Royalty Conditions.

(a) *Royalty Limitations*. Only one (1) royalty shall be due with respect to the sale of the same unit of Licensed Product or Targacept Returned Product. Only one (1) royalty shall be due on the sale of any unit of any Licensed Product or Targacept Returned Product, even if the manufacture, use, sale, offer for sale or importation of such Licensed Product would infringe more than one (1) Valid Claim of the Licensed Patents in the absence of the License and even if such Licensed Product or Targacept Returned Product incorporates more than one (1) Subject Compound.

(b) *Royalty Term*. Royalties will be payable on a country-by-country and a Licensed Product-by-Licensed Product or Targacept Returned Product-by-Targacept Returned Product basis from the date of the first commercial sale of such Licensed Product or Targacept Returned Product in such country following receipt of Regulatory Approval of such Licensed Product or Targacept Returned Product in such country until the later of (i) the expiration of the last Licensed Patent in such country that includes at least one (1) Valid Claim that covers the composition of matter of such Licensed Product or Targacept Returned Product or a method of using such Licensed Product or Targacept Returned Product to treat an indication for which such Licensed Product or Targacept Returned Product has received Regulatory Approval in such country, or (ii) the expiration of **[*********]** which the applicable **[*********]** with respect to such Licensed Product or Targacept Returned Product **[*********]** such Licensed Product or Targacept Returned Product **[*********]** such Licensed Product or Targacept Returned Product (the "Royalty Term"). With respect to each Licensed Product and country, upon the expiration of the Royalty Term, the License (and with respect to each Targacept Returned Product and country, the licenses granted by Targacept in Section 10.5(b)) in such country shall thereupon become fully paid-up, perpetual, irrevocable and unrestricted. With respect to each Licensed Product or Targacept Returned Product, the period beginning on the first day of the first Royalty Term and ending on the last day of the last to expire Royalty Term is referred to herein as the "Product Royalty Term."

(c) *Generic Erosion*. From and after when Generic Erosion first exists with respect to any Licensed Product or Targacept Returned Product in a particular country during the term of this Agreement, the applicable royalty rate set forth in Section 5.3 or Section 5.4, as the case may be, with respect to Net Sales of such Licensed Product or Targacept Returned Product in such country shall be reduced by **[*********]** (i.e., shall be **[*********]** of what it would be but for this Section 5.5(c)).

5.6 Payment Terms.

(a) *Manner of Payment*. All payments to be made by Licensee hereunder shall be made in United States dollars by wire transfer of immediately available funds to such bank account as Licensor may designate.

(b) *Reports and Royalty Payments*.

(i) If and for as long as payments are due and payable under Section 5.3 or Section 5.4, as the case may be, Licensee shall furnish to Licensor a written report, within **[********]** days after the end of each Calendar Quarter, showing the payments owed to Licensor with respect to such Calendar Quarter for Net Sales during such Calendar Quarter. Payments for each Calendar Quarter shall be due at the same time as such written report for such Calendar Quarter.

(ii) The report shall include, at a minimum, the following information for the applicable Calendar Quarter, each listed by Licensed Product or Targacept Returned Product, as the case may be, and by country of sale:

(A) the number of units of Licensed Products or Targacept Returned Products, as the case may be, sold by Licensee or its Affiliates or Sublicensees (or licensees) on which royalties are owed Licensor hereunder;

(B) the gross amount received for such sales;

(C) deductions taken from Net Sales as specified in the definition thereof;

(D) Net Sales;

(E) the royalties owed to Licensor under Section 5.3 or Section 5.4 as the case may be;

(F) the computations for any applicable currency conversions pursuant to Section 5.6(d); and

(G) any other information expressly required by the terms of this Agreement. All such reports shall be treated as Confidential Information of Licensee.

(c) *Records and Audits*.

(i) Licensee shall keep adequate books and records of accounting for the purpose of calculating all amounts payable to Licensor hereunder. For the two (2) years next following the end of the Calendar Year to which such books and records of accounting pertain, such books and records of accounting shall be open for inspection at reasonable times and upon reasonable prior written notice by an independent certified public accountant selected by Licensor, and which is reasonably acceptable to Licensee, for the sole purpose of inspecting the amounts owed to Licensor under this Agreement. In no event shall such inspections be conducted hereunder more frequently than once every **[********]** months or more than one (1) time with respect to any particular Calendar Quarter. Each audit conducted by Licensor under this Agreement shall be limited to a review of records pertaining to payments made by Licensee

during the immediately preceding **[********]** months. The accountant performing the audit must have executed and delivered to Licensee to be audited a confidentiality agreement as reasonably requested by Licensee, which shall include provisions limiting such accountant's disclosure to Licensor to only the results and basis for such results of such inspection. The results of such inspection, if any, shall be binding on both Parties.

(ii) Any underpayments from any such inspection shall be paid by Licensee within **[********]** days after written notification of the results of such inspection. Any overpayments from any such inspection shall be fully creditable against amounts payable in subsequent payment periods. Licensor shall pay for such inspections, except that in the event there is any upward adjustment in aggregate royalties payable for any Calendar Year shown by such inspection of more than the greater of (A) **[********]** U.S. dollars $**[********]**, or (B) **[********]** percent (**[********]**%) of the amount already paid for the audited period in question, Licensee shall reimburse Licensor for any reasonable out-of-pocket costs for such inspection.

(iii) Targacept acknowledges that amounts paid by it to Cornerstone under Section 5 are subject to Feinstein's rights to inspect Cornerstone (but, for clarity, not Targacept) under Article 4.2.2 of the Feinstein License and agrees to Feinstein's exercise thereof, including the disclosure of Targacept's Confidential Information solely as required to confirm the correctness of such amounts to Feinstein's independent certified public accountant.

(iv) Licensee shall maintain with its books of account such reports as it receives from any Sublicensee regarding the Sublicensee's Net Sales of any Licensed Product or Targacept Returned Product as the case may be. In addition, Licensee shall notify Licensor in the event Licensee conducts an audit of one of its Sublicensees and the outcome of such audit reveals an underpayment or overpayment from such Sublicensee to Licensee which, in turn, resulted in an underpayment or overpayment by Licensee to Licensor.

(d) *Currency Exchange*. With respect to Net Sales invoiced in U.S. dollars, the Net Sales and the amounts due to Licensor hereunder shall be expressed in U.S. dollars. With respect to Net Sales invoiced in a currency other than U.S. dollars, the Net Sales shall be expressed in the domestic currency of the entity making the sale, together with the U.S. dollar equivalent, calculated using the official rate of exchange of such domestic currency as quoted by The Wall Street Journal, Eastern U.S. Edition (the "WSJ Exchange Rate"), for the last business day of the Calendar Quarter for which the payment is made; provided that if the selling party employs a worldwide accounting system, such rate of exchange shall be its monthly rate of exchange prevailing on the last day of the month preceding the month in which such sales are recorded.

(e) *Tax Withholding*. The withholding tax, duties, and other levies (if any) applied by any government authority on payments made by Licensee to Licensor hereunder shall be borne by Licensor. Licensee shall cooperate with Licensor to enable Licensor to claim exemption therefrom under any double taxation or similar agreement in force and shall use commercially reasonable efforts to provide to Licensor proper evidence of payments of withholding tax and

assist Licensor by obtaining or providing in as far as possible the required documentation for the purpose of Licensor's tax returns.

(f) *Blocked Payments*. In the event that, by reason of applicable law in any country, it becomes impossible or illegal for Licensee to transfer, or have transferred on its behalf, payments owed Licensor hereunder, Licensee shall promptly notify Licensor of the conditions preventing such transfer and such payments shall be deposited in local currency in the relevant country to the credit of Licensor in a recognized banking institution designated by Licensor or, if none is designated by Licensor within a period of **[********]** days, in a recognized banking institution selected by Licensee and identified in a written notice given to Licensor.

(g) *Interest*. In the event a payment under this Agreement is not made when due, such outstanding payment will accrue interest (from the date such payment is due through and including the date upon which full payment is made) at the annual rate equal to the sum of **[********]** percent (**[********]**%) plus the Prime Rate (or the maximum applicable legal rate, if less than such sum) on the date when the payment was due, and calculated daily on the basis of a 360-day year. Payment of accrued interest will accompany payment of the outstanding payment. "Prime Rate" means the prime rate as reported in The Wall Street Journal, Eastern U.S. Edition.

Section 6. Prosecution, Maintenance, Enforcement and Defense of Licensed Patents.

6.1 Transfer. Within thirty (30) days after the Effective Date, Cornerstone shall transfer, or instruct its patent counsel to transfer, to Targacept's patent counsel true, complete and accurate original (in the case of Field Patents) or copies (in the case of Mixed Patents) files of Cornerstone's patent counsel relating to the prosecution, maintenance, defense, validity and enforceability of all Licensed Patents, including the complete file wrapper for each Licensed Patent, it being understood that Cornerstone's patent counsel shall retain copies of all documents delivered to Targacept's patent counsel. Cornerstone shall take all reasonable steps so as to ensure that the prosecution and maintenance of each Field Patent is not prejudiced during such transition. Cornerstone also shall promptly forward, or instruct Cornerstone's patent counsel to forward, to Targacept's patent counsel any correspondence or other communication relating to any Field Patent that Cornerstone or any counsel employed by Cornerstone may receive from any governmental office. Within **[********]** days of receiving Cornerstone's invoice therefor, Targacept shall reimburse Cornerstone for all out-of-pocket costs and reasonable expenses associated with the transfer of patent files and correspondence to Targacept's patent counsel under this Section 6.1.

