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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, 2013

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.)**
100 North Main Street, Suite 1510 **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, 2013, was approximately $97,526,569, based on the price at which the registrant's common stock was last sold on June 28, 2013 ($4.27).

As of February 28, 2014, the registrant had 33,743,856 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 2014 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, 2013, are incorporated by reference into Part III of this report.

TARGACEPT, INC.

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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-5619, TC-5214, 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, location, conduct, objective, duration or endpoints of any clinical trial, or the timing for initiation or completion of or availability of results from any clinical trial, for submission or approval of any regulatory filing, for interactions with regulatory authorities, or, where applicable, for a decision by AstraZeneca as to whether to conduct particular development;
- the benefits that may be derived from any of our product candidates or the commercial opportunity in any target indication;
- the timing or amounts of any payments that AstraZeneca may make to us;
- our operations, financial position, revenues, costs or expenses; or
- our strategies, prospects, plans, expectations or objectives

is a forward-looking statement made under the provisions of the Private Securities Litigation Reform Act of 1995. In some cases, words such as “may,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “ongoing,” “scheduled” or other comparable words identify forward-looking statements. Actual results, performance or experience may differ materially from those expressed or implied by any forward-looking statement as a result of various important factors, including our critical accounting policies and risks and uncertainties relating, among other things, to:

- whether findings from nonclinical studies and assessments of TC-5214 and clinical trials of TC-5214 in a different indication will be predictive of a positive outcome in our ongoing Phase 2b clinical trial of TC-5214 in overactive bladder;
- the conduct and results of clinical trials and non-clinical studies and assessments of TC-5619, TC-5214, TC-1734, AZD1446, TC-6987, TC-6499 or any of our other product candidates, including the performance of third parties engaged to execute them, delays resulting from any changes to the applicable protocols or difficulties and delays in subject enrollment and data analysis;
- 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 submit a new drug application for TC-5214 prior to October 1, 2017 or because the applicable statutory provision is re-authorized by the U.S. Congress;
- the control or significant influence that AstraZeneca has over the development of AZD1446, including as to the timing, scope and design of any future clinical trials and as to the conduct at all of further development;
- our ability to establish additional strategic alliances, collaborations or licensing or other comparable arrangements on favorable terms;
- our ability to protect our intellectual property; and
- the timing and success of submission, acceptance and approval of regulatory filings.

These and other risks and uncertainties are described in greater detail under the caption “Risk Factors” in Item 1A of Part I of this annual report and in other filings that we make with the Securities and Exchange Commission, or SEC. As a result of the risks and uncertainties to which our business is subject, the results or events indicated by any forward-looking statement may not occur. We caution you not to place undue reliance on any forward-looking statement.

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

PART I

Item 1. Business.

Overview

We are a biopharmaceutical company engaged in the development of novel NNR Therapeutics™ to treat patients suffering from serious nervous system and gastrointestinal/ genitourinary diseases and disorders. 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.

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 activity in the body by selectively affecting specific NNR subtypes.

We have multiple clinical-stage product candidates in areas in which we believe there are significant medical need and commercial potential, as well as an ongoing collaboration with AstraZeneca. Our most advanced product candidates are described briefly below.

TC-5214

TC-5214 acts as an antagonist on the α3ß4 NNR. We are currently conducting a Phase 2b clinical trial of TC-5214 as a treatment for overactive bladder.

TC-1734

TC-1734 (also referred to in previous filings as AZD3480) is a wholly-owned novel small molecule that modulates the activity of the α4ß2 NNR. We are currently conducting a Phase 2b clinical trial of TC-1734 as a treatment for mild to moderate Alzheimer's disease.

TC-6499

TC-6499 is a novel small molecule that modulates the activity of the α3ß4 and other NNRs as an agonist. We are evaluating potential future development options for this product candidate and are preparing to initiate in mid 2014 an exploratory study for the indication of diabetic gastroparesis, a disorder which is often debilitating and chronic that slows or stops the passage of food from the stomach to the small intestine.

AZD1446 (TC-6683)

AZD1446 is a novel small molecule that modulates the activity of the α4ß2 NNR and is subject to an ongoing collaboration agreement with AstraZeneca. Development decisions and activities for AZD1446 are substantially within the control of AstraZeneca.

TC-5619 and TC-6987

TC-5619 and TC-6987 are novel small molecules highly selective for the α7 NNR. The α7 NNR has been shown to play a role in a variety of biological pathways associated with various diseases and disorders. We previously conducted clinical studies of TC-5619 as a potential treatment for schizophrenia, Alzheimer's disease and attention deficit hyperactivity disorder and exploratory studies of TC-6987 as a treatment for inflammatory disorders. We do not have plans to pursue additional development of these compounds in these therapeutic areas.

Role of NNRs in the Body

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 have promise as treatments for these diseases and disorders.

In addition, NNRs located within various target organ systems in the body are involved in transmitting signals between those systems and the spinal cord and brain. As such, these receptors are thought to play a role in a variety of physiological functions, including heart rate, digestion, respiration, salivation and uro-genital function such as urination and sexual arousal.

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 conditions and that mutations of genes that are associated with specific NNR subunits can increase susceptibility to some 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

We are seeking to provide superior treatment options for complex diseases and disorders to improve the lives of patients by developing innovative new medicines. To achieve our goal, we are pursuing the following strategies:

- *Exploit our pipeline of NNR Therapeutics.* We believe that drugs designed to selectively target specific NNR subtypes can have positive medical effects with limited adverse side effects. Accordingly, we have historically focused our drug development activities on NNR Therapeutics. We currently have two chemically and pharmacologically distinct NNR Therapeutics in Phase 2b clinical development and an additional product candidate that is scheduled to be in an exploratory study later this year. The ongoing and planned clinical studies are in therapeutic areas where we believe there to be significant medical need and commercial potential. If we have clinical success in these areas, we intend to continue to progress these NNR Therapeutics through later stage clinical development with the objective of regulatory submission and approval.
- *Evaluate opportunities to expand our pipeline deliberatively.* To grow our business in the long term, we will need to expand our pipeline. We plan to continue to evaluate the scientific and commercial merits of internal opportunities for pipeline growth, either by pursuing clinical-stage NNR Therapeutics for additional indications or by advancing earlier-stage compounds with NNR-based mechanisms in our portfolio. We also expect to continue to consider prospects for complementing our pipeline with product candidates from external sources.
- *Collaborate selectively.* We have historically collaborated with significant pharmaceutical companies and currently have a collaboration with AstraZeneca focused on compounds that act on the α4ß2 NNR. We intend to selectively seek additional alliances and collaborations to assist us in furthering the development of some of our product candidates. In particular, we intend to enter into these alliances and collaborations for target indications for which a potential collaborator has unique expertise or that involve large primary care markets that are optimally 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, in the United States and, potentially in the future, other markets. Under our collaboration agreement with AstraZeneca, we have the option to co-promote AZD1446 and the other licensed compounds that arose out of the preclinical research collaboration that we conducted with AstraZeneca to specified classes of physicians in the United States.

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	Overactive bladder	Phase 2b clinical trial ongoing	Targacept
TC-1734	Mild to moderate Alzheimer's disease	Phase 2b clinical trial ongoing	Targacept
TC-6499	Diabetic gastroparesis	Phase 2a study planned to be initiated in mid 2014	Targacept
AZD1446 (TC-6683)	To be determined by AstraZeneca	Phase 2	AstraZeneca
TC-5619	To be determined	Inactive (Phase 2)	Targacept
TC-6987	To be determined	Inactive (Phase 2)	Targacept

Information regarding our research and development expenses for the fiscal years ended December 31, 2013, 2012 and 2011 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

We are currently conducting a Phase 2b clinical trial of TC-5214 as a treatment for overactive bladder. TC-5214 acts potently on α3ß4 and other NNRs located in or around the bladder that are believed to play a key role in bladder contraction and signaling of the urge to urinate. 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. TC-5214 had previously been in Phase 3 co-development with AstraZeneca as a treatment for major depressive disorder (MDD) under a now terminated collaboration agreement.

Ongoing Phase 2b Clinical Trial in Overactive Bladder

Our ongoing Phase 2b clinical trial of TC-5214 in overactive bladder is a double blind, placebo controlled, randomized, parallel group trial that is being conducted in the United States. The term "double blind" means that neither the subjects nor the investigators in the trial know which subjects receive the investigational drug (in this case, TC-5214) and which subjects receive placebo. The study, which is designed to enroll approximately 750 patients, includes a 3- to 5-week screening period followed by a 12-week treatment period during which patients receive either one of three doses of TC-5214 (0.5mg, 1mg or 2mg) or placebo twice daily. The study's co-primary endpoints are change in urination frequency per 24 hours and change in urinary incontinence episodes per 24 hours, in each case from baseline to 12 weeks.

We determined to pursue development of TC-5214 for overactive bladder based primarily on various nonclinical and clinical findings, including:

- exaggerated bladder effects in studies of TC-5214 in rodents, including urinary retention and beneficial changes in bladder contraction and capacity and urination frequency;
- potent activity of TC-5214 at nicotinic receptors located in or around the bladder considered to play a key role in bladder contraction and believed to be involved in signaling of the urge to urinate;
- greater than 90% elimination of TC-5214 in humans unchanged through the bladder, supporting use of a low dose and creating the potential to minimize unwanted side effects;
- a well-established safety and tolerability profile for TC-5214 resulting from prior clinical evaluation in approximately 2,400 subjects; and
- elements of the side effect profile for TC-5214 arising from the completed MDD program that are qualitatively similar to observations made with marketed medications for overactive bladder.

Completed Clinical Program in MDD

We and AstraZeneca previously conducted a multi-clinical trial Phase 3 program for TC-5214 as an adjunct therapy, and a Phase 2b clinical trial of TC-5214 as a "switch" monotherapy, in each case in adults with MDD who do not respond adequately to initial therapy. None of these clinical trials met its primary endpoint (as used in this annual report, the terms "endpoint" and "outcome measure" have the same meaning). In the first quarter of 2012, we and AstraZeneca announced that, based on the totality of the results of the Phase 3 program, a regulatory filing for TC-5214 as an adjunct therapy for MDD would not be pursued and we reported the discontinuation of a "switch" monotherapy trial. AstraZeneca subsequently terminated our collaboration agreement for TC-5214, effective in May 2012.

TC-1734

TC-1734 is a novel small molecule that modulates the activity of the α4ß2 NNR. We are currently conducting a Phase 2b clinical trial of TC-1734 as a treatment for mild to moderate Alzheimer's disease. Our ongoing Phase 2b clinical trial of TC-1734 is a potential registration study that is the subject of a Special Protocol Assessment agreement with the U.S. Food and Drug Administration, or FDA. It is a double blind study designed to evaluate TC-1734 head-to-head against donepezil, which is marketed as Aricept and is the medication most often prescribed for mild to moderate Alzheimer's disease. The trial design provides for approximately 300 subjects diagnosed with probable Alzheimer's disease classified as mild or moderate in severity to be randomly assigned to receive donepezil or a fixed 30mg dose of TC-1734 daily over 12 months. We are conducting the study at sites predominantly in Eastern Europe and also in the United States. The study has co-primary outcome measures, change from baseline after 12 months of treatment with TC-1734 as compared to donepezil on the Alzheimer's Disease Assessment Scale-cognitive subscale, or ADAS-Cog, and on a functional measure. The functional measure for European sites is the Alzheimer's Disease Cooperative Study — Activities of Daily Living Inventory, and the functional measure for U.S. sites is the Clinician's Interview Based Impression of Change Plus Caregiver Input, each of which assesses subjects' ability to perform typical day-to-day activities.

Our ongoing study is the second clinical trial of TC-1734 in mild to moderate Alzheimer's disease. The first was conducted by AstraZeneca under our collaboration agreement, and its outcome was inconclusive. On March 5, 2013, AstraZeneca exercised its right to terminate TC-1734 from our collaboration agreement. As a result, all rights and licenses for TC-1734 that we granted under the agreement to AstraZeneca terminated and reverted to us effective June 5, 2013. Previously, we had received $6.2 million in nonrefundable payments from AstraZeneca in connection with our ongoing clinical trial.

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

In 2008, AstraZeneca completed a Phase 2b double blind, placebo controlled, dose finding, multi-center clinical trial of TC-1734 in mild to moderate Alzheimer's disease, known as the "Sirocco" trial. The Sirocco trial was conducted at sites in Western Europe, Eastern Europe and Canada. In the trial, 567 subjects diagnosed with probable Alzheimer's disease classified as mild or moderate in severity were randomly assigned to one of three dose groups of TC-1734, to donepezil, or to placebo and dosed over a 12-week period. The primary outcome measure of the trial was change from baseline on ADAS-Cog after 12 weeks of treatment with TC-1734 as compared to placebo. Some of the secondary outcome measures of the trial included the Alzheimer's Disease Cooperative Study—Clinical Global Impression of Change, or ADCS-CGIC, which is a 7-point clinician assessment of change in behavior and the ability to function, the Mini Mental State Examination, or MMSE, which is a quantitative, 30-point cognition scale, and a computer-based test battery developed by CDR Ltd. to test cognitive function.

The results of the Sirocco trial were inconclusive in that the active comparator, donepezil, did not meet the trial's criteria for statistical significance versus placebo on the primary outcome measure. TC-1734 also did not meet the trial's criteria for statistical significance versus placebo on the primary outcome measure. However, in an analysis conducted post hoc in which the most mildly impaired subjects (MMSE = 25 or 26) were excluded, the middle dose of TC-1734 tested achieved a favorable outcome (one-sided p-value = 0.04) and donepezil showed a strong trend (one-sided p-value = 0.065).

Subjects dosed with TC-1734 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 TC-1734 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 TC-1734 dose groups as compared to the placebo dose group.

Completed Clinical Trials in Other Indications

In addition to the previous trial in Alzheimer's disease, we or AstraZeneca have completed Phase 2 clinical trials of TC-1734 in various other indications characterized by cognitive impairment. These studies have generated a range of efficacy results, including: (1) achievement of the primary outcome measure(s) (in age associated memory impairment, or AAMI, a common condition characterized by gradual memory loss or other cognitive impairment that generally occurs with normal aging, and in adults with ADHD); (2) encouraging signals (in early-stage trials in AAMI and mild cognitive impairment, or MCI); and (3) failure to achieve the primary outcome measure (in cognitive dysfunction in schizophrenia). These trials are summarized below.

AAMI (later study)	• a double blind, placebo controlled, multi-center study that we conducted in the United States • subjects were between the ages of 50 and 80 and classified with AAMI based on inclusion criteria reflecting both subjective and objective memory impairment • there were three co-primary endpoints, change from baseline on the Power of Attention and Episodic Memory factors of the CDR test battery and on the Subject Global Impression– Cognition scale at the end of 16 weeks of dosing with TC-1734 as compared to placebo • TC-1734 met all three co-primary endpoints ($p < 0.05$) at 50mg and met the Power of Attention endpoint at 25mg
Adults with ADHD	• a double blind, placebo controlled crossover design study that we and AstraZeneca conducted at a single site in the United States in which each subject served as his or her own control • two doses of TC-1734 tested • the primary outcome measure was change from baseline on the CAARS-INV total score after two weeks dosing with TC-1734 as compared to placebo, and the result was statistically significant in favor of one of the doses (50mg TC-1734, $p < 0.01$) on an intent to treat basis
AAMI (earlier study); MCI	• two double blind, placebo controlled, crossover design Phase 2 studies that we conducted, one in each indication, assessing the effects of multiple doses of TC-1734 at various time points using the CDR test battery • TC-1734 demonstrated positive effects in the AAMI study at some, but not all, dose levels and measures tested, with the results most favorable at 50mg • the results of the MCI trial were more favorable at 100mg TC-1734 and did not favor 50mg TC-1734 on any measure
Cognitive Dysfunction in Schizophrenia	• a double blind, placebo controlled, dose finding, multi-center study that AstraZeneca conducted in the United States and Canada • subjects were clinically stable schizophrenics who were active smokers and taking a marketed atypical antipsychotic • TC-1734 did not meet pre-defined success criteria on the primary endpoints, change from baseline on scores for attention/vigilance, working memory, verbal learning, speed of processing and reasoning and problem solving as measured by a computerized test battery after 12 weeks of treatment with TC-1734 as compared to placebo

TC-6499

We currently plan to initiate in mid-2014 an exploratory study of TC-6499 in diabetic gastroparesis. TC-6499 is a novel small molecule that modulates the activity of the α3ß4 and other NNRs. The α3ß4 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 TC-6499 may have potential as a treatment for gastrointestinal disorders. In an exploratory four-week study of TC-6499 that we completed in 24 subjects with constipation-predominant irritable bowel syndrome at a single site in 2011, 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).

AZD1446 (TC-6683)

AZD1446 (TC-6683) is a novel small molecule that modulates the activity of the α4ß2 NNR. We discovered and advanced AZD1446 as part of a now completed preclinical research collaboration that we and AstraZeneca conducted under our collaboration agreement. AstraZeneca is responsible for conducting and funding the development and potential future commercialization of AZD1446 and has previously completed various early-stage clinical studies. Under a March 2013 amendment to our collaboration agreement, AstraZeneca has the right to pursue development and commercialization of AZD1446, as well as other compounds licensed from us under our collaboration agreement, in any therapeutic area, rather than only in cognitive disorders or schizophrenia. Development decisions and activities for AZD1446 are substantially within the control of AstraZeneca.

TC-5619

TC-5619 is a novel small molecule that modulates the activity of the α7 NNR. We have completed Phase 2 clinical trials of TC-5619 in various indications. We currently do not have plans to pursue additional development with TC-5619.

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

We completed in December 2013 a Phase 2b clinical trial of TC-5619 in negative symptoms and cognitive dysfunction in schizophrenia. The trial was a double blind, placebo controlled, parallel group study conducted at sites in Eastern Europe and the United States. The trial enrolled 477 subjects with stable psychotic symptoms and taking an approved atypical antipsychotic medication. The trial design provided for a four-week screening period, followed by a 24-week treatment period during which subjects received either one of two daily doses of TC-5619 (5mg or 50mg) or placebo together with continued treatment with an atypical antipsychotic.

The primary outcome measure in the trial was change from baseline on the Scale for the Assessment of Negative Symptoms, or SANS, at the end of the treatment period with TC-5619 as compared to placebo. SANS is an investigator assessment of improvement on the negative symptoms of schizophrenia. The key secondary outcome measures for the trial were the composite score on the CogState Schizophrenia Battery, or CSB, a computerized battery of neuropsychiatric tests that assess specific cognitive domains, and the University of California, San Diego Performance-Based Skills Assessment, brief version.

TC-5619 did not meet the primary outcome measure and did not demonstrate improvement on the key secondary measures.

Completed Phase 2 Clinical Trial in Cognitive Dysfunction in Schizophrenia

Previously, we completed a Phase 2 clinical trial of TC-5619 in cognitive dysfunction in schizophrenia. The trial was a double blind, placebo controlled, multi-center study conducted in the United States and India. In the trial, 185 subjects with schizophrenia who had stable psychotic symptoms were randomly assigned to receive either TC-5619 or placebo, together with continued treatment with an atypical antipsychotic (either quetiapine, marketed as Seroquel, or risperidone, marketed as Risperdal), for 12 weeks. Approximately half of the subjects

were users of tobacco products. Subjects who received TC-5619 received a 1mg daily dose for the first four weeks, a 5mg daily dose for the next four weeks and a 25mg daily dose for the last four weeks. This type of scheduled dosing adjustment is sometimes referred to as "forced titration."

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

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

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

Completed Phase 2 Clinical Trials in Adults with ADHD and Adults with ADHDi

Previously, we completed a Phase 2 clinical trial of TC-5619 in adults with attention deficit/hyperactivity disorder, or ADHD, and a subsequent Phase 2 clinical trial of TC-5619 in adults with inattentive-predominant attention deficit/hyperactivity disorder, or ADHDi. The ADHD trial was a double blind, placebo controlled, forced titration, multi-center, 12-week study conducted in the United States. Each subject in the trial was randomly assigned to receive a daily dose of either TC-5619, beginning with 1mg and increasing to 5mg and then to 25mg, or placebo. TC-5619 did not meet the primary outcome measure of the trial, but showed encouraging signals on some of the trial's efficacy measures in the subpopulation of subjects with ADHDi. The ADHDi trial was a double blind, placebo controlled, parallel group, multi-center, 12-week study conducted in the United States. Subjects in the trial were randomly assigned to receive a daily dose of 5mg TC-5619, 25mg TC-5619 or placebo. TC-5619 did not meet the primary outcome measure of the trial, and we are not pursuing further development of TC-5619 in ADHD or ADHDi.

TC-6987

TC-6987 is a novel small molecule that modulates the activity of the α7 NNR. We are evaluating potential future development options for TC-6987. Previously, we completed two exploratory Phase 2 clinical trials of TC-6987, one in asthma and one in Type 2 diabetes. We will not pursue further development of TC-6987 in Type 2 diabetes and have no current plans to conduct additional development of TC-6987 in asthma.

Medical Need and Commercial Opportunity in Our Target Indications

The indications for which our most advanced product candidates are currently in development include overactive bladder and Alzheimer's disease, and we are currently planning to initiate a clinical study in diabetic gastroparesis.

Overactive bladder is a disorder that causes a sudden and frequent urge to urinate that may be difficult to suppress and may lead to incontinence and the need to wake up at night to urinate. Overactive bladder poses a significant reduction in quality of life due to a decreased ability to socialize and participate in normal life activities, sleep disturbances and decreased emotional well-being. Decision Resources estimated that by 2014 there would be approximately 73.2 million people in the world's seven major pharmaceutical markets with overactive bladder.

Alzheimer's disease, the most common form of dementia, is a progressive, debilitating disorder that attacks neurons in the brain, resulting in loss of memory, thinking and language skills and behavioral changes. Decision Resources estimated that by 2013 there would be approximately 21.2 million people in the world's seven major pharmaceutical markets with diagnosed Alzheimer's disease or who would develop Alzheimer's disease in the coming years. Alzheimer's disease progresses in stages from mild to moderate to severe and gradually destroys a person's memory and ability to learn, reason, make judgments, communicate and carry out daily activities. Mild Alzheimer's disease is characterized by mild forgetfulness and difficulty acquiring basic information and communicating. Patients generally exhibit the symptoms of mild Alzheimer's disease for two to four years before progressing to the moderate stage. Moderate Alzheimer's disease is characterized by increasing forgetfulness, failure to recognize friends and family, disorientation regarding time and place even in familiar locations and personality changes. Patients can exhibit the symptoms of moderate Alzheimer's disease for several years before progressing to the severe stage. Severe Alzheimer's disease is characterized by difficulty performing simple tasks and activities associated with daily living. Patients with severe Alzheimer's disease require continuous care and generally do not survive for more than three years.