6.2 Division of Mixed Patents. Subsequent to the Effective Date, Targacept shall identify which of the pending patent applications included in the Mixed Patents, if any, it believes in good faith should be separated into discrete patent applications with (i) claims that apply exclusively in the Excluded Field and (ii) claims that apply exclusively in the Field, whether by filing divisionals, continuations, continuations-in-part or other like patent applications claiming priority to the applicable Mixed Patent). Promptly following such determination by Targacept, Cornerstone shall request SetPoint's written concurrence with and agreement to such determination and Targacept and Cornerstone shall as soon as reasonably practicable thereafter

implement such separation; provided that (i) in furtherance of identifying and implementing such separation, Cornerstone agrees to let Targacept instruct Cornerstone's counsel and (ii) each Party shall pay its own costs and expenses (including the cost of its counsel) associated with identifying and implementing such separation. With respect to each Mixed Patent that is separated into discrete patent applications pursuant to this Section 6.2, upon consummation of such separation, the resulting patent application(s) with claims that apply exclusively in the Excluded Field shall thereupon become Excluded Field Patents and the resulting patent application(s) with claims that apply exclusively in the Field shall thereupon become Field Patents. Each Mixed Patent that has not been determined by Targacept to be separated into discrete patent applications pursuant to this Section 6.2 shall be and remain a Mixed Patent.

6.3 Prosecution and Maintenance of Field Patents and Mixed Patents.

(a) *Prosecution and Maintenance*.

(i) Following the Effective Date and subject to Feinstein's rights with respect to the selection of patent counsel pursuant to Article 5.1 of the Feinstein License, (A) Targacept or any of its Affiliates or Sublicensees shall have the right, but not the obligation, to prepare, prosecute (including with respect to any interferences, oppositions, reissue proceedings, re-examinations and term extensions) and maintain the Field Patents at Targacept's or such Affiliate's or Sublicensee's sole expense in such jurisdictions as Targacept or its Affiliate or Sublicensee shall determine in its sole discretion and (B) Cornerstone shall have the obligation to prepare, prosecute (including with respect to any interferences, oppositions, reissue proceedings, re-examinations and term extensions) and maintain the Mixed Patents at its sole expense.

(ii) With respect to the preparation and prosecution of each "Specified Outside Patent" (as defined as of the Effective Date in the SetPoint License), Targacept shall not include in such Specified Outside Patent any claim that applies in the Excluded Field (A) unless (1) the failure to include such claim would materially prejudice the prosecution of claims that apply in the Field or (2) either Cornerstone or, for so long as the SetPoint License is in force and effect, SetPoint shall have provided written consent and (B) without prior consultation with either Cornerstone or, for so long as the SetPoint License is in force and effect, SetPoint and without attempting to incorporate all reasonable comments thereof with respect to such claim.

(b) *Cornerstone Support for Field Patents*. Cornerstone shall provide, and shall cause its licensors, sublicensees and patent counsel to provide, information and assistance in connection with the prosecution and maintenance of the Field Patents as reasonably requested by Targacept or any of its Affiliates or Sublicensees, at Targacept's or such Affiliate's or Sublicensee's reasonable expense.

(c) *Communication*.

(i) Field Patents. Targacept shall (A) direct its patent counsel to keep Cornerstone reasonably informed as to the status of Field Patents, (B) consult from time to time with Cornerstone concerning the prosecution of such Field Patents and (C) provide Cornerstone

copies of all applications that are Field Patents and any other documents specifically relating to a Field Patent that Targacept files with or receives from any patent office and Targacept agrees that Cornerstone may provide such copies to Feinstein.

(ii) Mixed Patents. Cornerstone shall (A) direct its patent counsel to keep Targacept reasonably informed as to the status of Mixed Patents, (B) consult from time to time with Targacept concerning the prosecution of such Mixed Patents and (C) provide Targacept copies of any material documents specifically relating to the prosecution and maintenance of each Mixed Patent that Cornerstone files with or receives from any patent offices where such Mixed Patent is being prosecuted or maintained.

(d) *Abandonment and Lapse*. In the event that Targacept decides to abandon, or not to pursue in any Major Country or in Australia, Canada or China, the prosecution or maintenance of a Field Patent, Targacept shall provide Cornerstone with notice in a manner so as to provide Cornerstone with sufficient notice to allow Cornerstone to assume prosecution or maintenance of such Field Patent. If Cornerstone does assume filing, prosecution or maintenance of such Field Patent, such Field Patent shall no longer be a Licensed Patent. In the event that Cornerstone (or, for so long as SetPoint has the valid right to file, prosecute and maintain the applicable Mixed Patent, SetPoint) decides to abandon the prosecution or maintenance of a Mixed Patent, Cornerstone shall provide Targacept with notice in a manner so as to provide Targacept with sufficient notice to allow Targacept to assume, in its sole discretion, prosecution or maintenance of such Mixed Patent; provided that, for clarity, to the extent such Mixed Patent continues to be licensed by Feinstein to Cornerstone, Targacept shall retain all of its rights under this Agreement with respect to such Mixed Patent whether or not it assumes prosecution or maintenance thereof.

(e) *Priority*. Notwithstanding anything in this Agreement to the contrary, with respect to the prosecution and maintenance of any Field Patent, Targacept shall be entitled to give priority to any Licensed Product over any other compound or product.

6.4 Patent Term Extension. Targacept shall have the sole right to make all decisions in each country or jurisdiction in the world regarding patent term extensions for each Licensed Patent (other than **[********]** Patents) and each Licensed Product, including (a) in the United States with respect to extensions pursuant to 35 U.S.C. §156 et. seq., (b) outside of the United States pursuant to supplementary protection certificates and (c) anywhere in the world with respect to any other extensions that are now or become available in the future. Upon request by Targacept, Cornerstone shall timely implement, or cooperate in all reasonable respects in the timely implementation of, Targacept's decisions under this Section 6.4.

6.5 Enforcement and Defense of Licensed Patents.

(a) *Notification of Infringement*. In the event that Cornerstone or Targacept becomes aware of (i) a suspected infringement (including a deemed infringement under the Drug Price Competition and Patent Term Restoration Act of 1984, as amended) of any Licensed Patent (an "Infringement") or (ii) any challenge to a Licensed Patent, including any claim of invalidity or unenforceability of a Licensed Patent, then in each case, such Party shall notify the other Party promptly, and following such notification, the Parties shall confer.

(b) *Targacept First Right for Field Patent Actions*.

(i) Targacept (or, at Targacept's election, any Affiliate or Sublicensee thereof) shall have the first right, but shall not be obligated, to bring an enforcement action, including for infringement, or to defend any action or proceeding alleging non-infringement of any Field Patent, or to defend against any action or proceeding alleging invalidity or unenforceability of any Field Patent (any of the foregoing, a "Field Patent Action"), at its own expense, in its own name and under its own direction and control, or settle any such Field Patent Action by sublicense or otherwise. The first right pursuant to this Section 6.5(b)(i) shall be subject to Feinstein's rights as set forth in Article 5.5 of the Feinstein License.

(ii) *Assistance by Cornerstone*. Cornerstone shall assist Targacept (or any Affiliate or Sublicensee thereof) in all reasonable respects in any Field Patent Action if so requested by Targacept (or any Affiliate or Sublicensee thereof) and shall (i) join such Field Patent Action if reasonably requested by Targacept (or any Affiliate or Sublicensee thereof) or required by applicable law or (ii) require, if empowered by the applicable Third Party In-License, or otherwise use its best efforts to cause the owner of the applicable Field Patent to do the same.

(c) *Cornerstone First Right for Mixed Patent Actions*. Cornerstone shall have the first right, but shall not be obligated, to bring an enforcement action, including for infringement, or to defend any action or proceeding alleging non-infringement of any Mixed Patent, or to defend against any action or proceeding alleging invalidity or unenforceability of any Mixed Patent (any of the foregoing, a "Mixed Patent Action"), at its own expense, in its own name and under its own direction and control, or settle any such Mixed Patent Action by sublicense or otherwise. The first right pursuant to this Section 6.5(c) shall be subject to Feinstein's rights as set forth in Article 5.5 of the Feinstein License.

(d) *Step In Rights*. If Targacept (and, if applicable, its Affiliates and Sublicensees), in the case of a Field Patent Action, or Cornerstone (or, for so long as SetPoint has the valid right to bring or defend the applicable Mixed Patent Action, SetPoint), in the case of a Mixed Patent Action, makes a final decision, documented in writing, not to bring or defend any action, then Targacept (in the case of a Field Patent Action) or Cornerstone (in the case of a Mixed Patent Action) shall notify the other Party and such other Party or any of its Affiliates, Third Party licensors or licensees (or (S)sublicensees) may, but shall not be obligated to, bring or defend such Field Patent Action or Mixed Patent Action (as the case may be, a "Patent Action"), at its own expense, in its own name and under its own direction and control.

(e) *Participation*. If Cornerstone or any of its Affiliates or licensees (or sublicensees) brings or defends any Field Patent Action in accordance with Section 6.5(d), or if Targacept or any of its Affiliates or licensees (or sublicensees) brings or defends any Mixed Patent Action in accordance with Section 6.5(d), the other Party (or any Affiliate or Sublicensee thereof) shall have the right to participate in such Patent Action with its own counsel at its own expense and without reimbursement hereunder. If such other Party (or any Affiliate or Sublicensee thereof) elects to so participate, the bringing or defending Party shall provide, or cause the enforcing

entity to provide, the other Party (or any Affiliate or Sublicensee thereof) with an opportunity to consult regarding such Patent Action.

(f) *Withdrawal*. If either (i) Targacept (or any Affiliate or Sublicensee thereof) or (ii) Cornerstone or any of its Affiliates or licensees (or sublicensees) brings or defends a Patent Action under this Section 6.5 and subsequently ceases to pursue or defend or withdraws from such Patent Action, it shall promptly notify the other so that the other may exercise any rights available to it under the terms of this Section 6.5.

(g) *Exclusion of* **[********]** *Patents*. Notwithstanding anything in this Section 6.5 to the contrary, Targacept shall not have any (i) defense or enforcement rights with respect to the **[********]** Patents or (ii) obligation to pay any expenses of any kind (including prosecution, filing, issuance, maintenance, filing, defense and prosecution-related expenses) with respect to **[********]** Patents.

6.6 Prosecution, Maintenance, Enforcement and Defense of Excluded Field Patents. In the prosecution, maintenance, enforcement or defense of each Excluded Field Patent (or, if applicable, Licensed Patent), Cornerstone shall not and shall not permit any of its Third Party licensors or licensees (or sublicensees) to:

(a) take any action in the prosecution and maintenance of any Excluded Field Patent (or, if applicable, Licensed Patent) that it knows or should know has or would have a material adverse effect on the commercial exploitation of Licensed Products by Targacept or any Affiliate or Sublicensee thereof; or

(b) enter into any agreement that is inconsistent with this Section 6; or

(c) list any Excluded Field Patent (or, if applicable, Licensed Patent) in the Orange Book without providing Targacept at least **[********]** days advance notice.

6.7 Settlements and Recoveries in Patent Actions.

(a) *Settlement*. With respect to any Patent Action brought or defended by Cornerstone or any of its Affiliates, Third Party licensors or licensees (or sublicensees) as permitted by Section 6.5(d), no settlement of such Patent Action that restricts or may restrict the scope, or adversely affects or may adversely affect the validity or enforceability, of a Licensed Patent, or that does not include a full release of Targacept (and its directors, officers and employees) from any liability, may be entered into by Cornerstone or any Affiliate or licensee (or sublicensee) thereof (and Cornerstone shall not to consent to such a settlement) without the prior written consent of Targacept, not to be unreasonably withheld.

(b) *Recoveries to Cover Costs*. In the event that either Party exercises the rights conferred in this Section 6 and recovers any damages or other sums in a Patent Action or in settlement thereof, such damages or other sums recovered shall first be applied to all out-of-pocket costs and expenses incurred by the Parties in connection therewith (including attorneys fees), unless such Party is expressly not entitled to reimbursement hereunder. If such recovery is

insufficient to cover all such costs and expenses of both Parties, the controlling Party's costs shall be paid in full first before any of the other Party's costs. Each party seeking reimbursement under this Section 6.7(b) shall furnish promptly to the other Party appropriate documentation of its out-of-pocket costs and expenses incurred.

(c) *Remaining Funds*. If, after reimbursement pursuant to Section 6.7(b), any funds shall remain from such damages or other sums recovered, such funds shall be retained by the Party that controlled the Patent Action; provided, however, that (A) if Targacept is the Party that controlled such Patent Action, Targacept shall pay Cornerstone an amount equal to the royalties payable hereunder, if any, as if such remaining recovery were Net Sales, except that if amounts are owed Cornerstone pursuant to this clause (A), solely to the extent such recovery is expressly designated by the applicable court as including lost profits of Targacept, Cornerstone shall instead be entitled to receive a portion of such recovered lost profits in the same proportion as Targacept's aggregate royalties paid or payable to Cornerstone hereunder on Net Sales of Licensed Products in the country in question during the four completed Calendar Quarters immediately preceding the date of such recovery twelve (12) full bears to Targacept's profits with respect to the sale of the Licensed Product that gave rise to such Net Sales for the same period and (B) if Cornerstone is the Party that controlled such Patent Action, Cornerstone shall pay Targacept an amount equal to one-half of such remaining recovery. All payments under this Section 6.7(c) shall be due and payable within **[********]** days after the controlling Party's receipt of any damages or other sums.

6.8 Escrow in Certain Circumstances.

(a) *Deposit of Funds*. With respect to each Licensed Product and each country, in any Patent Action in which a Third Party challenges the validity or enforceability of all (and not less than all) of the Valid Claims under the Licensed Patents in such country that would give rise to a Royalty Term (or a continued Royalty Term) in such country (including by way of interference, opposition, reissue proceeding or re-examination or in response to enforcement pursuant to this Section), then, beginning upon filing of such action or proceeding by a Third Party, **[********]** percent (**[********]**%) of all amounts that would otherwise be paid to Cornerstone under Sections 5.2 or 5.3 with respect to such Licensed Product for such country affected by such action or proceeding, shall be deposited in an interest bearing escrow account pursuant to a separate written escrow agreement signed by the Parties and a Third Party escrow agent until such time as all such Valid Claims expire, subject to Section 6.8(b).

(b) *Release of Funds*. All monies in any escrow account established pursuant to Section 6.8(a), together with all accrued interest, shall be (A) released to Targacept if all such Valid Claims are found invalid or unenforceable by a court of proper jurisdiction in a decision unappealable or unappealed within the time allowed for appeal, or (B) if at least one such Valid Claim is found not invalid and not unenforceable by a court of proper jurisdiction in such decision, after giving effect to Section 6.7, all monies in such escrow account, together with all accrued interest, shall be released to Cornerstone immediately.

6.9 Feinstein License. Solely to the extent any of the rights of Targacept pursuant to this Section 6 (including the rights to file, prosecute, maintain, enforce and defend Field Patents or, if

applicable, Mixed Patents as provided in this Section 6) requires an assignment by Cornerstone of rights of Cornerstone arising under the Feinstein License (the "Requisite Assigned Rights"), Cornerstone hereby assigns the Requisite Assigned Rights to Targacept and its Affiliates and Sublicensees.

Section 7. Confidential Information; Non-Disclosure of Agreement; Use of Name.

7.1 Confidential Information. The Parties agree that Confidential Information shall be handled in accordance with the terms and conditions of the Confidentiality Agreement, subject to the terms of Sections 7.3, 7.4, 7.5 and 7.6; provided, however, that: (i) the purpose described in Section 1 of the Confidentiality Agreement is amended to include the performance of and exercise of rights under this Agreement; (ii) the term of the Confidentiality Agreement set forth in Section 8 thereof is hereby amended to end five (5) years after the expiration or termination of this Agreement; and (iii) in the event of any inconsistency between the terms of the Confidentiality Agreement and the terms of this Agreement, the terms of this Agreement shall control. The terms of the Confidentiality Agreement, as amended hereby, are hereby incorporated in this Agreement by this reference.

7.2 Non-Disclosure of Agreement. Except as specifically authorized herein (including in Section 7.4), neither Party shall make, directly or indirectly, any public comment, statement, or communication with respect to, or otherwise to disclose or to permit any disclosure relating to, this Agreement or the transactions contemplated hereby, without the other Party's prior written consent, provided that: (i) notwithstanding the foregoing, to the extent information regarding this Agreement or the transactions contemplated hereby has been publicly disclosed (or disclosed in a scientific or other conference) other than as a result of a breach of this Agreement, either Party may subsequently disclose the same information without the consent of the other Party; and (ii) nothing herein shall prevent: (A) either Party from, upon notice to and opportunity to review and comment by the other, making such public announcements as such Party's legal obligations require, including under any federal or state securities laws and under any rule or regulation of any securities exchange or market on which such Party's or any of its Affiliates' securities are listed or quoted; provided that, for clarity, prior to the first filing with the United States Securities and Exchange Commission or other public announcement describing the terms of this Agreement and prior to each subsequent filing that includes material terms of this Agreement disclosed for the first time, the filing Party shall give the other Party a reasonable opportunity to review prior to submission and shall give due consideration to any reasonable comments by the non-filing Party relating to such filing, including the provisions of this Agreement for which confidential treatment should be sought; or (B) Targacept from making any public comment, statement, or communication with respect to, or otherwise to disclose or to permit any disclosure relating to, any Licensed Product.

7.3 Confidential Information During Term of License. Cornerstone acknowledges and agrees that the Field Patents and the Licensed Know-How are valuable assets and, following the Effective Date and for so long as the License is in force and effect, shall be controlled by Targacept and constitute

Targacept's Confidential Information, subject in the case of the Licensed Know-How only to SetPoint's rights under the SetPoint License. Cornerstone agrees to use diligent efforts to cause SetPoint to treat the Licensed Know-How as Confidential Information of Targacept and not to make use of such information for its own purposes or for the benefit of any other Person, subject only to SetPoint's rights in the Excluded Field under the SetPoint License.

7.4 Publications. Notwithstanding anything herein to the contrary, Targacept shall be free to present or publish any information, studies or data generated as a result of the research, development and commercialization of Licensed Products or other exploitation of the Licensed Intellectual Property by Targacept in the Field.

7.5 Confidential Information After Term of License. If the License is terminated in full for any reason, then the Licensed Intellectual Property shall no longer be deemed Confidential Information of Targacept.

7.6 Disclosure to Feinstein. Targacept acknowledges, notwithstanding the Confidentiality Agreement and Section 7.2, that this Agreement and information regarding the transactions contemplated hereby have been and will be made available by Cornerstone to Feinstein solely as and to the extent required by Article 3.1 of the Feinstein License.

7.7 Use of Name. Except as required by law (including any federal or state securities laws and under any rule or regulation of any securities exchange or market on which a Party's or any of its Affiliates' securities are listed or quoted), neither Targacept nor Cornerstone shall use the name or any insignia, symbol or logotype of the other in any advertising or promotional materials or public statement or press release without the prior consent of the other party.

Section 8. Covenants of Cornerstone.

8.1 Cornerstone Non-Competition Covenant. For a period of **[********]** years following the Effective Date, Cornerstone shall not, and shall ensure that its Affiliates do not, either directly or indirectly, research, develop, market, sell, manufacture, distribute or otherwise commercialize any product in the Restricted Field, or grant to a Third Party a license to any Patent Rights or Technology Controlled by Cornerstone or any of its Affiliates to research, develop, market, sell, manufacture, distribute or otherwise commercialize any product in the Restricted Field.

8.2 Acquisition Exemption for Non-Competition Covenants. The restriction in Section 8.1 shall not limit in any way the activities of any Person or group of Persons that acquires all or any part of the business of Cornerstone (through any acquisition of stock, assets, or otherwise) or any Affiliate of such acquiring Person(s) that is not an Affiliate of Cornerstone at the date of this Agreement, provided that such Person or group of Persons is engaged in substantial development or commercialization efforts in the Restricted Field on the date of such acquisition.