Gastroparesis, also referred to as delayed gastric emptying, is a debilitating, chronic disorder that slows or stops the passage of food from the stomach to the small intestine. The most common symptoms of gastroparesis are nausea, a feeling of fullness after eating only a small amount of food, vomiting, gastroesophageal reflux, abdominal pain and bloating. Gastroparesis affects an estimated 5% to 12% of patients with diabetes and can cause a significant reduction in quality of life. Complications from the disorder may lead to hospitalizations and emergency room visits, which can have significant economic impact on individuals and society.

Preclinical Assets and Pentad Drug Discovery Technologies

In addition to our clinical-stage product candidates, we have a library of discovery or preclinical stage compounds. The most advanced of these compounds is a late-preclinical compound included in our Parkinson's disease program, which is not currently active. We have previously been awarded three grants from The Michael J. Fox Foundation for Parkinson's Research. Two of the grants were to test the potential of compounds with novel NNR pharmacologies to address abnormal involuntary movements, or dyskinesias, that are a side effect of a treatment commonly used to treat the motor deficits of Parkinson's disease called levodopa. The third grant was 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.

We also have 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. In our previous drug discovery activities, we used Pentad to assess the likelihood that novel compounds will interact with various NNRs, the degree of the interaction and the potential of these compounds to be developed as drugs based on projected pharmacokinetic and pharmaceutical profiles.

Discontinued Product

As a result of increased fees charged by the FDA and declining prescriptions, we discontinued the commercialization of Inversine®, which is currently our only approved product, effective as of September 30, 2009. Inversine® is approved in the United States for the management of moderately severe to severe essential hypertension and uncomplicated cases of malignant hypertension, which are high blood pressure disorders. Inversine® was first approved for marketing in the 1950s. We acquired marketing rights to the product in August 2002 from Layton Bioscience, Inc., which had previously acquired the rights from Merck & Co., Inc.

Strategic Alliances and Collaborations

AstraZeneca AB

In December 2005, we entered into a collaborative research and license agreement with AstraZeneca AB. The agreement became effective in January 2006 and was initially focused in cognitive disorders. As amended through the date of this Form 10-K, the agreement permits AstraZeneca to pursue development and commercialization of compounds that it has licensed from us in any therapeutic area.

Our agreement with AstraZeneca initially included a number of different elements, including a multi-year preclinical research collaboration that we and AstraZeneca conducted until January 2010. AZD1446 is the most advanced compound that arose from the research collaboration, and future development decisions and activities with respect to AZD1446 are substantially within the control of AstraZeneca.

In addition, we granted to AstraZeneca under the agreement a license to develop and commercialize TC-1734. In March 2013, AstraZeneca exercised its right to terminate TC-1734 from the agreement. As a result, all rights and licenses for TC-1734 that we granted under the agreement to AstraZeneca terminated and reverted to us effective June 5, 2013. AstraZeneca also had the right under the agreement to license TC-5619 following completion of our prior Phase 2 clinical trial in cognitive dysfunction in schizophrenia. In 2011, AstraZeneca elected not to exercise this license right.

*Payment Term*s. AstraZeneca has paid us a total of $88.1 million, including an initial fee, milestone and other product candidate-related payments, and research support payments, under the agreement since inception. We are eligible to receive other payments of up to $57 million, if development, regulatory and first commercial sale milestone events for AZD1446 are achieved for a specified indication under consideration for development and sales-related milestone events are then achieved for AZD1446, and up to $73 million, if development, regulatory and first commercial sale milestone events for AZD1446 are achieved for any other indication. We are also eligible to receive stepped royalties on any future AZD1446 product sales for any indication. If AZD1446 is subsequently developed under the agreement for other indications, we would also be eligible to receive payments of up to $35 million for each successive indication, if development, regulatory and first detail milestone events are achieved.

AstraZeneca's obligation to pay royalties to us for AZD1446 and each other compound subject to the collaboration expires on a country-by-country basis on the later of expiration of our patent rights that provide exclusivity for that compound in that country or 12 years after the first commercial sale in that country of either that compound or any related compound that meets specified criteria. If AstraZeneca obtains a patent covering the composition of a compound that is derived within a specified period from a compound that is subject to the collaboration, the term of AstraZeneca's patent would also be taken into account in determining the term of AstraZeneca's obligation to pay royalties to us for that derived compound. The U.S. patent rights with respect to AZD1446 expire in 2028. The foreign patent rights with respect to AZD1446 that have issued and correspond to our U.S. patent rights expire in 2027. We also have pending U.S. and foreign patent applications with respect to AZD1446 that, if issued as patents, would expire in 2027. None of these 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 AZD1446 in any particular country. Royalty rates are subject to reduction under the agreement in specified circumstances, including in any country if the licensed compound is no longer subject to adequate patent protection in that country or if AstraZeneca licenses patent rights from any third party under circumstances in which the product that we license to AstraZeneca might infringe the third party's patent rights.

Completed Preclinical Research Collaboration. The agreement provided for a preclinical research collaboration that we and AstraZeneca conducted between January 2006 and January 2010 to discover and develop additional compounds that act on the α4ß2 NNR. AstraZeneca paid us research fees based on an agreed reimbursement rate for research services rendered by us in the collaboration. AstraZeneca has exclusively

licensed these compounds, including AZD1446, together with metabolites of these compounds and derivatives and other compounds related to these compounds that meet specified criteria.

Development and Commercialization Costs. AstraZeneca is responsible for the clinical development and commercialization of AZD1446 and any other licensed compounds that arose from the research collaboration that it elects to advance and for funding substantially all associated costs. In addition, we have received $6.2 million in payments from AstraZeneca in connection with events associated with our ongoing clinical trial of TC-1734 in mild to moderate Alzheimer's disease. We have the option to co-promote AZD1446 and any other licensed compounds that arose from the research collaboration that are selected for advancement to specified classes of specialist physicians in the United States. If we exercise our co-promotion option, AstraZeneca is required to provide training to our sales force and compensate us for our detailing efforts following regulatory approval.

Exclusivity Rights and Restrictions. We are not permitted outside of the collaboration to develop or commercialize compounds that act on the α4ß2 NNR and meet pre-defined criteria for the treatment of Alzheimer's disease, ADHD, cognitive dysfunction in schizophrenia or other conditions characterized by cognitive impairment, or schizophrenia. AstraZeneca was previously also subject to this restriction, but the restriction on AstraZeneca has lapsed. This restriction on us will lapse if AstraZeneca commences clinical development outside of the collaboration for a compound that acts on the α4ß2 NNR and meets pre-defined criteria.

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.

Previous Collaboration Agreements

In December 2009, we entered into a collaboration and license agreement with AstraZeneca AB for the global development and commercialization of TC-5214 in MDD. Following completion of a Phase 3 clinical program for TC-5214 conducted under the agreement, we and AstraZeneca announced that a regulatory filing for TC-5214 as an adjunct therapy for MDD would not be pursued and we reported the discontinuation of a "switch" monotherapy trial. AstraZeneca subsequently terminated the agreement effective in May 2012. As a result of the termination, all rights and licenses for TC-5214 that we granted under the agreement to AstraZeneca terminated and reverted to us.

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

Patents and Proprietary Rights

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

As of February 28, 2014, our patent estate included 60 patents issued in the United States, 45 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 (pending)	March 2033 (projected assuming issuance, patent not issued)
TC-1734	Composition of matter for TC-1734	July 2018
	Composition of matter for a family of compounds that includes TC-1734	April 2016
	Composition of matter for the preferred salt form of TC-1734	August 2026
	Methods of use of a family of compounds that includes TC-1734 for treatment and prevention of central nervous system, or CNS, disorders	February 2017
	Methods of use for TC-1734 for treatment and prevention of CNS disorders	July 2018
	Composition of matter for the preferred polymorphic form of the preferred salt form of TC-1734	March 2030
AZD1446 (TC-6683)	Composition of matter for AZD1446	August 2028
	Composition of matter for a family of compounds that includes AZD1446	January 2028
TC-6499	Composition of matter for TC-6499	February 2024
	Composition of matter for the preferred salt form of TC-6499	September 2032
TC-5619	Composition of matter for a racemic mixture that includes TC-5619	March 2019
	Composition of matter for a family of racemic compounds that includes a racemic mixture that includes TC-5619	August 2019
	Composition of matter for a sub-family of racemic compounds that includes a racemic mixture that includes TC-5619	December 2018
	Composition of matter for salt forms of TC-5619, including the preferred salt	January 2029
	Commercial method and composition of matter for synthetic intermediates for manufacture of TC-5619	August 2028

In addition to these patents, for some of these product candidates, we have later-expiring patents and patent applications that cover the product candidate, its use as part of combination therapy or otherwise or methods for synthesis or composition of matter coverage for synthetic intermediates. These patents, including any patents that issue from other pending applications, could provide additional protection or a longer period of protection. We also have issued patents and pending patent applications with equivalent or substantially comparable protection for our product candidates in jurisdictions internationally that we consider key pharmaceutical markets.

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

License Agreements

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

University of South Florida Research Foundation

Pursuant to a license agreement with University of South Florida Research Foundation, or USFRF, we hold an exclusive worldwide license under patents and patent applications owned by USFRF to develop and commercialize TC-5214, mecamylamine hydrochloride and other specified compounds. The licensed patent rights include issued patents covering the pharmaceutical composition of TC-5214.

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

- an annual license fee of $50,000 until we or a sublicensee files an NDA or foreign equivalent for use of a product subject to the license;
- 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 a 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 may receive for a sublicense from a 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. 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.

University of Kentucky Research Foundation

Pursuant to a sponsored research agreement, University of Kentucky Research Foundation, or UKRF, agreed to assign its rights to inventions that resulted in patents related to TC-1734 to R.J. Reynolds Tobacco Company. These patents were subsequently assigned by R.J. Reynolds Tobacco Company to us in August 2000. Under the sponsored research agreement and a subsequent license agreement with UKRF, we are obligated to pay royalties to UKRF based on amounts received for a license to these patents from any licensee.

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. We seek to protect our proprietary information, in part, by using confidentiality agreements with our commercial partners, collaborators, employees and consultants and invention assignment agreements with our employees.

Sales and Marketing

We currently have limited sales, marketing and distribution experience with respect to pharmaceutical products and no internal sales or distribution capabilities. Our current strategy is to selectively seek alliances and collaborations, particularly for target indications for which a potential collaborator has unique expertise or that involve large primary care markets that must be served by large sales and marketing organizations. In entering into these alliances and collaborations, our goal will generally be to maintain co-promotion or co-commercialization rights in the United States and, potentially in the future, other markets. To be successful if we exercise these rights, we would have to develop a specialized sales and marketing organization with sufficient technical expertise.

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 rely and expect to continue to rely on a number of contract manufacturers to manufacture our product candidates for use in any preclinical research and 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 FDA and other 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 in development that target NNRs, including AbbVie, Bristol-Myers Squibb, Novartis, EnVivo Pharmaceuticals, Upsher Smith, Psychogenics, Asmacure, Bionomics, Aniona, Savant HWP, Alpharmagen (a joint venture formed by CoMentis and Anvyl), Extab, SK Biopharmaceuticals and Neuroderm. We expect that we will face increased competition in the future if therapies that target NNRs are further validated and if companies initiate or expand programs focused on NNRs or otherwise pursue the development and commercialization of therapeutics for diseases and disorders that we target, whether independently or by alliance, collaboration or acquisition.

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

- for overactive bladder, anticholinergics such as Vesicare from Astellas Pharma, Detrol LA from Pfizer/Almirall, Enablex from Warner Chilcott/Bayer, Toviaz from Pfizer, Sanctura XR from Allergan, Ditropan XL from Ortho-McNeil Pharma and Oxytrol, an over-the-counter treatment from Merck, beta3-adrenergic receptor agonists such as Mybretiq from Astellas Pharma, and the botulinum toxin Botox from Allergan; and
- for mild to moderate Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer/Eisai, Razadyne from Johnson & Johnson and Exelon from Novartis; Aricept is also indicated for severe Alzheimer's disease and Namenda from Forest Laboratories, which acts by regulating the neurotransmitter glutamate, is indicated for moderate to severe Alzheimer's disease.

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

We expect to compete based upon, among other things, the efficacy and favorable side effect profiles of our products. Our ability to compete successfully will depend on our continued ability to attract and retain skilled and experienced scientific, clinical development and executive personnel, to identify and develop viable product candidates into products and to exploit these products commercially before others are able to develop competitive products. In addition, our ability to compete may be affected by insurers and other third-party payors favoring the use of lower priced generic products over branded products.

Regulatory Matters

Government Regulation and Product Approval

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

U.S. 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 complying with applicable federal, state, local and foreign laws and regulations require the expenditure of substantial time and financial resources. Failure to comply with United States requirements at any time during the product development process, the approval process or after approval may subject a company 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 or untitled letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, refusals of government contracts, restitution, disgorgement, civil or criminal penalties, and criminal prosecution.

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

- completion of nonclinical 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 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 processes require substantial time, effort and financial resources.

Once a drug is identified for development it enters the nonclinical testing stage. Nonclinical tests include laboratory evaluations of chemistry, toxicity and formulation, as well as animal studies to assess the characteristics and potential effects of the drug and may continue throughout the entire drug development process. The conduct of the nonclinical tests must comply with federal regulations and requirements, including good laboratory practices, or GLP. The results of nonclinical 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. The IND becomes effective 30 days after receipt by the FDA, unless within the 30-day time period the FDA places the subject clinical trial on a clinical hold. In such a case, the company responsible for the clinical trial (the sponsor) and the FDA must resolve any outstanding concerns before the clinical trial can begin. Clinical holds also may be imposed by the FDA at any time before or during studies due to safety concerns or non-compliance with applicable law or regulation.

All clinical trials must be conducted under the supervision of one or more qualified investigators. Clinical trials must be conducted: (i) in compliance with federal regulations, including regulations requiring that all research subjects provide informed consent; (ii) in compliance with good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing, among other things, the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Further, an institutional review board, or IRB, for each institution participating in a clinical trial must review and approve the plan for the clinical trial before it commences at the institution. An IRB considers, among other things, whether the risks to individuals participating in the trials are minimized and reasonable in relation to the anticipated benefits. The IRB also approves the information regarding the trial and the consent form that must be provided to each trial subject or his or her legal representative and monitors the study until completed. An IRB may impose conditions to the initiation or continued conduct of trial at the institution for which the IRB is responsible. Each new clinical protocol must be submitted to the IND for FDA review and to the applicable IRBs for approval.

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 subjects to evaluate safety, dosage tolerance, absorption, metabolism, distribution and excretion. In the case of some drugs for severe or life-threatening diseases, the initial human testing may be conducted in patients, particularly where the drug may be too inherently toxic to administer ethically to healthy subjects;
- *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 clinical trial, whether Phase 1, Phase 2 or Phase 3, may fail to 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 trial participants 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 under investigation has been associated with unexpected serious harm to patients.

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

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

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

The Food and Drug Administration Safety and Innovation Act, which was enacted in 2012, enables a sponsor to request that a drug be designated as a breakthrough therapy. Breakthrough therapy designation is intended to expedite the development and review of drugs for serious or life-threatening conditions. The request is submitted concurrently with or as an amendment to an IND. The request must include supporting information, including the basis for considering the drug as intended to treat a serious condition and a summary of the preliminary clinical evidence that the drug may demonstrate substantial improvement over available therapies. A sponsor must describe the preliminary clinical evidence, including, for example, justification for the clinical study endpoint used and a brief description of statistical analyses. The FDA will make a determination whether or not to grant the request within 60 days after receipt of the submission.

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

U.S. Review and Approval Processes

The results of product development, nonclinical studies and clinical trials, along with descriptions of the manufacturing process, analytical chemistry tests, proposed labeling, and other relevant information, are submitted to the FDA as part of an NDA requesting approval to market the product. FDA approval of the NDA is required before marketing of the product may begin in the United States. The cost of preparing and submitting an NDA is substantial. Under federal law, the submission of most NDAs is additionally subject to a substantial application user fee and the manufacturer or sponsor under an approved NDA is also subject to annual establishment registration and product listing fees. These fees are typically increased annually. A waiver or reduction of the fees may be obtained under specified limited circumstances.

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

The FDA has 60 days from its receipt of an NDA to determine whether the application will be accepted for filing based on the agency's threshold determination that it is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review. The FDA has agreed to certain performance goals in the review of NDAs. Most such applications for standard review drug products are reviewed within ten to twelve months; most applications for priority review drugs are reviewed in six to eight months. Priority review can be applied to drugs that the FDA determines offer major advances in treatment, or provide a treatment where no adequate therapy exists. The review process for both standard and priority review may be extended by FDA for three additional months to consider certain late-submitted information, or information intended to clarify information already provided in the submission.

The FDA may also refer applications for novel drug products, or drug products that present difficult questions of safety or efficacy, to an advisory committee—typically a panel that includes clinicians and other experts—for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is

manufactured. The FDA will not approve the product unless compliance with current good manufacturing practice, or GMP—a quality system regulating manufacturing—is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After FDA evaluates the NDA and the manufacturing facilities, it issues either 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 application. If, or when, those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. FDA has committed to reviewing such resubmissions in two or 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 a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug's safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

Changes to some of the conditions established in an approved application, including changes in indications, labeling, or manufacturing processes or facilities, require submission and FDA approval of a new NDA or NDA supplement before the change can be implemented. An NDA supplement for a new indication typically requires clinical data similar to that in the original application, and the FDA uses the same procedures and actions in reviewing NDA supplements as it does in reviewing NDAs.

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 that 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 nonclinical 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.

An ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. The ANDA applicant may also elect to submit a section viii statement certifying that its proposed ANDA label does not contain (or carves out) any language regarding the patented method-of-use rather than

certify to a listed method-of-use patent. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. A certification that the new product will not infringe the already approved product's listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the ANDA applicant has provided a Paragraph IV certification to the FDA, the applicant must also send notice of the Paragraph IV certification to the NDA and patent holders once the ANDA has been accepted for filing by the FDA. The NDA and patent holders may then initiate a patent infringement lawsuit in response to the notice of the Paragraph IV certification. The filing of a patent infringement lawsuit within 45 days of the receipt of a Paragraph IV certification automatically prevents the FDA from approving the ANDA until the earlier of 30 months, expiration of the patent, settlement of the lawsuit, or a decision in the infringement case that is favorable to the ANDA applicant.

Most drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA, which enables the applicant to rely, in part, on FDA's previous approval of a similar product or published literature in support of its application. Section 505(b)(2) NDAs often provide an alternate path to FDA approval for new or improved formulations or new uses of previously approved products. Section 505(b)(2) of the FDCA permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of reference. If the Section 505(b)(2) applicant can establish that reliance on FDA's previous approval is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all, or some, of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

To the extent that the Section 505(b)(2) applicant is relying on studies conducted for an already approved product, the applicant is required to certify to the FDA concerning any patents listed for the approved product in the Orange Book to the same extent that an ANDA applicant would. Thus approval of a Section 505(b)(2) NDA can be stalled until all the listed patents claiming the referenced product have expired, until any non-patent exclusivity, such as exclusivity for obtaining approval of a new chemical entity, listed in the Orange Book for the referenced product has expired, and, in the case of a Paragraph IV certification and subsequent patent infringement suit, until the earlier of 30 months, settlement of the lawsuit or a decision in the infringement case that is favorable to the Section 505(b)(2) applicant.

Marketing Exclusivity

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

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

Orphan Drug Designation

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

If a product that has orphan drug designation subsequently receives the first FDA approval for the disease for which it has such designation, the product is entitled to orphan product exclusivity, which means that the FDA may not approve any other applications to market the same drug for the same indication for seven years, except in very limited circumstances (such as a showing of clinical superiority to the product with orphan drug exclusivity). Orphan drug exclusivity does not prevent the FDA from approving a different drug for the same disease or condition or from approving the same drug for a different disease or condition.

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

Patent Term Extension

After NDA approval, owners of relevant drug patents may apply for up to a five year patent extension. The allowable patent term extension is calculated as half of the drug's testing phase (the time between IND application and NDA submission) and all of the review phase (the time between NDA submission and approval) up to a maximum of five years. The time can be shortened if FDA determines that the applicant did not pursue approval with due diligence. The total patent term after the extension may not exceed 14 years.

For patents that might expire during the application phase, the patent owner may request an interim patent extension. An interim patent extension increases the patent term by one year and may be renewed up to four times. For each interim patent extension granted, the post-approval patent extension is reduced by one year. The director of the United States Patent and Trademark Office must determine that approval of the drug covered by the patent for which a patent extension is being sought is likely. Interim patent extensions are not available for a drug for which an NDA has not been submitted.

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 applicable state agencies and are subject to periodic unannounced inspections for compliance with cGMP and other laws and regulations.

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

As part of the sales and marketing process, pharmaceutical companies frequently provide samples of approved drugs to physicians. The Prescription Drug Marketing Act, or the PDMA, imposes requirements and limitations upon the provision of drug samples to physicians and prohibits states from licensing distributors of prescription drugs unless the licensing program meets federal guidelines that include minimum standards for storage, handling and record keeping. The PDMA sets forth civil and criminal penalties for violations.

From time to time, legislation is drafted, introduced and passed by the U.S. Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of products regulated by the FDA.

Foreign Regulation

In addition to regulations in the United States, we are subject to a variety of foreign regulations governing clinical trials of our product candidates and commercial sales and distribution of any products. Whether or not we obtain FDA approval for a product candidate or product, we must obtain approval by the comparable regulatory authorities of foreign countries, or of economic areas such as the European Union, before we can commence clinical trials of the product candidate or marketing of the product in those countries or areas. The approval process and requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary greatly from place to place, and the time required may be longer or shorter than the time required for FDA approval.

Under European Union regulatory systems, we may submit marketing authorization applications either under a centralized or a decentralized procedure. The centralized procedure, which provides for the grant of a single marketing authorization that is valid for all European Union member states, is compulsory for medicines produced by biotechnology or intended to treat AIDS, cancer, neurodegenerative disorders or diabetes and optional for medicines that are highly innovative. For drugs without approval in any member state, the decentralized procedure provides for approval by one or more other, or concerned, member states of an assessment of an application performed by one member state, which is known as the reference member state. Under this procedure, an applicant submits an application, or dossier, and related materials (including a draft summary of product characteristics, draft labeling and package leaflet) to the reference member state and concerned member states. The reference member state prepares a draft assessment and drafts of the related materials within 120 days after receipt of a valid application. Within 90 days of receiving the reference member state's assessment report, each concerned member state must decide whether to approve the assessment report and related materials. If a member state cannot approve the assessment report and related materials on the grounds of potential serious risk to public health, any disputed issues may eventually be referred to the European Commission and the decision of the European Commission would be binding on all member states.