8.3 Prohibition Against Challenging the Licensed Patents. Without the consent of the other Party, neither Party nor any of its Affiliates shall challenge, or induce any Third Party to challenge, the validity or enforceability of the Licensed Patents, or any claim therein, or initiate or participate in any re-examination or other proceeding related to the validity, enforceability or patentability of any claim of the Licensed Patents before any tribunal or patent office. Notwithstanding the foregoing, nothing in this Agreement shall restrict either Party or its Affiliates from responding to a subpoena, process, or discovery requests in any litigation or administrative proceeding.

8.4 Prohibition re: Non-Feinstein Licensed Patents. Without the consent of Targacept, in no event shall Cornerstone or any of its Affiliates file, prosecute or maintain any Licensed Patent (other than the Feinstein Licensed Patents) that includes any claim that applies outside the Field.

8.5 Notification of Third Party Inventions. Cornerstone agrees that, if after the Effective Date any Third Party to an agreement listed on Schedule 9.1 hereto notifies Cornerstone that an invention or other intellectual property was made, conceived or created under such agreement or with respect to a Cornerstone Compound, Cornerstone shall provide notice to Targacept within **[********]** days of receiving such notice and, if Targacept requests, cooperate in all reasonable respects, at Targacept's reasonable cost, to cause such invention or other intellectual property to become Licensed Intellectual Property.

Section 9. Warranties; Limitations of Liability; Indemnification.

9.1 Cornerstone Representations, Warranties and Covenants. Cornerstone covenants, represents and warrants to Targacept that as of the Effective Date:

(a) Cornerstone is a corporation duly organized, validly existing and in good standing under the laws of state or jurisdiction in which it is incorporated, and it has full right and authority to enter into this Agreement and to grant the licenses and other rights to Targacept as herein described.

(b) This Agreement has been duly authorized by Cornerstone by all requisite corporate action and, when executed and delivered, shall become a valid and binding contract of Cornerstone enforceable against Cornerstone in accordance with its terms, subject to applicable bankruptcy, insolvency, reorganization, moratorium and other laws affecting creditors' rights generally from time to time in effect, and to general principles of equity.

(c) The execution, delivery and performance of this Agreement do not conflict with any other agreement, contract, instrument, or understanding, oral or written, to which Cornerstone is a party, or by which it is bound, nor does such execution, delivery and performance of this Agreement violate any law applicable to Cornerstone.

(d) All necessary consents, approvals and authorizations of all regulatory and governmental authorities and other Persons required to be obtained by Cornerstone in connection

with the execution and delivery of this Agreement and the performance of its obligations hereunder have been obtained.

(e) The Patent Rights listed on (i) Exhibit A constitute, to Cornerstone's knowledge after due inquiry of Feinstein, all of the Feinstein Licensed Patents as of the Effective Date, (ii) Exhibit B constitute all Patent Rights (other than the Feinstein Licensed Patents) Controlled by Cornerstone or any of its Affiliates, or in which Cornerstone or any of its Affiliates has any ownership, license, sublicense, covenant not to sue, option or other interest, in each case as of the Effective Date that are necessary or reasonably useful to make, use, sell, offer to sell, import or otherwise exploit any product in the Primary Field, (iii) Exhibit C constitute all of the Excluded Field Patents as of the Effective Date and (iv) the Mixed Patents listed on Exhibit A constitute all of the Licensed Patents licensed by Cornerstone to SetPoint and such license is limited to the Excluded Field. To Cornerstone's knowledge, all claims included in the issued Licensed Patents are, and, upon issuance, all claims included in the pending Licensed Patents will be, valid and enforceable. No written claim has been made to Cornerstone or, to Cornerstone's knowledge, to Feinstein or any Third Party (except by a patent examiner during prosecution of the patent application(s) that resulted in any such issued Licensed Patent), and no action or proceeding has been commenced or, to Cornerstone's knowledge, threatened, alleging to the contrary of the preceding sentence. Except as provided on Schedule 9.1, no Licensed Patent (other than the Feinstein Licensed Patents) and, to Cornerstone's knowledge, no Feinstein Licensed Patent has ever been the subject of litigation, an interference, an opposition, a reissue proceeding, a re-examination or other like action or proceeding. To Cornerstone's knowledge, the conception and reduction to practice of the inventions claimed in or covered by the Licensed Patents (the "Inventions") have not constituted or involved the misappropriation of trade secrets or other rights or property of any Third Party. To Cornerstone's knowledge, there has been no infringement or threatened infringement by any Third Party of any Licensed Patents. Cornerstone has the right to enforce the Licensed Patents. No rights or licenses are required under Patent Rights or Technology Controlled by Cornerstone or, to Cornerstone's knowledge, under any Third Party Patent Rights or Technology for Targacept or its Affiliates or Sublicensees to exploit Licensed Products in the Field other than those granted herein.

(f) Each Cornerstone Compound is a "Product" (as defined in the Feinstein License). The "Research Term" (as defined in the Feinstein License) has expired; there is no further research being conducted under the Feinstein License; and there is no pending or, to Cornerstone's knowledge, planned publication with respect to research previously conducted thereunder or otherwise with respect to any Cornerstone Compound.

(g) To Cornerstone's knowledge, all filings or actions required to be made or taken by Cornerstone or any of its Affiliates, or by Feinstein, with any government agency or authority to secure and maintain title to each Invention and each Licensed Patent have been timely made or taken.

(h) Cornerstone is the sole and exclusive owner of and Controls all right, title and interest in and to the Licensed Intellectual Property, other than the Feinstein Licensed Patents and Feinstein Know-How, and is entitled to grant the License and other rights with respect thereto specified herein. To Cornerstone's knowledge after due inquiry of Feinstein, except as

provided on Schedule 9.1, Cornerstone is the sole and exclusive licensee of and Controls all right, title and interest in and to the Feinstein Licensed Patents and Feinstein Know-How, subject only to the rights in the Excluded Field Patents and Mixed Patents granted by Cornerstone to SetPoint in the Excluded Field under the SetPoint License and the rights in the **[********]** Patents granted by Feinstein to third parties outside the Field, and Cornerstone is entitled to grant the License and other rights with respect thereto specified herein. There are no Licensed Patents to which Cornerstone is a non-exclusive licensee in the Field (subject to the rights of the U.S. government under the Feinstein License). None of the Licensed Intellectual Property is subject to any lien, security interest, encumbrance or claim of ownership by any Third Party, other than Feinstein's claim of ownership of the Feinstein Licensed Patents and Feinstein Know-How.

(i) There are no claims, judgments or settlements against or amounts with respect thereto owed by Cornerstone or any of its Affiliates (or SetPoint) relating to the Licensed Intellectual Property, and, to Cornerstone's knowledge, Targacept's exploitation of Licensed Products under this Agreement will not infringe the Patent Rights or misappropriate other intellectual property rights of any Third Party. The grant, use or practice of the License shall not trigger any payment obligation by Cornerstone or any of its Affiliates to any Third Party, other than to Feinstein under the Feinstein License. The only Third Party In-License (including, for clarity, agreements whereby a Third Party Controls Patent Rights and Technology licensed to Targacept hereunder) is the Feinstein License.

(j) Neither Cornerstone nor, to its knowledge, Feinstein is in breach of the Feinstein License and the Feinstein License is in full force and effect. Cornerstone has not received notice that it is in breach of its obligations under the Feinstein License. To the knowledge of Cornerstone, there is no basis for a claim that it is or was in breach of its obligations under the Feinstein License. No term or provision of this Agreement constitutes or gives rise to, or shall constitute or give rise to, a breach of the Feinstein License.

(k) Neither Cornerstone nor, to its knowledge, SetPoint, is in breach of the SetPoint License, and the SetPoint License is in full force and effect. Cornerstone has not received notice that it is in breach of its obligations under the SetPoint License. To the knowledge of Cornerstone, there is no basis for a claim that it is or was in breach of its obligations under the SetPoint License, nor is there any basis for a claim that SetPoint is or was in breach of its obligations under the SetPoint License. No term or provision of this Agreement constitutes or gives rise to, or shall constitute or give rise to, a breach of the SetPoint License.

(l) True, complete and correct copies of the Feinstein License and the SetPoint License have been provided or made available to Targacept prior to the Effective Date. Targacept will not have any financial obligations under the Feinstein License or the SetPoint License. Except for the Feinstein License, there is no other agreement to which Cornerstone is a party that would impose any obligations on Targacept's exploitation of Licensed Products in the Field.

(m) There is no pending action or proceeding alleging, nor has Cornerstone received any written communication alleging, that the manufacture, use, sale, offer for sale, importation, performance, research, development, commercialization or other exploitation of any Licensed

Intellectual Property or Licensed Product has infringed or misappropriated, or will infringe or misappropriate, any Patent Rights or other intellectual property rights of any Third Party.

(n) Cornerstone has not previously granted to any Third Party any licenses, sublicenses, covenants not to sue or any other rights under the Licensed Intellectual Property in or outside the Field, except for the licenses granted to SetPoint in the Excluded Field pursuant to the SetPoint License.

(o) To Cornerstone's knowledge and except as provided on Schedule 9.1: (i) Kevin J. Tracey, M.D. and the other individuals named as inventors in the respective Licensed Patents (collectively, the "Inventors") are the only persons who contributed to either the conception or first reduction to practice of the corresponding Inventions; and (ii) Feinstein has secured a valid and binding written assignment to each Invention from each Inventor. Cornerstone has no reason to believe that any of the named inventors in the respective Licensed Patents has granted, purported to grant or agreed to grant any right or license to any Invention or any of the Licensed Patents to any Third Party.

(p) The Licensed Patents are being diligently prosecuted in the United States Patent and Trademark Office and equivalent foreign patent offices in accordance with all applicable laws and regulations. The Licensed Patents have been filed and maintained properly and correctly in all material respects and all applicable fees have been paid on or before the deadline for payment. In respect of the pending United States patent applications included in the Licensed Patents, (i) Cornerstone has presented all relevant prior art of which it and, to its knowledge, the Inventors, have knowledge to the relevant patent examiner at the United States Patent and Trademark Office and (ii) no action has been taken in the prosecution thereof to give priority to claims directed to the Excluded Field over claims directed to the Field.