As in the United States, we may apply for designation of a product as an orphan drug for the treatment of a specific indication in the European Union before the application for marketing authorization is made. Orphan

drugs in Europe receive economic and marketing benefits, including up to 10 years of market exclusivity for the approved indication unless another applicant can show that its product is safer, more effective or otherwise clinically superior to the orphan-designated product.

Reimbursement

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

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

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

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

The American Recovery and Reinvestment Act of 2009 provides funding for the federal government to compare the effectiveness of different treatments for the same illness. A plan for the research would be developed by the Department of Health and Human Services, the Agency for Healthcare Research and Quality and the National Institutes of Health, and periodic reports on the status of the research and related expenditures would be made to the U.S. Congress. Although the results of the comparative effectiveness studies are not intended to mandate coverage policies for public or private payors, it is not clear whether research would have any effect on the sales of any of our products that is successfully developed and approved, if the product or the condition that it is intended to treat becomes the subject of a study. It is also possible that comparative effectiveness research demonstrating benefits of a competitor's product could adversely affect the sales of any of

our products that is successfully developed and approved. If third-party payors do not consider our products to be cost-effective compared to other available therapies, they may not cover our products after approval as a benefit under their plans or, if they do, the level of payment may not be sufficient to allow us to sell our products on a profitable basis.

The Patient Protection and Affordable Care Act, or the ACA, as amended by the Health Care and Education Affordability Reconciliation Act of 2010, has had and is expected to have a significant impact on the health care industry. The ACA expanded coverage for the uninsured while at the same time containing overall healthcare costs. Among other things, the ACA expanded and increased industry rebates for drugs covered under Medicaid programs and made changes to the coverage requirements under the Medicare Part D program. We cannot predict the full impact of the ACA on pharmaceutical companies because many of the ACA's reforms require the promulgation of detailed regulations to implement the statutory provisions, which has not yet occurred. In addition, although the United States Supreme Court has upheld the constitutionality of most of the ACA, some states have indicated that they intend not to implement certain sections of the ACA and some members of the U.S. Congress are still working to repeal the ACA. These challenges add to the uncertainty of the effects of the ACA.

The Physician Payment Sunshine Act, or Sunshine Act, which was enacted as part of ACA, requires covered manufacturers of drugs covered under Medicare, Medicaid or the Children's Health Insurance Program to report annually to the Secretary of the Department of Health and Human Services payments or other transfers of value made by that entity, or by a third party as directed by that entity, to physicians and teaching hospitals, or to third parties on behalf of physicians or teaching hospitals, during the course of the preceding calendar year. The final rule implementing the Sunshine Act, published on February 8, 2013, required data collection on payments to begin on August 1, 2013. The first reports are currently due in the second quarter of 2014, and the information will be made publicly available on a searchable website in September 2014. Failure to submit required information may result in civil monetary penalties of up to $150,000 per year (up to $1 million per year for "knowing failures") for all payments, transfers of value or ownership or investment interests not reported in an annual submission.

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

In some foreign countries, the proposed pricing for a drug must be approved before it may be lawfully marketed. The requirements governing drug pricing vary widely from country to country. For example, the European Union provides options for its member states to restrict the range of medicinal products for which their respective national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. A member state may approve a specific price for the medicinal product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the medicinal product on the market. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any of our products for which we receive marketing approval. Historically, the price structures for products launched in the European Union do not follow those of the United States and tend to be significantly lower.

Employees

As of February 28, 2014, we had 39 full-time employees and one part-time employee. Our management believes that relations with our employees are good. None of our employees is represented under a collective bargaining agreement.

Our Corporate Information

We were incorporated in Delaware in 1997 as a wholly owned subsidiary of R.J. Reynolds Tobacco Company. In August 2000, we became an independent company when we issued and sold stock to venture capital investors. Our principal executive offices are located at 100 North Main Street, Suite 1510, Winston-Salem, North Carolina 27101 and our telephone number is (336) 480-2100.

Our internet address is www.targacept.com. The information contained on, or that can be accessed through, our website is not incorporated by reference into this annual report. We have included our website address as a factual reference and do not intend it as an active link to our website. Our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K, and all amendments to those reports, are available to you free of charge through the Investor Relations page of our website as soon as reasonably practicable after such materials have been electronically filed with, or furnished to, the SEC.

Targacept®, Pentad™ and NNR Therapeutics™ are trademarks of ours. Other service marks, trademarks and trade names appearing in this annual report are the properties of their respective owners.

Item 1A. Risk Factors.

Risks Related to Our Financial Results

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

We were incorporated in 1997 and operated as a wholly owned subsidiary of R.J. Reynolds Tobacco Company until August 2000. As of December 31, 2013, we had an accumulated deficit of $280.6 million. We had net loss of $46.7 million, $7.0 million and $8.5 million for the years ended December 31, 2013, 2012 and 2011, respectively. 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 product candidates advance into later-stage development and as we progress our programs and invest in additional product opportunities. As a result, we will need to generate significant revenues to achieve profitability in the future or, if we do achieve profitability for any particular period, to sustain or grow our profitability on a quarterly or annual basis.

We derived a substantial portion of our revenue for 2013, 2012 and 2011 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:

- the scope, progress, duration, results and cost of clinical trials, as well as non-clinical studies and assessments, of our product candidates and programs;
- whether we establish additional strategic alliances, collaborations or licensing or other comparable arrangements, or whether we pursue and complete any merger, acquisition or other significant corporate transaction, and, if we do, the associated terms in each case; and
- whether and to what extent milestone events are achieved for AZD1446 under our collaboration agreement with AstraZeneca.

Sources that have contributed to our revenue for any particular year may not continue. For example, we received $245 million in aggregate payments under two collaborations with global pharmaceutical companies that are now terminated and no longer sources of future revenue. Additionally, we do not currently have any source of product revenue.

If we are unable to develop and commercialize one or more of our product candidates, if development is delayed or if revenue from sales of any product candidate that receives marketing approval is insufficient, we may not achieve profitability in the future. Even if we are profitable for any particular period, we may not be able to sustain or grow our profitability on a quarterly or annual basis.

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

Successful drug development and commercialization requires significant amounts of capital. It is foreseeable that we will in the future require substantial additional capital in order to continue to conduct the development 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 potential future collaborator of ours may assume responsibility under the terms of the applicable agreement for funding further development and subsequent commercialization) and potentially to establish sales and marketing capabilities. Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the scope, progress, duration, results and costs of clinical trials, as well as non-clinical studies and assessments, of our product candidates and programs;
- whether we establish additional strategic alliances, collaborations or licensing or other comparable arrangements, or whether we pursue and complete any merger, acquisition or other significant corporate transaction, and, if we do, the associated terms in each case;
- whether and to what extent milestone events are achieved for AZD1446 under our collaboration agreement with AstraZeneca;
- the extent to which we retain development or commercialization rights or responsibilities for our product candidates and incur associated development costs, manufacturing costs or costs to establish sales and marketing functions;
- the number and characteristics of product candidates that we pursue and programs that we conduct;
- the costs to satisfy our obligations under potential future alliances and collaborations;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending patents and other intellectual property rights;
- the costs of manufacturing-related services for our product candidates in development;
- the costs, timing and outcomes of regulatory reviews or other regulatory actions;
- the timing, receipt and amount of sales or royalties, if any, from our potential products;
- the extent of our general and administrative expenses; and
- the rate of technological advancements for the indications that we target.

In addition, we may seek additional capital, whether through offerings of securities utilizing our currently effective Registration Statement on Form S-3, our at the market sales agreement or otherwise, if the conditions for raising capital are favorable or based on strategic considerations even if we believe we have sufficient funds for our current or future operating plans. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our stockholders may be diluted, and the terms of the securities may include liquidation or other preferences that materially and adversely affect the rights of our stockholders. Debt financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions such as incurring additional debt, making capital expenditures or declaring dividends. If we raise additional funds through alliance, collaboration or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies or product candidates or grant licenses on terms that are not favorable to us.

We plan to continue, whether alone, with AstraZeneca where applicable or with potential future collaborators, to advance our product candidates through the development process. We currently expect that our existing capital resources will enable us to fund our operations through at least the end of 2015. However, our operating plan may change as a result of many factors, including those described above, and we may need additional funds sooner than planned to meet operational needs and capital requirements for product development and commercialization. Our ability to raise additional funds if and when needed on terms that are acceptable to us, or at all, is uncertain. If adequate funds are not available on a timely basis, we may:

- terminate, delay or downsize clinical trials or manufacturing or other development activities for one or more of our product candidates;
- delay establishment of any sales and marketing capabilities or other activities that may be necessary to commercialize our product candidates; or
- scale back or eliminate programs that are designed to expand our product pipeline.

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

Our success depends substantially on our most advanced product candidates, which are still under development. If we are unable to bring 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 in future periods will depend substantially on the successful development and commercialization of our clinical-stage product candidates, including in particular TC-5214 and TC-1734 (which are both currently in Phase 2b clinical development).

Any of our product candidates could be unsuccessful if it:

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

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

TC-5214 has not yet demonstrated efficacy in clinical trials in overactive bladder, and our previous findings from nonclinical studies and assessments and clinical trials in a different indication may not be predictive of a benefit for TC-5214 as a treatment for overactive bladder. If our planned and any future clinical trials of TC-5214 in overactive bladder are not successful, we will not obtain the regulatory approvals required to market and sell TC-5214.

We are developing TC-5214 as a treatment for overactive bladder. Our decision to conduct this development was based primarily on various findings from nonclinical studies and assessments of TC-5214 and clinical trials of TC-5214 in a different indication that we believe indicate potential benefits of TC-5214 as an overactive bladder therapy. We have not yet completed any clinical trials of TC-5214 in patients with overactive bladder, and our previous findings may not be predictive of clinical success in this patient population. If our current and any future clinical trials of TC-5214 in overactive bladder are not successful, we will not obtain the regulatory approvals required to market and sell TC-5214 as a treatment for overactive bladder.

If we are unable to complete the development program for TC-5214 and submit a new drug application to the FDA on or before September 30, 2017 or if other statutory conditions are not met, TC-5214 may not receive the five-year exclusivity period provided by applicable law, in which case our ability to exclude third parties from themselves marketing TC-5214 in the United States would be substantially dependent on patents after three years.

The Federal Food, Drug, and Cosmetic Act, or FDCA, provides a five-year period of marketing exclusivity in the United States to the first applicant to obtain approval of a new drug application, or NDA, for a drug that qualifies as a new chemical entity. The exclusivity period runs concurrently with any patents that cover the new chemical entity, but provides exclusivity independent from and irrespective of the patents. Accordingly, a new chemical entity approved in the United States has assurance of a statutory period of marketing exclusivity in the United States whether or not the patents that cover it are sufficiently strong to withstand challenge.

TC-5214 is one of two enantiomers of a racemate previously marketed in the United States. Enantiomers are mirror images of each other that have the same chemical but potentially different biological properties, and a racemate is a chemical mixture comprised of two corresponding enantiomers. Under Section 505(u) of the FDCA as currently in effect, 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, 2017, when the statutory provision that permits the election is scheduled to expire unless it is re-authorized by the U.S. Congress. It is uncertain whether the statutory provision will be re-authorized. If for any reason we are unable to submit an NDA for TC-5214 on or before September 30, 2017, or if other statutory conditions are not met, and the statutory provision is not reauthorized, TC-5214 will not receive the five-year exclusivity period and will be limited to a three-year exclusivity period that is provided by the FDCA for certain applications. In that case, we 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 potentially 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 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, any future commercialization of TC-5214 would be materially and adversely affected and our business would suffer.

TC-6499 has not yet demonstrated efficacy in clinical trials in diabetic gastroparesis, and our previous findings from clinical and nonclinical studies and assessments may not be predictive of a benefit for TC-6499 as a treatment for diabetic gastroparesis. If our planned and any future clinical trials of TC-6499 in diabetic gastroparesis are not successful, we will not obtain the regulatory approvals required to market and sell TC-6499.

We plan to conduct an exploratory study of TC-6499 as a treatment for diabetic gastroparesis. Our decision to conduct this development was based primarily on various findings from a previous clinical trial of TC-6499 in another indication and nonclinical studies and assessments of TC-6499 that we believe may indicate potential benefits of TC-6499 as a diabetic gastroparesis therapy. We have not yet conducted any clinical trials of TC-6499 in patients with diabetic gastroparesis, and our previous findings may not be predictive of clinical success in this patient population. If our planned and any future clinical trials of TC-6499 in diabetic gastroparesis are not successful, we will not obtain the regulatory approvals required to market and sell TC-6499 as a treatment for diabetic gastroparesis.

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

The nonclinical 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 must receive regulatory approval of each product candidate before we can market and sell it. We have only limited experience in pursuing regulatory approvals. Securing FDA approval requires the submission of extensive nonclinical and clinical data and information about the chemistry and manufacture of, and control procedures for, each potential product. In addition, the supporting information submitted to the FDA must establish the safety and efficacy of the product candidate for each indicated use. The drug development and marketing approval process takes many years, requires the expenditure of substantial resources, is subject to delays and can vary substantially based upon the type, complexity and novelty of the product candidates involved. In addition to the time and expense involved, the process is uncertain and we may never receive the required regulatory approvals. In addition, the FDA, the U.S. Congress or foreign 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 receive regulatory approval to market a particular product candidate, the approval will be subject to limitations on the indicated uses for which it may be marketed and may not permit labeling claims that are necessary or desirable for its promotion.

A Phase 1 clinical trial program typically takes several months to complete, a Phase 2 clinical trial program typically takes several months to two years to complete and a Phase 3 clinical trial program typically takes one to four years to complete. Moreover, Phase 3 clinical trials may not follow successful completion of Phase 2 clinical trials directly, as additional non-clinical assessments or clinical trials may first be required. Industry sources have reported that the preparation and submission of an NDA, which is required for regulatory approval in the United States, generally takes six months to one year to complete after completion of 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. Precise estimates vary, but a great majority of investigational drugs that enter clinical trials will never be approved by the FDA for commercial sale.

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

- clinical trial results may indicate that the product candidate is not safe;
- clinical trial results may indicate that the product candidate is not effective, whether because the product candidate does not have its intended effects in the clinical trial, because subjects given an inactive comparator (i.e., placebo) in the clinical trial experience benefits comparable to the benefits experienced by subjects given the product candidate, which obscures the effects of the product candidate, or for any other reason;
- the product candidate may not have a favorable risk: benefit profile;
- 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 interpret the same results differently;
- the FDA may require development of a Risk Evaluation and Mitigation Strategy, or REMS, as a condition of approval;
- 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, or the facilities of our third party manufacturers may not pass inspection by the FDA; or
- the FDA may change its approval policies or adopt new regulations.

If we obtain the requisite regulatory approval for a particular product candidate, the approval may not extend to all indications for which approval was sought, which could limit the use of the product and materially and adversely impact our revenue.

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

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

To obtain the requisite regulatory approvals to market and sell any of our product candidates, we must demonstrate, through extensive nonclinical 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. Nonclinical studies and clinical trials are lengthy and expensive, difficult to design and implement and subject to a historically high rate of failure. The development of each of our product candidates involves significant risks at each stage of testing. A failure of one or more clinical trials of any of our product candidates could occur at any stage of testing. For example, TC-5214 did not achieve the primary endpoint in multiple Phase 3 clinical trials in major depressive disorder completed in 2011 and 2012, and TC-5619 did not meet the primary endpoint in the Phase 2b clinical trial in schizophrenia in 2013. If we experience failures in our ongoing or future clinical trials, or if we are 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 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 the initial clinical trial for a product candidate may commence in the United States, we must submit an IND containing nonclinical studies, chemistry, manufacturing, control and other information and a study protocol to the FDA. If the FDA does not object within 30 days after submission of the IND, then the trial may commence. If a clinical trial is commenced, we, 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 do not prove in clinical trials that our product candidates are safe and effective, we will not 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 product candidates target diseases or disorders that are not well understood. For example, there is only limited scientific understanding of the causes of overactive bladder, Alzheimer's disease and diabetic gastroparesis. 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 pathways targeted by our product candidates. 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 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 will encounter problems with any ongoing or planned clinical trials of our product candidates that will cause us or any regulatory authority to delay or suspend those clinical trials or delay the analysis of data derived from them. A number of events, including 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 by the FDA or any foreign regulatory authority regarding the scope or design of the clinical trial;
- delays in recruiting and enrolling subjects into the clinical trial;
- delays in obtaining, or our inability to obtain, required approvals from institutional review boards, ethics committees or other reviewing entities at clinical sites selected for participation in the clinical trial;
- insufficient supply or deficient quality of the product candidate or other materials necessary to conduct the clinical trial;
- lower than anticipated retention rate of subjects in the clinical trial;
- negative or inconclusive results from the clinical trial, or results that are inconsistent with earlier results, that necessitate additional study;
- serious and unexpected drug-related side effects experienced by subjects in the clinical trial; or
- failure of our third-party contractors to comply with regulatory requirements or otherwise meet their contractual obligations to us in a timely manner.

Clinical trials require sufficient subject enrollment, which is a function of many factors—including the size of the patient population, the extent to which other clinical trials are being conducted concurrently that involve the same patient population, the number of participating clinical sites, the proximity of subjects to clinical sites, the nature of the trial protocol, the availability of effective treatments for the relevant disease, the eligibility criteria for the clinical trial and the emphasis placed on ensuring a rigorous adherence to the eligibility criteria. Delays in subject enrollment can result in increased costs and longer development times. The failure to enroll subjects in a clinical trial could delay the completion of the clinical trial beyond our current expectations. For example, we experienced enrollment delays in our ongoing Phase 2b study of TC-1734 in mild to moderate Alzheimer's disease that delayed our initial projected completion dates for that study.

In addition, the FDA or foreign regulatory authorities could require us to conduct clinical trials for any of our product candidates with a larger number of subjects than we project. We may not be able to enroll a sufficient number of subjects in a timely or cost-effective manner. Furthermore, enrolled subjects may drop out of clinical trials, which could impair the validity or statistical analysis of those clinical trials.

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

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

The FDA or foreign regulatory authorities may require more nonclinical or clinical data for any of our product candidates or more time to evaluate data than we currently anticipate because drugs that act on NNRs are

not a well-established class of drugs, because nicotine, which interacts with all nicotinic receptors, has addictive properties and potential for abuse, because of experiences with drugs that act on NNRs that are developed or marketed by third parties or for any other reason. In particular, the FDA has issued a public health advisory with regard to Pfizer's aid to smoking cessation product, Chantix, and requires Chantix (as well as Zyban, which is GlaxoSmithKline's aid to smoking cessation product) to include a boxed warning on its prescribing information. The warning makes prominent the risk of serious mental health events, including changes in behavior, depressed mood, hostility, agitation and suicide-related events, that have been reported in some patients attempting to quit smoking while taking these drugs. The FDA has also issued a separate safety alert reporting a higher incidence of cardiovascular events with Chantix than placebo in completed clinical trials. Chantix acts on several NNR subtypes, as well as other molecular targets in the body. All of our product candidates currently in development affect the activity of one or more NNR subtypes.

It is uncertain whether any adverse medical experiences associated with Chantix will impact the view of the FDA or foreign regulatory authorities regarding our product candidates. If the FDA or any foreign regulatory authority determines that any adverse medical experiences associated with Chantix have relevance to one or more of our product candidates or that compounds that interact with NNRs may have potential for abuse, it may require us to generate more clinical data than we currently anticipate to establish that the affected product candidate is safe or does not have abuse potential, which could increase the cost of the development program for the affected product candidate, extend the development timeline for the affected product candidate or delay our receipt of revenue from potential product sales of the affected product candidate.

Our ongoing Phase 2b clinical trial of TC-1734 in mild to moderate Alzheimer's disease is evaluating our product candidate as compared to a commonly used marketed medication rather than placebo, which may make a positive outcome more difficult to achieve.

Our ongoing Phase 2b clinical trial of TC-1734 is designed to evaluate TC-1734 as a treatment for mild to moderate Alzheimer's disease as compared to donepezil, the marketed medication most often prescribed for the disease. As a result, the trial will not have a positive outcome if TC-1734 does not statistically outperform donepezil, even if TC-1734 could be an effective treatment for mild to moderate Alzheimer's disease. This requirement of superiority to donepezil may make a positive outcome comparatively less likely than if we were evaluating TC-1734 in the trial as compared to an inactive comparator (i.e., placebo). If the trial is not successful, it will not support regulatory approval to market and sell TC-1734 as a treatment for mild to moderate Alzheimer's disease.

We currently have limited supplies of TC-1734. Therefore, even if our ongoing Phase 2b clinical trial of TC-1734 in mild to moderate Alzheimer's disease has a favorable outcome, and we decide to proceed to the next clinical testing phase of TC-1734, there will be some delay due to the need to manufacture additional supplies of TC-1734 to support that testing.

When AstraZeneca terminated its rights to TC-1734 under our 2005 collaboration agreement, and all rights to the compound reverted to Targacept in June of 2013, we became responsible for the cost and execution of the ongoing Phase 2b clinical trial of TC-1734 in mild to moderate Alzheimer's disease and any potential future development and commercialization of TC-1734. While our current supply of TC-1734 is sufficient to support our ongoing Phase 2b trial, it is not sufficient to support potential additional clinical trials. Based on the challenging therapeutic area and the high success hurdle we established for the current Phase 2b trial, we have not made investments to manufacture additional supplies of TC-1734, and we do not expect to make such an investment, if at all, unless the ongoing Phase 2b trial is favorable. This means any decision to make such an investment is not expected to be made until after the results of the ongoing Phase 2b trial are known, which is currently anticipated to be in mid-2014. If a decision is made to conduct additional clinical testing, such testing will therefore be delayed until sufficient supplies of TC-1734 are manufactured, at the earliest.

Our Special Protocol Assessment agreement with the FDA for our ongoing Phase 2b clinical trial of TC-1734 in mild to moderate Alzheimer's disease does not guarantee regulatory approval or any particular outcome from any future regulatory review of TC-1734, even if we believe that the outcome of the trial when completed is favorable.