(q) Cornerstone has made available to Targacept prior to the Effective Date true, complete and correct copies of all information in its possession or Control as of the Effective Date regarding any or all of the safety, tolerability, potency or efficacy of Licensed Products or the validity and enforceability of the Licensed Patents.

(r) All works of authorship and all other materials subject to copyright protection included in Licensed Know-How are original and were either created by Cornerstone employees within the scope of their employment or are otherwise works made for hire, or all right, title and interest in and to such materials have been legally and fully assigned and transferred to Cornerstone, and all rights in all inventions and discoveries, made, developed or conceived by any employee or independent contractor of Cornerstone during the course of employment (or other retention) by Cornerstone and relating to or included in Licensed Know-How or that are the subject of one or more Licensed Patents have been or will be assigned in writing to Cornerstone.

(s) Cornerstone owns the Material and has the full power and right to provide the Material to Targacept without violating the terms of any agreement or arrangement with any Third Party. Cornerstone has provided to Targacept prior to the Effective Date a complete and correct copy of the agreement pursuant to which the Material was manufactured and provided to

Cornerstone. To the knowledge of Cornerstone, the supplier of the Material is not in violation or breach of or default under the agreement pursuant to which the Material was manufactured and provided to Cornerstone. To Cornerstone's knowledge, the Material: (i) has been manufactured in accordance with applicable written specifications and all applicable laws; and (ii) at the time of delivery to Targacept or its designee, will not be adulterated or misbranded within the meaning of the U.S. Federal Food, Drug and Cosmetic Act and other applicable laws. To Cornerstone's knowledge, no process, procedure or material used in the manufacture of Material delivered to Targacept hereunder infringed the Patent Rights other intellectual property rights of a Third Party. Neither Cornerstone nor, to Cornerstone's knowledge, the Material supplier nor any personnel of any of the foregoing who participated in the manufacture of the Material has been debarred or is subject to debarment pursuant to Section 306 of the U.S. Federal Food, Drug and Cosmetic Act, 21 U.S.C. § 335a, or is the subject of a conviction described in such section (or under any analogous provisions of applicable laws outside the United States).

(t) Except as provided on Schedule 9.1 hereto, no Cornerstone Compound has been provided by Cornerstone in any quantity at any time prior to the Effective Date to any Third Party. No Third Party to any agreement listed on Schedule 9.1 hereto has notified Cornerstone that an invention or other intellectual property was made, conceived or created under such agreement or with respect to a Cornerstone Compound.

(u) The intellectual property licensed and rights granted to Cornerstone pursuant to the License Agreement between Cornerstone and Feinstein effective July 1, 2001, as may have been amended thereafter, do not include any patent rights or technology necessary to develop, commercialize or otherwise exploit any Licensed Product, except and to the extent that such Licensed Product contains **[*********]** (or a **[*********]**), or **[*********]** (or a **[*********]**), or an **[*********]** (or a **[*********]**) or other **[*********]** that **[*********]** any of the foregoing.

(v) All information, documentation and other materials furnished or made available by Cornerstone upon the request of Targacept during Targacept's period of diligence prior to the Effective Date are true, complete and correct copies of what they purport to be.

9.2 Targacept Representations and Warranties. Targacept represents and warrants to Cornerstone that as of the Effective Date:

(a) Targacept is a corporation duly organized, validly existing and in good standing under the laws of state in which it is incorporated, and it has full right and authority to enter into this Agreement and to accept the rights and licenses granted as herein described.

(b) This Agreement has been duly authorized by Targacept by all requisite corporate action and, when executed and delivered, shall become a valid and binding contract of Targacept enforceable against Targacept in accordance with its terms, subject to applicable bankruptcy, insolvency, reorganization, moratorium and other laws affecting creditors' rights generally from time to time in effect, and to general principles of equity.

(c) The execution, delivery and performance of this Agreement do not conflict with any other agreement, contract, instrument or understanding, oral or written, to which Targacept is a party, or by which it is bound, nor does such execution, delivery and performance of this Agreement violate any law applicable to Targacept.

(d) All necessary consents, approvals and authorizations of all regulatory and governmental authorities and other Persons required to be obtained by Targacept in connection with the execution and delivery of this Agreement and the performance of its obligations hereunder have been obtained.

9.3 Disclaimer. EXCEPT FOR THE EXPRESS WARRANTIES SET FORTH IN THIS AGREEMENT, NONE OF CORNERSTONE, TARGACEPT, NOR ANY OF THEIR RESPECTIVE AFFILIATES, OFFICERS, DIRECTORS, EMPLOYEES OR REPRESENTATIVES MAKES OR HAS MADE ANY OTHER REPRESENTATION OR WARRANTY, EXPRESS OR IMPLIED, WRITTEN OR ORAL, AT LAW OR IN EQUITY, IN ANY FORM RELATING TO THE PARTIES, THE TRANSACTIONS CONTEMPLATED HEREBY, THE LICENSED PATENTS, THE LICENSED KNOW-HOW, OR THE LICENSED PRODUCTS. ANY REPRESENTATION OR WARRANTY OTHER THAN THE EXPRESS WARRANTIES SET FORTH IN THIS AGREEMENT IS HEREBY EXPRESSLY DISCLAIMED, INCLUDING ANY IMPLIED REPRESENTATION OR WARRANTY WITH RESPECT TO (I) MERCHANTABILITY, NON-INFRINGEMENT, SUITABILITY OR FITNESS FOR ANY PARTICULAR PURPOSE OR (II) THE PROSPECTS (FINANCIAL OR OTHERWISE), RISKS AND OTHER INCIDENTS OF THE LICENSED PRODUCTS.

NO OFFICER, DIRECTOR, AGENT, EMPLOYEE, OR REPRESENTATIVE OF CORNERSTONE HAS ANY AUTHORITY, EXPRESS OR IMPLIED, TO MAKE ANY REPRESENTATIONS OR WARRANTIES NOT SPECIFICALLY SET FORTH IN THIS AGREEMENT. TARGACEPT ACKNOWLEDGES THAT CORNERSTONE DOES HEREBY SPECIFICALLY DISCLAIM ANY SUCH OTHER REPRESENTATION OR WARRANTY MADE BY ANY PERSON.

9.4 Acknowledgments. Targacept acknowledges that **[********]** Cornerstone that (i) all of the research and development work of Cornerstone with respect to the Licensed Intellectual Property, including with respect to the Cornerstone Compounds, was **[********]** by which **[********]**, (ii) **[********]** of all of **[********]** in connection with **[********]**, (iii) **[********]** for the **[********]**, and (iv) **[********]** in the **[********]** and that such **[********]** in the **[********]**. Cornerstone acknowledges that **[********]** any of the foregoing.

9.5 Limitation of Liability. NOTWITHSTANDING ANYTHING IN THIS AGREEMENT OR OTHERWISE, EXCEPT WITH RESPECT TO A BREACH OF SECTION 7, NEITHER PARTY SHALL BE LIABLE TO THE OTHER OR ANY THIRD PARTY WITH RESPECT TO ANY SUBJECT MATTER OF THIS AGREEMENT FOR ANY INDIRECT, SPECIAL OR CONSEQUENTIAL DAMAGES, WHETHER UNDER ANY CONTRACT, WARRANTY, NEGLIGENCE,

STRICT LIABILITY OR OTHER LEGAL OR EQUITABLE THEORY; PROVIDED THAT, FOR CLARITY, THIS SECTION 9.5 SHALL NOT BE DEEMED TO LIMIT EITHER PARTY'S OBLIGATION UNDER SECTION 9.6, IF APPLICABLE, TO INDEMNIFY AND HOLD HARMLESS THE OTHER PARTY FROM AND AGAINST "LOSSES" ACTUALLY PAID BY SUCH OTHER PARTY TO THIRD PARTIES.

IN NO EVENT SHALL TARGACEPT OR ANY OF ITS DIRECTORS, OFFICERS, EMPLOYEES, ATTORNEYS, AGENTS OR REPRESENTATIVES BE LIABLE TO CORNERSTONE, ANY OF ITS AFFILIATES OR ANY THIRD PARTY (INCLUDING FEINSTEIN AND SETPOINT) FOR ANY DIRECT, INDIRECT, SPECIAL, CONSEQUENTIAL OR OTHER DAMAGES ARISING IN ANY RESPECT OUT OF (1) THE PREPARATION, NEGOTIATION OR CONSUMMATION OF EITHER THE AMENDMENT TO THE FEINSTEIN LICENSE EXECUTED ON OR ABOUT THE EFFECTIVE DATE OR THE AMENDMENT TO THE SETPOINT LICENSE EXECUTED ON OR ABOUT THE EFFECTIVE DATE OR (2) ANY ACT, OMISSION, DEFAULT OR NEGLECT TAKEN OR OMITTED IN GOOD FAITH (INCLUDING THE MAKING OF ANY DECISION OR DETERMINATION) IN CONNECTION WITH THE EXERCISE OF TARGACEPT'S RIGHTS UNDER SECTION 6, WHETHER UNDER ANY CONTRACT, WARRANTY, NEGLIGENCE, STRICT LIABILTY, AGENCY OR ANY OTHER LEGAL OR EQUITABLE THEORY.

9.6 Indemnification.

(a) *Targacept Indemnity*. Targacept hereby agrees to indemnify and hold Cornerstone and its Affiliates, each of their respective employees, directors, agents and contractors, and each of their respective successors, heirs and assigns and representatives ("Cornerstone Indemnitees") harmless from and against all claims, liabilities, damages, expenses (including reasonable attorneys' fees), suits, proceedings, losses or judgments, whether for money or equitable relief, of any kind (collectively, "Losses"), except to the extent subject to indemnification by Cornerstone pursuant to Section 9.6(b), arising from (i) the manufacture, use, sale, offer for sale, importation, performance, research, development, commercialization or other exploitation of any Licensed Products by or for Targacept or any of its Affiliates or Sublicensees, (ii) any breach of any representation, warranty or covenant of Targacept under this Agreement, or (iii) any act or omission by a Targacept Indemnitee that constitutes gross negligence, recklessness, or willful misconduct.