We have obtained a Special Protocol Assessment, or SPA, agreement with the FDA for our ongoing Phase 2b clinical trial of TC-1734 in mild to moderate Alzheimer's disease. The purpose of an SPA is to memorialize an agreement with the FDA on the protocol design and statistical analysis plan for the clinical trials that will form the primary basis of an efficacy claim. Clinical trials that are designed to support a determination that a drug is safe and effective for a particular use are sometimes referred to as "pivotal" trials. Our SPA with the FDA provides that the ongoing Alzheimer's disease trial will not alone be sufficient to support regulatory approval for TC-1734. If we submit an NDA following completion of the ongoing trial and any additional clinical trials of TC-1734 that we conduct in mild to moderate Alzheimer's disease, the NDA may not be approved by the FDA notwithstanding our SPA, even if we believe that the data from the trials support approval.

Approval of an NDA for TC-1734 is not guaranteed because a final determination by the FDA that an agreed-upon protocol satisfies a specific objective, such as the demonstration of efficacy, or supports an approval decision will be based on a complete review of all of the data in the NDA. The FDA retains significant latitude and discretion in interpreting the terms of an SPA, the data and results from clinical trials and all other information included in the NDA. For example, the FDA may require trial design changes or additional studies if issues arise that it believes to be relevant to determining safety or efficacy, the FDA may reconsider the agreed upon scope of review based on data that subsequently becomes available and the FDA may raise concerns that arise after grant of the SPA that override it. In particular, the FDA may determine that our ongoing study of TC-1734 in mild to moderate Alzheimer's disease, which we are conducting at sites predominantly in Eastern Europe and also in the United States, did not when completed include a sufficient number of subjects at sites in the United States to support regulatory approval to market and sell TC-1734. In addition, in previous toxicology studies of TC-1734 in male rats, testicular abnormalities were observed. These nonclinical abnormalities, which were provided to the FDA prior to receiving our SPA agreement and initiating our ongoing study, were seen only in rats and not in any of the four other species studied. The findings in rats could adversely affect the likelihood that the FDA will grant approval to market and sell TC-1734, or the FDA could grant approval of TC-1734 only for a limited population of patients with mild to moderate Alzheimer's disease or require a warning on the prescribing information that limits the overall commercial potential of TC-1734. As a result, even with an SPA, we cannot be certain that the FDA will find any particular clinical trial results acceptable to support regulatory approval to market and sell TC-1734 as a treatment for mild to moderate Alzheimer's disease.

We have closed our laboratory operations and no longer have the capability to identify or discover internal product candidates. If development of our product candidates currently in clinical development proves to be unsuccessful, we may not be able to overcome the pipeline attrition, which would have a material adverse effect on our business.

In 2012, we completed two workforce reductions and closed our laboratory operations. Following these actions, we do not have internal discovery and research capabilities or the ability to identify and discover new internal product candidates. We have no current plan to resume discovery or research activities. If in the future we were to resume these activities, we would need to recruit additional scientific and technical personnel and obtain access to laboratory facilities. We currently have two active and one planned clinical development programs and, without internal discovery and research, we may not be able to expand our pipeline with internal candidates or at all. If our current development activities are unsuccessful and we experience attrition, our business would be materially and adversely affected, which would materially and adversely impact our stock price.

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

Even if we receive regulatory approval to market a particular product candidate, the approval could be conditioned on us conducting additional costly post-approval studies or could limit the indicated uses included in our labeling. The FDA has significant postmarket authority, including, for example, the authority to require labeling changes based on new safety information and to require postmarket studies or clinical trials to evaluate serious safety risks related to the use of a drug. The FDA also has the authority to require, as part of an NDA, the submission of a REMS. A REMS plan could, for example, limit prescribing to certain physicians or medical centers that have undergone specialized training, limit treatment to patients who meet certain safe-use criteria or require treated patients to enroll in a registry. Any REMS required by the FDA may lead to increased costs to assure compliance with new post-approval regulatory requirements and potential requirements or restrictions on the sale of approved products, all of which could lead to lower sales volume and revenue. Moreover, a product may later cause adverse medical experiences that limit or prevent its widespread use or commercial potential, force us to withdraw it from the market or impede or delay our ability to obtain regulatory approvals in additional countries. If any of our product candidates that becomes an approved product either causes adverse medical experiences or becomes associated with a third-party product that is associated with adverse medical experiences such as those related to Chantix described above under "*Regulatory authorities may require more data for any of our product candidates than we currently anticipate, which could cause us to incur additional costs, extend our development timelines or delay our receipt of any revenue from potential product sales.,*" the overall commercial success of the affected product may be negatively impacted.

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

Also, although we have not received any notice that we are the subject of any FDA 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 fail to comply with the requirements of the FDA and other applicable U.S. or foreign governmental or regulatory authorities or previously unknown problems with our products or product candidates, manufacturers or manufacturing processes are discovered, we could be subject to administrative or judicially imposed sanctions, including:

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

Because we have multiple compounds and are considering a variety of target indications, we may apply our finite resources to pursue a particular product candidate or indication, fail to capitalize on product candidates or indications that may be more profitable or for which there is a greater likelihood of success, or relinquish valuable rights to our disadvantage.

Because we have finite financial and managerial resources, we must focus on product candidates for the specific indications that we believe are the most promising. As a result, we may forego or delay pursuit of opportunities with other product candidates or other indications that later prove to have greater commercial potential. Our resource allocation decisions may cause us to fail to capitalize on viable commercial products or profitable market opportunities. Furthermore, if we do not accurately evaluate the commercial potential or target market for a particular product candidate, or if we incorrectly conclude that utilizing the expertise and resources of a collaborator in the development or potential commercialization of a particular product candidate would benefit us, we may relinquish valuable rights to that product candidate through strategic alliances, collaborations or licensing or other comparable arrangements in cases in which it would have been advantageous for us to retain sole development and commercialization rights. Any of these decisions or conclusions could have a material adverse effect on our business.

Risks Related to Our Dependence on Third Parties

The successful development and commercialization of AZD1446 depends substantially on our collaboration with AstraZeneca, and AstraZeneca may decide not to conduct any further development of AZD1446.

Our collaboration agreement with AstraZeneca involves a complex allocation of rights, provides for milestone payments to us if specified development, regulatory and first commercial sale milestone events are achieved and provides us with royalty-based revenue if AZD1446 or another product candidate in the collaboration is successfully commercialized. AstraZeneca has decision-making authority for most matters under the agreement, including, provided it meets its diligence obligations, whether to proceed with further development and potential commercialization of any particular product candidate in the collaboration and, if so, for what indication(s). Under the terms of the agreement, we are not permitted to conduct development of AZD1446 (or any other product candidate in the collaboration) independently or with another collaborator. Although we are currently in discussions with AstraZeneca regarding the next development steps for AZD1446, AstraZeneca may decide not to conduct any further development of AZD1446.

AstraZeneca has significant control and we have little control over the conduct and timing of development efforts for AZD1446. If AstraZeneca fails to devote sufficient financial and other resources to the development of AZD1446, the development and potential commercialization of AZD1446 would be delayed. This would result in a delay in potential milestone payments and, if regulatory approval to market and sell AZD1446 is obtained, royalties that we could receive on any future AZD1446 product sales.

AstraZeneca has the right to terminate our collaboration agreement in its entirety upon 90 days' notice. Termination of the agreement by AstraZeneca at any time could negatively impact our business. In particular, we would have to fund any further clinical development and commercialization of AZD1446 on our own, which could accelerate our need for additional capital, or alternatively seek another collaborator or licensee for clinical development and commercialization or abandon the development and commercialization of 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 collaboration agreement with AstraZeneca, we intend to selectively enter into alliances and collaborations, particularly for target indications for which a potential collaborator has unique expertise or that represent large primary care markets that must be served by large sales and marketing organizations. Our

ability to generate revenue from our alliances and collaborations will depend on our collaborators' abilities to establish the safety and efficacy of our product candidates, to obtain regulatory approvals and to achieve market acceptance. Strategic alliances and collaborations involving our product candidates, including our collaboration 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 nonclinical 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, either in their entirety or as to particular product candidates or programs, which may result in a need for a reallocation of internal funds or additional capital to pursue further development of the applicable product candidates. As examples, we previously had a collaboration agreement with AstraZeneca for the development and commercialization of TC-5214 in MDD and a product development and commercialization agreement with GlaxoSmithKline that have been terminated. In addition, AstraZeneca exercised its right to terminate TC-1734 and other compounds from our ongoing collaboration agreement. Some of these terminations caused us to reallocate internal resources.

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

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

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

Our drug development programs and potential commercialization of our product candidates will require substantial additional cash to fund expenses. Our strategy includes selectively seeking alliances and collaborations to assist us in furthering development and potential commercialization of some of our product candidates. We intend to do so particularly for target indications for which a potential collaborator has unique expertise or that involve large primary care markets that must be served by large sales and marketing organizations.

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

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

We have a supply agreement with Euticals S.p.A. (as successor to Poli Industria Chimica, S.p.A.) and Interchem Corporation for the pharmaceutical development and supply of the active ingredient form of TC-5214. The agreement with Euticals and Interchem provides for us to purchase our requirements for the active ingredient form of TC-5214 exclusively from Euticals through Interchem during the term of the agreement, subject to specified conditions. Because of the exclusive supply relationship, if Euticals 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 circumstances give us the right to change the manufacturer for the active ingredient form of TC-5214 and we 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*.," we would be dependent on Euticals to effect or facilitate a successful transfer of the manufacturing technology for TC-5214 to a replacement contract manufacturer. Following any future regulatory approval of TC-5214, such a technology transfer would require review and approval by the FDA or applicable 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 any future 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 depend on independent clinical investigators and, in many cases, contract research organizations and other third-party service providers to conduct the clinical trials of our product candidates and expect to continue to do so. We rely heavily on these parties for successful execution of our

clinical trials, but we do not control many aspects of their activities. Nonetheless, we are responsible for confirming that each of our clinical trials is conducted in accordance with its general investigational plan and protocol. Moreover, the FDA and foreign regulatory authorities require us to comply with regulations and guidelines, commonly referred to as good clinical practice, or GCP, for conducting and recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the trial participants are adequately protected. Our reliance on third parties that we do not control does not relieve us of these responsibilities and requirements.

Third parties may not complete activities on schedule or may not conduct our clinical trials in accordance with regulatory requirements or the respective trial plans and protocols. These risks may be heightened for clinical trials that we conduct outside of North America and Western Europe. In particular, we have previously conducted trials of multiple product candidates at sites in India and we are conducting our ongoing Phase 2b trial of TC-1734 in mild to moderate Alzheimer's disease at sites in Eastern Europe, as well as in the United States.

Language barriers and the limited experience of some clinical investigators in Eastern Europe or other countries in conducting clinical trials in accordance with standards set forth by the FDA and applicable regulatory authorities may increase the risk of non-compliance. The failure of third parties to carry out their obligations could impair the credibility or reliability of the data generated in clinical trials of our product candidates, require a trial to be repeated and increase the overall cost of a development program, delay or prevent the development, approval and commercialization of our product candidates or result in enforcement action against us.

If the performance of our contract manufacturers or any present or future collaborator of ours with manufacturing responsibility for a particular product candidate is substandard, our clinical trials and product introductions may be delayed or there may be a shortage of commercial supply.