(b) *Cornerstone Indemnity*. Cornerstone hereby agrees to indemnify and hold Targacept and its Affiliates, each of their respective employees, directors, agents and contractors, and each of their respective successors, heirs and assigns and representatives ("Targacept Indemnitees") harmless from and against all Losses arising from (i) any breach of any representation or warranty of Cornerstone under this Agreement, (ii) any breach of any covenant of Cornerstone under this Agreement, (iii) the manufacture, use, sale, offer for sale, importation, performance, research, development, commercialization or other exploitation of any Targacept Returned Product by or for Cornerstone or any of its Affiliates or Sublicensees (or licensees), (iv) the manufacture, use, sale, offer for sale, importation, performance, research, development, commercialization or other exploitation of any product or service in the Excluded Field, (v) any

breach by Cornerstone of the Feinstein License or other Third Party In-License, (vi) any breach by Cornerstone or SetPoint of the SetPoint License or (vii) any act or omission by a Cornerstone Indemnitee that constitutes gross negligence, recklessness, or willful misconduct.

(c) *Indemnification Procedure*.

(i) A claim to which indemnification applies under Section 9.6(a) or Section 9.6(b) shall be referred to herein as a "Claim." If any Person (each, an "Indemnitee") intends to claim indemnification under this Section 9.6, the Indemnitee shall notify the other Party (the "Indemnitor") in writing promptly upon becoming aware of any claim that may be a Claim (it being understood and agreed, however, that the failure by an Indemnitee to give such notice shall not relieve the Indemnitor of its indemnification obligation under this Agreement except and only to the extent that the Indemnitor is actually prejudiced as a result of such failure to give notice). The Indemnitor shall have the right to assume and control the defense of such Claim at its own expense with counsel selected by the Indemnitor and reasonably acceptable to the Indemnitee; provided, however, that an Indemnitee shall have the right to retain its own counsel, with the fees and expenses to be paid by the Indemnitor if representation of such Indemnitee by the counsel retained by the Indemnitor would be inappropriate due to actual or potential differing interests between such Indemnitee and any other party represented by such counsel in such proceedings and otherwise by the Indemnitee. If the Indemnitor does not assume the defense of such Claim as aforesaid, the Indemnitee may defend such Claim, with the fees and expenses to be paid by the Indemnitor, but shall have no obligation to do so. The Indemnitee shall reasonably cooperate with the Indemnitor at the Indemnitor's expense and shall make available to the Indemnitor all pertinent information under the control of the Indemnitee, which information shall be subject to the terms of the Confidentiality Agreement.

(ii) The Indemnitee shall not settle or compromise any Claim without the prior written consent of the Indemnitor, and the Indemnitor shall not settle or compromise any Claim in any manner that would have an adverse effect on the Indemnitee's interests, without the prior written consent of the Indemnitee, which consent, in each case, shall not be unreasonably withheld.

9.7 Insurance.

(a) Targacept shall procure and maintain insurance policies for the following coverages with respect to personal injury, bodily injury and property damage arising out of Targacept's performance under this Agreement: (i) comprehensive general liability, including indemnification obligations and other contractual liability, in a minimum amount of $**[********]** combined single limit per occurrence and in the aggregate; (ii) before the commencement of clinical trials involving any Licensed Product, clinical trials coverage in a minimum amount of $**[********]** combined single limit per occurrence and in the aggregate; and (iii) prior to the first commercial sale of the first Licensed Product, product liability coverage, in a minimum amount of $**[********]** combined single limit per occurrence and in the aggregate, with the coverage provided for in clauses (ii) and (iii) to remain in force during the term of this Agreement and for at least **[********]** years thereafter.

(b) Cornerstone shall procure and maintain insurance policies for the following coverages with respect to personal injury, bodily injury and property damage arising out of Cornerstone's performance of this Agreement: (i) comprehensive general liability, including indemnification obligations and other contractual liability, in a minimum amount of $**[********]** combined single limit per occurrence and in the aggregate; (ii) before the commencement of clinical trials involving any Targacept Returned Product, clinical trials coverage in a minimum amount of $**[********]** combined single limit per occurrence and in the aggregate; and (iii) prior to the first commercial sale of the first Targacept Returned Product, product liability coverage, in a minimum amount of $**[********]** combined single limit per occurrence and in the aggregate, with the coverage provided for in clauses (ii) and (iii) to remain in force during the term of this Agreement and for at least **[********]** years thereafter. With respect to each Targacept Returned Product, all rights and licenses granted by Targacept to Cornerstone shall be expressly subject to and conditional on compliance by Cornerstone with this Section 9.7(b).

9.8 Bayh-Dole. Cornerstone shall ensure that Feinstein takes all actions in the future necessary under the Patent and Trademark Law Amendments Act of 1980, as amended, codified at 35 USC §§200-212, as amended (the Bayh-Dole Act), as well as any regulations promulgated pursuant thereto, to secure ownership of all Feinstein Patent Rights for Feinstein, including complying with all reporting requirements as set forth in 37 C.F.R. 401.14 and in the funding agreement between the U.S. government (or the National Institutes of Health) and Feinstein.

Section 10. Term, Termination and Survival.

10.1 Term. This Agreement shall commence as of the Effective Date and, unless sooner terminated in accordance with the terms hereof or by mutual written consent, shall continue until the expiration of the Product Royalty Term for the last Licensed Product, subject to Section 5.5(b).

10.2 Termination based on Certain Events.

(a) *Termination for Failure to Timely Complete the Preclinical Milestone*. If Targacept does not complete the Preclinical Milestone within the applicable period for completion set forth in Section 4.1(b)(i), as such period may be extended or eliminated as set forth therein, then, subject to Section 4.1(b)(ii), Cornerstone may terminate immediately this Agreement, but must do so, if at all, within **[*********]** days after first having such termination right.

(b) *Material Default*. Subject to Section 10.2(c), either Party shall have the right to terminate this Agreement upon delivery of written notice to the other Party in the event of any default in the performance by such other Party of any of such other Party's material obligations under this Agreement that has not been cured within **[*********]** days (**[*********]** business days in the case of a payment breach) after written notice thereof is given by the non-defaulting Party to the defaulting Party specifying the nature of the alleged default; provided that, except in the case of a payment breach, if the defaulting Party has during such **[*********]**-day period commenced and diligently continued conducting activities designed to cure such default but such cure is not possible during such **[*********]**-day period, the defaulting Party shall have an additional **[*********]** days in which to cure such default.

(c) *Disputed Default*. If the defaulting Party disputes in good faith the existence or materiality of a default specified in a notice provided by the non-defaulting Party pursuant to Section 10.2(b), and the defaulting Party provides notice to the non-defaulting Party of such dispute within the **[*********]** day (**[*********]** days in the case of a payment breach) cure period , the non-defaulting Party shall not have the right to terminate this Agreement unless and until the existence of such material default or failure by the defaulting Party has been determined in accordance with Section 11.7 and the period(s) set forth in Section 10.2(b) have expired without a cure. It is understood and agreed that during the pendency of such a dispute, all of the terms and conditions of this Agreement shall remain in effect and the Parties shall continue to perform all of their respective obligations hereunder.

10.3 Termination for Convenience by Targacept. Targacept may terminate this Agreement in full for any reason effective upon thirty (30) days prior written notice to Cornerstone.

10.4 Insolvency.

(a) *Licensor Bankruptcy*. All rights and licenses granted under or pursuant to this Agreement by Licensor to Licensee (including the License) are, and shall be deemed to be, for purposes of Section 365(n) of the Bankruptcy Code, licenses of rights to "intellectual property" as defined under Section 101(35A) of the Bankruptcy Code (the "Intellectual Property"). The Parties agree that Licensee, as a licensee of the Intellectual Property under this Agreement, shall retain and may fully exercise all of its rights and elections under the Bankruptcy Code in the event a case is commenced by or against the Licensor under the Bankruptcy Code and the Licensor rejects this Agreement pursuant to Section 365 of the Bankruptcy Code, including the right of the Licensee to elect under Section 365(n)(l)(B) to retain all of the its rights and licenses granted by Licensor that are in existence immediately before the commence of such case,

including any rights granted to the Licensee with respect to any patents that issue on any patent applications pending at the time of commencement of such case or any then-existing rights with respect to patents issued, or works of authorship protected, under the law of any foreign jurisdiction.

(b) *Liquidation of a Party*. Either Party may terminate this Agreement, or the rights and licenses of the other Party under this Agreement, upon written notice to such other Party given at any time upon or after:

(i) the appointment of a receiver, supervisor or liquidator for all or substantially all of the property of such other Party or a money judgment against such other Party which remains unsatisfied for more than **[********]** days after entry of judgment and such judgment has not been appealed;

(ii) the institution of any proceedings for the liquidation or winding up of the business of such other Party or for the termination of its corporate existence; or

(iii) such other Party files a petition in bankruptcy, or enters into an agreement with its creditors, makes an assignment for the benefit of creditors, or suffers or permits the entry of any order adjudicating it to be bankrupt or insolvent and such order is not discharged within 30 days or takes any equivalent or similar action in consequence of debt in any jurisdiction.

10.5 Effects of Certain Terminations. Upon termination of this Agreement by Cornerstone pursuant to Section 10.2 or Section 10.4 or by Targacept pursuant to Section 10.3, the following provisions shall apply.

(a) The License shall terminate, and Section 2.2(c) shall survive.

(b) Within **[********]** days after Cornerstone's written request (if accompanied by a written representation certifying as to its compliance with Section 9.7(b)), Targacept shall: (i) grant to Cornerstone a worldwide, paid-up (except as set forth in Section 10.5(c)), irrevocable (unless Cornerstone shall cease to comply with Section 9.7(b)), exclusive (even as to Targacept) license, with right to further sublicense to the same extent, and subject to the same conditions, as the License pursuant to Section 2.2, to any Technology generated by, and any Patent Rights filed or obtained by, Targacept prior to such termination that (A) relate solely to a Cornerstone Compound and (B) are necessary or reasonably useful to make, use, sell, offer to sell, import or otherwise exploit any pharmaceutical or medicinal item, substance or formulation that is comprised of or contains such Cornerstone Compound (each, a "Targacept Returned Product") in the Cornerstone Restricted Field, such license to be solely to make, use, sell, offer to sell, import or otherwise exploit, or to perform services that utilize, Targacept Returned Products in the Cornerstone Restricted Field; and (ii) provide to Cornerstone, at Cornerstone's expense, one (1) copy (in electronic form, if available) of all reports and documents in Targacept's or its Affiliates' possession as of the effective date of such termination of this Agreement to the extent that such reports and documents solely describe or solely contain any data with respect to such Cornerstone Compound. "Cornerstone Restricted Field" means all fields of use, but excluding, with respect to each Cornerstone Compound, all fields and indications in or for which Targacept

would not be permitted, or would not have the unrestricted right, to develop such Cornerstone Compound, or would not be permitted to, or would not have the unrestricted right to, commercialize (or make, use or sell) such Cornerstone Compound under any of (i) Targacept's Collaboration and License Agreement with AstraZeneca AB dated December 3, 2009, as may be amended from time to time, (ii) Targacept's Collaborative Research and License Agreement with AstraZeneca AB dated December 27, 2005, as amended and as may be further amended from time to time, (iii) Targacept's Product Development and Commercialization Agreement with SmithKline Beecham Corporation (d/b/a GlaxoSmithKline) and Glaxo Group Limited, as may be amended from time to time, or (iv) any other collaboration, alliance, licensing, corporate partnering or other arrangement entered into after the Effective Date by Targacept or any Affiliate thereof.

(c) With respect to each Targacept Returned Product (or, for clarity, corresponding Cornerstone Compound) subject to Section 10.5(b) for which for which Targacept has initiated human clinical development prior to such termination of this Agreement:

(i) Cornerstone shall pay royalties to Targacept on Net Sales of the Targacept Returned Product by Cornerstone or any Sublicensee (or licensee) in accordance with Section 5.4 of this Agreement; and

(ii) within **[********]** days after receipt of a written request from Cornerstone (accompanied by a written representation certifying as to its compliance with Section 9.7(b)), Targacept shall assign to Cornerstone all regulatory filings made by Targacept or any of its Affiliates solely for such Targacept Returned Product; provided that Targacept shall have and retain a right of reference to each such regulatory filing.

10.6 Return of Confidential Information. Within **[********]** days following termination of this Agreement for any reason, (a) each Party shall return all Confidential Information of the other Party in such Party's possession, and (b) except where this Agreement is terminated by Targacept under Section 10.2(b) or Section 10.4(b), Targacept shall return all of the Licensed Know-How delivered to Targacept pursuant to Section 3.1, including all reproductions and copies thereof in any medium (except that Targacept may retain one copy for its legal files).

10.7 Right to Sell-Off Inventory. Upon termination of this Agreement for any reason, should Targacept have any inventory of any Licensed Products, Targacept shall have **[*********]** months thereafter in which to dispose of such inventory (subject to the payment to Cornerstone of any amounts due Cornerstone with respect to the Net Sales of such inventory hereunder).

10.8 Survival. In addition to the consequences set forth in Section 10.5, if applicable, the following provisions shall survive: (i) expiration or termination of this Agreement for any reason: Sections 2.3(a), 2.3(b)(ii), 2.3(g), 2.5, 4.2(b), 4.2(c), 5.4, 5.5(a), 5.5(b) (penultimate sentence only), 5.6, 6.5 (solely to the extent that any action or proceeding was instituted before any such termination or expiration), 6.7 (solely to the extent that any action or proceeding was instituted before any such termination or expiration), 6.8, 9.3, 9.4, 9.5, 9.6,

9.7, 11.1, 11.2, 11.4, 11.5, 11.6, 11.7, 11.8, 11.10, 11.11, 11.12, 11.13 and 11.14; Sections 7 and 10; and, for purposes of interpreting any of the foregoing sections, all other sections referenced in such section, and Section 1); and (ii) termination of this Agreement by Targacept pursuant to Section 10.2 or Section 10.4, Section 2.1, 2.2(a), 2.3(c), 2.3(d), 2.3(e), 2.3(f), 2.4, 6.2, 6.3, 6.4(a), 6.4(b), 6.4(e), 6.5, 6.6(d), 6.7, 6.8, 8.1 and 8.2. Expiration or termination of this Agreement for any reason shall not relieve the Parties of any liability or obligation which accrued hereunder prior to the effective date of such termination or expiration or preclude either Party from pursuing all rights and remedies it may have hereunder or at law or in equity, subject to Section 11.7, with respect to any breach of this Agreement prior to the effective date of such termination or expiration.

Section 11. General Provisions.

11.1 Performance by Contract Service Providers. The Parties recognize that Licensee or its Sublicensees may perform some or all of its obligations under this Agreement through contract service providers such as manufacturers, clinical research organizations, and similar Third Parties that customarily provide services to, or conduct research with or for, companies in the pharmaceutical industry. Licensee or its Sublicensees may engage such providers and may permit such companies to utilize the intellectual property licensed by Licensor hereunder to the extent necessary for such providers to provide services or research directly related to Licensee's or any of its Sublicensee's manufacture, use, sale, offer for sale, importation, performance, research, development, commercialization or other exploitation of any Licensed Products.

11.2 Assignment. Except as set forth in Section 2.2 and Section 11.1, neither this Agreement nor any rights or performance hereunder may be assigned, transferred or delegated by either Party without the other Party's advance written consent (not to be unreasonably withheld or delayed), except that: (i) a Party may assign this Agreement in its entirety (a) to the bona fide successor to all or substantially all of the business of such Party (whether by merger, consolidation, asset transfer or similar transaction) to which this Agreement relates or (b) to an Affiliate of such Party, provided in each case that the assigning Party provides written notice to the other Party of such assignment and such assignee agrees in writing to be bound hereunder to the same extent as such assigning Party; (ii) Targacept may assign this Agreement in its entirety, or assign, transfer or delegate any of its rights or performance hereunder, to a Sublicensee; and (iii) Cornerstone may delegate its performance under Sections 6.3(a)(i)(B)), 6.3(c)(ii) and 6.5(c) to SetPoint for so long as the SetPoint License remains in effect; provided, in the case of clause (ii) or clause (iii), the delegating Party, if applicable, provides written notice to the other Party of such delegation and such delegatee agrees in writing to be bound hereunder with respect to such obligation to the same extent as such delegating Party. Any assignment, transfer, or delegation in violation of this Section 11.2 shall be void ab initio. This Agreement shall inure to the benefit of, and be binding upon, the legal representatives, successors, and permitted assigns of the Parties.

11.3 Force Majeure. Neither Party shall be held liable or responsible to the other Party nor be deemed to have defaulted under or breached this Agreement for failure or delay in fulfilling or performing any term of this Agreement if such

failure or delay results from causes beyond the reasonable control of the affected Party, potentially including fire, floods, embargoes, terrorism, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts or other labor disturbances, acts of God or acts, omissions or delays in acting by any governmental authority or any other Party; provided that the Party affected shall promptly notify the other of the force majeure condition and shall exert reasonable efforts to eliminate, cure or overcome any such causes and to resume performance of its obligations as soon as practicable. Force majeure does not apply to any obligations for the timely payment by the Parties of amounts due unless banks are closed due to the force majeure event, and then delay will be excused only for the period of time that the banks are so closed.

11.4 Severability. If any one or more of the provisions contained in this Agreement is held invalid, illegal or unenforceable in any respect, the validity, legality and enforceability of the remaining provisions contained herein shall not in any way be affected or impaired thereby, unless the absence of the invalidated provision(s) adversely affects the substantive rights of the Parties. The Parties shall in such an instance use diligent efforts to replace the invalid, illegal or unenforceable provision(s) with valid, legal and enforceable provision(s) which, insofar as practicable, implement the purposes of this Agreement.

11.5 Amendment; Waiver. This Agreement may not be modified, amended or rescinded, in whole or part, except by a written instrument signed by the Parties; provided that any waiver granted by one Party in favor of the other shall be enforceable if in a writing signed by the Party to be charged with the waiver. No delay or omission by either Party hereto in exercising any right or power occurring upon any noncompliance or default by the other Party with respect to any of the terms of this Agreement shall impair any such right or power or be construed to be a waiver thereof. A waiver by either of the Parties of any of the covenants, conditions or agreements to be performed by the other shall not be construed to be a waiver of any succeeding breach thereof or of any other covenant, condition or agreement herein contained.

11.6 Notices. Except as otherwise provided herein, all notices and other communications provided for hereunder shall be in writing, shall specifically refer to this Agreement, shall be addressed to the receiving Party’s address set forth below or to such other address as a Party may designate by notice hereunder, and shall be deemed to have been sufficiently given for all purposes when received or, if earlier, (a) three (3) business days after being mailed by first class certified or registered mail, postage prepaid, (b) the next business day after being sent by nationally recognized overnight courier for next business day delivery, in each case with all charges prepaid, (c) upon being personally delivered, or (d) made by telecopy or facsimile transmission with confirmed receipt:

If to Targacept, to:

Targacept, Inc.
Attn: SVP, Business and Commercial Development
200 East First Street, Suite 300
Winston Salem, NC 27101-4165
Telephone: 336-480-2100
Telecopier: 336-480-2285

With a copy to (which shall not constitute notice):

Targacept, Inc.
Attn: General Counsel
200 East First Street, Suite 300
Winston Salem, NC 27101-4165
Telephone: 336-480-2100
Telecopier: 336-480-2103

If to Cornerstone, to:

Cornerstone Therapeutics Inc.
Attn: Chief Financial Officer
1255 Crescent Green Drive, Suite 250
Cary, NC 27518
Telephone: (919) 678-6514
Telecopier: (919) 678-6599

With a copy to (which shall not constitute notice):

Smith, Anderson, Blount, Dorsett,
Mitchell & Jernigan, L.L.P.
Attn: David B. Clement
2500 Wachovia Capitol Center
Post Office Box 2611
Raleigh, NC 27602-2611
Telecopier: (919) 821-6800

11.7 Dispute Resolution. Disputes arising under or in connection with this Agreement shall be resolved pursuant to this Section 11.7; provided, however, that in the event a dispute cannot be resolved without an adjudication of the rights or obligations of a Third Party (other than any Parties' Affiliates or any Cornerstone Indemnitee or Targacept Indemnitee identified in Sections 9.6(a) or 9.6(b), as applicable), the dispute procedures set forth in this Section 11.7 shall be inapplicable as to such dispute.

(a) In the event of a dispute between the Parties, the Parties shall first attempt in good faith to resolve such dispute by negotiation and consultation between themselves. In the event that such dispute is not resolved on an informal basis within **[********]** days, either Party may, by written notice to the other, have such dispute referred to each of the Parties' respective chief executive officers or his or her designee (who shall be a senior executive), who shall attempt in good faith to resolve such dispute by negotiation and consultation for a **[********]** day period following receipt of such written notice.

(b) In the event the Parties' chief executive officers (or designees) are not able to resolve such dispute, either Party may pursue all rights and remedies it may have at law or in equity, subject to Section 11.7(c).

(c) The state or federal courts located within the State of North Carolina shall have exclusive jurisdiction over any and all disputes between the Parties, whether in law or equity, arising out of or relating to this Agreement and the agreements, instruments and documents contemplated hereby and the Parties consent to and hereby submit to the exclusive jurisdiction of such courts. Each of the Parties hereby waives and agrees not to assert in any such dispute, to the fullest extent permitted by applicable law, any claim that (i) such Party is not personally subject to the jurisdiction of such courts, (ii) such Party and such Party's property is immune from any legal process issued by such courts or (iii) any litigation or other proceeding commenced in such courts is brought in an inconvenient forum. The Parties agree that the exclusive choice of forum set forth in this Section 11.7(c) does not prohibit the enforcement of any judgment, whether obtained in that forum or any other appropriate forum, in any other jurisdiction.

11.8 Applicable Law. This Agreement shall be governed in all respects, including validity, interpretation and effect, by and construed in accordance with the laws of North Carolina, without regard to its conflicts of law provisions, provided that any dispute relating to the scope, validity, enforceability or infringement of any Patent Rights or other intellectual property rights shall be governed by, and construed and enforced in accordance with, the substantive laws of the jurisdiction in which such Patent Rights or other right applies.

11.9 Further Assurances. Each Party agrees to do and perform all such further acts and things and shall execute and deliver such other agreements, certificates, instruments and documents necessary or that the other Party may deem advisable in order to carry out the intent and accomplish the purposes of this Agreement and to evidence, perfect or otherwise confirm its rights hereunder.

11.10 Relationship of the Parties; Third Party Beneficiaries. Each Party is an independent contractor of the other Party under this Agreement. Nothing contained herein is intended or is to be construed so as to constitute Cornerstone and Targacept as partners, agents or joint venturers. Neither Party shall have any express or implied right or authority to assume or create any obligations on behalf of or in the name of the other Party or to bind the other Party to any contract, agreement or undertaking with any Third Party. There are no express or implied third party beneficiaries hereunder (except for Targacept Indemnitees other than Targacept and Cornerstone Indemnitees other than Cornerstone, in each case solely for purposes of Section 9.6).

11.11 Entire Agreement. This Agreement (along with the Exhibits attached hereto) contains the entire understanding of the Parties with respect to the subject matter hereof and supersedes and replaces any and all previous arrangements and

understandings (other than the Confidentiality Agreement), whether oral or written, between the Parties with respect to the subject matter hereof **[********]**.

11.12 Headings. The captions to the several Sections hereof are not a part of this Agreement, but are merely guides or labels to assist in locating and reading the several Sections hereof.

11.13 Waiver of Rule of Construction; Interpretation. Each Party has had the opportunity to consult with counsel in connection with the review, drafting and negotiation of this Agreement and to amendments to the Feinstein License and SetPoint License executed on or about the Effective Date. Accordingly, the rule of construction that any ambiguity in this Agreement (or any ambiguity resulting from such amendments to the Feinstein License and SetPoint License) shall be construed against the drafting party shall not apply, regardless of which Party was generally responsible for the preparation of this Agreement (or such amendments to the Feinstein License and SetPoint License). Whenever any provision of this Agreement uses the term "including" (or "includes"), such term shall be deemed to mean "including without limitation" (or "includes without limitation"). The term "or" is used in this Agreement in the inclusive sense (and/or). "Herein," "hereby," "hereunder," "hereof" and other equivalent words refer to this Agreement as an entirety and not solely to the particular portion of this Agreement in which any such word is used. All definitions set forth herein shall be deemed applicable whether the words defined are used herein in the singular or the plural. Unless otherwise provided, all references to Sections and Exhibits in this Agreement are to Sections and Exhibits of this Agreement. References to any Section includes the broader Section of which such Section is a part and the narrower subsections that are part of such Section (e.g., a section numbered "Section 2.2" would be part of "Section 2," and references to "Section 2.2" would also refer to material contained in the subsection described as "Section 2.2(a)")

11.14 Execution of Agreement; Counterparts. This Agreement and any amendment hereto may be executed in any number of counterparts, 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. The exchange of copies of this Agreement or amendments thereto and of signature pages by facsimile transmission or by email transmission in portable document format, or similar format, shall constitute effective execution and delivery of such instrument(s) as to the Parties and may be used in lieu of the original Agreement or amendment for all purposes. Signatures of the Parties transmitted by facsimile or by email transmission in portable document format, or similar format, shall be deemed to be original signatures for all purposes.

[signature page follows]

[Signature Page to Exclusive License Agreement]

IN WITNESS WHEREOF, the Parties have caused this Exclusive License Agreement to be executed by their respective duly authorized officers as of the respective dates set forth below.

TARGACEPT, INC.

By: /s/ Jeffrey P. Brennan
Name: Jeffrey P. Brennan
Title: Sr. Vice President, Business & Commercial Development & Chief Business Officer

Date: 8/3/2010

CORNERSTONE THERAPEUTICS INC.

By: /s/ Craig A. Collard
Name: Craig A. Collard
Title: President and CEO

Date: 8/2/2010

EXHIBIT A

Field Patents

[********]

[********]*Patents*

[********]

Mixed Patents

[********]

EXHIBIT B

[********]

EXHIBIT C

[********]

Exhibit 10.19

Description of Annual Cash Incentive Program

Targacept, Inc. (the "Company") maintains an incentive award program (the "Program") under which all of its employees, including its named executive officers, are eligible to receive an annual cash incentive bonus. Under the terms of the Program, each employee is assigned a target bonus percentage of his or her base salary. The target bonus percentages for the Company's named executive officers (and other members of its executive (management) committee) are determined by the Compensation Committee of the Board of Directors. At or about the beginning of each fiscal year, the Compensation Committee establishes performance objectives for the Company for that year and ascribes a percentage weight to each objective. The aggregate weight for all of the performance objectives is at least equal to 100%. The performance objectives may include additional weighting associated with events considered by the Compensation Committee to be particularly challenging that, if achieved, would be expected to provide substantial benefit to the Company and its stockholders. In that event, the aggregate weight for all of the objectives exceeds 100%. The performance objectives typically relate to one or more of the following areas — the discovery, progression or advancement of the Company's product candidates, clinical or nonclinical development, preclinical research, regulatory operations, business development, alliance management, cash management and capital efficiency.

Following the end of the fiscal year, the Compensation Committee determines the achievement level for the Program for that year. In determining the achievement level, the Compensation Committee calculates the weights ascribed to those performance objectives that have been met, the circumstances surrounding any performance objective that has not been met and whether to award all or any portion of the weight ascribed to that objective, and determines whether to make any adjustment based on other Company accomplishments that occurred during the year.

For a group of employees that includes the Company's principal executive officer, principal financial officer and other executive officers, as well as other employees at the level of vice president or above, 100% of the annual cash incentive bonus is determined based on the achievement level for the Program determined by the Compensation Committee as described above. Accordingly, the annual cash incentive bonus for a particular year for each employee in this group is determined by multiplying the amount of his or her base salary received for that year times his or her assigned target bonus percentage times the achievement level for the Program determined by the Compensation Committee. For the Company's remaining employees, 50% of the annual cash incentive bonus is based on the achievement level for the Program determined by the Compensation Committee and the other 50% is based on individual performance.

Exhibit 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

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

- Registration Statement (Form S-8 No. 333-133882) pertaining to the Targacept, Inc. 2000 Equity Incentive Plan,
- Registration Statement (Form S-8 No. 333-160331) 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 11, 2011, 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, 2010.

/s/ Ernst & Young LLP

Raleigh, North Carolina
March 11, 2011

EXHIBIT 31.1

CERTIFICATION

I, J. Donald deBethizy, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: March 11, 2011

By: /S/ J. DONALD DEBETHIZY

J. Donald deBethizy
President and Chief Executive Officer

EXHIBIT 31.2

CERTIFICATION

I, Alan A. Musso, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: March 11, 2011

BY: /S/ ALAN A. MUSSO

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

EXHIBIT 32.1

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

In connection with the Annual Report on Form 10-K of Targacept, Inc. (the "Company") for the period ended December 31, 2010 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, J. Donald deBethizy, President and Chief Executive Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

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

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

Date: March 11, 2011

By: /S/ J. DONALD DEBETHIZY
J. Donald deBethizy
President and Chief Executive Officer

EXHIBIT 32.2

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

In connection with the Annual Report on Form 10-K of Targacept, Inc. (the "Company") for the period ended December 31, 2010 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; 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 11, 2011

BY: /S/ ALAN A. MUSSO

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