Our product candidates require precise, high quality manufacturing. We no longer have 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 substantially all manufacturing responsibility for AZD1446 under our collaboration 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 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, based on its own business priorities, at a time that is costly or inconvenient for us; or
- breach or fail to perform as agreed under the applicable manufacturing agreement.

We expect to rely initially on a single contract manufacturer for any product candidate that we successfully bring to market. Changing any manufacturer that we engage for a particular product or product candidate may be difficult, as the number of potential manufacturers is limited and we will have to compete with third parties for access to those manufacturing facilities. cGMP manufacturing processes and procedures are described in an NDA or supplement that typically must be reviewed and approved by the FDA or foreign regulatory authorities and the facilities typically must pass inspection by the FDA or foreign regulatory authorities before such approval. Changing manufacturers may require re-validation of any new facility for cGMP compliance, which would likely be costly and time-consuming. We may not be able to engage replacement manufacturers on acceptable terms quickly or at all. In addition, contract manufacturers located in foreign countries may be subject to import limitations or bans. As a result, if any contract manufacturer 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 Administration (in the case of controlled substances) and corresponding state and foreign agencies to ensure strict compliance with cGMP, other government regulations and corresponding foreign standards. While we are ultimately responsible for ensuring the quality of any products manufactured by third party contractors and obligated to audit the performance of such third-party contractors, we do not have control over third-party manufacturers' compliance with these regulations and standards. Failure by us 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 our ability to obtain and maintain meaningful intellectual property protection for our product candidates, technology and know-how. We generally seek to protect our compounds and technologies by, among other methods, filing U.S. and foreign patent applications related to our proprietary technology that is important to the development of our business. We file patent applications directed to our product candidates in an effort to establish intellectual property positions regarding new chemical entities, pharmaceutical compositions, formulations 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 have in obtaining valid 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. 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. The Leahy-Smith America Invents Act was signed into U.S. law September 26, 2011, and includes significant changes to patent law. One of the most notable changes is the transition from a "first-to-invent" to a "first-inventor-to-file" patent system. This is effective for patent applications filed on or after March 16, 2013. 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 patent applications filed on or before March 16, 2013, or that we were or will be the first to file for protection of the inventions claimed in any of our U.S. patent applications filed after March 16, 2013 or in any of our issued foreign patents or pending foreign 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. We may enter into additional licenses in the future. Our existing licenses impose, and we expect future licenses will impose, various diligence, milestone payment, royalty, insurance and other obligations on us. If we fail to comply with these obligations, whether as a result of actions or inactions by us or by any potential future collaborator of ours to which we out-license patent rights that we have in-licensed from a third party, the licensor may have the right to terminate the license, in which event we may not be able to market any product that is covered by the licensed patents.

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 a different indication, we could be subject to competition arising from off-label use.

Although we generally seek the broadest patent protection available for our compounds, we may not be able to obtain patent protection for the actual composition of any particular compound and may be limited to protecting a new method of use for the compound or otherwise restricted in our ability to prevent others from exploiting the compound. If we are unable to obtain patent protection for the actual composition of any compound that we seek to develop and commercialize and must rely on method of use patent coverage, we would likely be unable to prevent others from manufacturing or marketing that compound for any use that is not protected by our patent rights. If a third party were to receive marketing approval of any compound for which we rely on method of use patent coverage for another use, physicians could nevertheless prescribe it for indications that are not described in the product's labeling or approved by the FDA or foreign regulatory authorities. Even if we have patent protection for the indication for which the product is prescribed, as a practical matter, we would have little recourse as a result of this off-label use. In that event, our revenue from the commercialization of the compound would likely be 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 of TC-5214, one of the enantiomers of mecamylamine hydrochloride. We do not have patent rights covering the composition of matter for mecamylamine hydrochloride. As a result, we may be limited in our ability to prevent others from exploiting mecamylamine hydrochloride, which could have a negative impact on the commercial potential of TC-5214. We believe another company, Cary Pharmaceuticals Inc., may be developing mecamylamine hydrochloride in a fixed dose combination with bupropion as a smoking cessation aid. In addition, racemic mecamylamine hydrochloride is the active ingredient in our approved product Inversine®, which we are no longer commercializing. We are aware of Abbreviated New Drug Application No. 20-4054 by Nexgen Pharma for mecamylamine hydrochloride, approved March 19, 2013, for the forms of hypertension for which Inversine® is approved. Physicians, therefore, could prescribe mecamylamine hydrocloride 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 hydrochloride as a treatment for overactive bladder despite differences in the biological properties between TC-5214 and mecamylamine hydrochloride. 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 could be materially and adversely affected.

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

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

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

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

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

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

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

Risks Related to Commercialization

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

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

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

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

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

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

We currently have limited sales, marketing and distribution experience and no internal sales or distribution capabilities. Although we intend to focus any future internal sales and marketing resources in areas where specialists heavily influence our target markets, such as neurology and urology, we also intend to seek to further augment our sales, marketing and distribution capabilities through arrangements with third parties, such as our collaboration with AstraZeneca. In particular, our strategy includes selectively entering into strategic alliances and collaborations with respect to product candidates for indications that require service by large sales and marketing organizations. There are risks involved with establishing our own sales force and marketing and distribution capabilities, as well as in entering into arrangements with third parties to perform these services. Developing our own sales force would be expensive and time-consuming and could delay any product launch. We may not be successful in entering into arrangements with third parties on terms that are favorable to us or at all. Also, we have little control over AstraZeneca's performance under our collaboration agreement and would have little control over the performance of potential future collaborators, any of which may fail to devote the necessary resources and attention to sell, market or distribute our products effectively. If we do not establish sales and distribution capabilities successfully, either on our own or in collaboration with third parties, we may not successfully commercialize our products.

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

Successful commercialization of any of our product candidates for which regulatory approval is obtained will depend in part on the extent to which coverage and adequate payment is available from government health programs, such as Medicare and Medicaid, private health insurers and other third-party payors. If we succeed in bringing a product candidate to the market, it may not be considered cost-effective and reimbursement may not be available or sufficient to allow us 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 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 government and third party payors will continue to look for ways to contain or reduce the cost of health care in ways that are likely to affect the business and financial condition of pharmaceutical companies. We cannot predict the impact of these efforts on the coverage of, or prices for, any of our product candidates if they are approved.

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 and development 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 and development, regulatory and drug commercialization than we have. Our competitors may:

- develop products that are more effective, safer, more tolerable, more convenient, less costly or otherwise more competitive than our product candidates;
- obtain FDA or foreign regulatory approval for their products more rapidly than we do;
- adapt more quickly to new technologies and scientific advances than we do;
- initiate or withstand substantial price competition more successfully than we do;
- 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 do;
- 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 AbbVie, Bristol-Myers Squibb, Novartis, EnVivo Pharmaceuticals, Upsher Smith, Psychogenics, Asmacure, Bionomics, Aniona, Savant HWP, Alpharmagen (a joint venture formed by CoMentis and Anvyl), Extab, SK Biopharmaceuticals and Neuroderm. We expect that we will face increased competition in the future if therapies that target NNRs are further validated and if companies initiate or expand programs focused on NNRs or otherwise pursue the development and commercialization of therapeutics for diseases and disorders that we target, whether independently or by alliance, collaboration or acquisition.

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

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

If approved, our product candidates will compete for a share of the existing market with numerous approved products. We believe that the primary competitive products for use in indications that we are currently targeting with our most advanced product candidates include:

- for overactive bladder, anticholinergics such as Vesicare from Astellas Pharma, Detrol LA from Pfizer/Almirall, Enablex from Warner Chilcott/Bayer, Toviaz from Pfizer, Sanctura XR from Allergan and Ditropan XL from Ortho-McNeil Pharma, beta3-adrenergic receptor agonists such as Mybretiq from Astellas Pharma, and the botulinum toxin Botox from Allergan; and
- for mild to moderate Alzheimer's disease, acetylcholinesterase inhibitors such as Aricept from Pfizer/Eisai, Razadyne from Johnson & Johnson and Exelon from Novartis; Aricept is also indicated for severe Alzheimer's disease and Namenda from Forest Laboratories, which acts by regulating the neurotransmitter glutamate, is indicated for moderate to severe Alzheimer's disease.

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

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

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

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

Physicians may prescribe drugs for uses that are not described in the product's labeling or for uses that differ from those tested in clinical studies and approved by the FDA or foreign regulatory authorities. Regulatory authorities generally do not regulate the behavior of physicians in their choice of treatments. Regulatory authorities do, however, restrict communications on the subject of off-label use. Companies cannot actively promote approved drugs for off-label uses but may in some jurisdictions and under specified conditions disseminate articles published in peer-reviewed journals that discuss off-label uses of approved products to physicians. To the extent allowed, we may in the future disseminate peer-reviewed articles on our products to physicians. If we undertake any promotional activities in the future for any product candidate for which we receive regulatory approval and our activities fail to comply with these regulations or guidelines, we may be subject to warnings from, or enforcement action by, these authorities.

Risks Related to Employees

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

Our performance depends substantially on the performance of our senior management team, including our President and Chief Executive Officer, Stephen A. Hill, who joined us in December 2012, as well as our other scientific, technical and managerial personnel. Our key personnel, including Dr. Hill, can terminate their employment with us at any time. The loss of the services of any of our senior management team or other key personnel may significantly delay or prevent the achievement of product development and other business objectives. In addition, we rely on consultants and advisors, including scientific and clinical 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 consulting or advisory contracts with other organizations or other commitments that could limit their availability or otherwise affect their ability to contribute to us.

Potential future growth of our business and replacement of any key personnel that may terminate their employment with us will depend on our ability to identify, recruit and retain the appropriate personnel. We may have difficulty attracting senior management, scientific and technical personnel as a result of previous workforce reductions and a perceived risk of future workforce reductions. We face intense competition for skilled executives and individuals with relevant scientific and technical expertise in our industry, and this competition is likely to continue. We may not be able to continue to attract and retain personnel with the advanced qualifications necessary for the success of our business.

Risks Related to Our Common Stock

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

The trading price of our common stock has historically been highly volatile, and 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:

- the scope, progress, duration, results and cost of clinical trials, as well as non-clinical studies and assessments, of our product candidates and programs;
- our inability, or the inability of any current or 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;
- whether we establish additional strategic alliances, collaborations or licensing or other comparable arrangements, or whether we pursue and complete any merger, acquisition or other significant corporate transaction, and, if we do, the associated terms in each case;
- the expiration or termination of our collaboration agreement with AstraZeneca or agreements with any potential future collaborator;
- whether and to what extent milestone events are achieved for AZD1446 under our collaboration agreement with AstraZeneca;
- the cost, timing and outcomes of regulatory approvals or other regulatory actions;
- the extent of our general and administrative expenses;
- general and industry-specific economic conditions that may affect the research and development expenditures of AstraZeneca or any potential future collaborator of ours; and
- general conditions in the pharmaceutical, biopharmaceutical or biotechnology industries or in the U.S. or global credit or financial markets.

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

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

Our current trading volumes are modest, and sales of a substantial number of shares of our common stock in the public market could cause the market price to decline. Such sales also might make it more difficult for us to sell equity securities in the future at a time and at a price that we deem appropriate. If there are more shares of our common stock offered for sale than buyers are willing to purchase, the market price of our common stock may decline to a market price at which buyers are willing to purchase the offered shares and sellers remain

willing to sell the shares. The number of shares of our common stock owned by our stockholders and available for sale in the public market is limited only to the extent provided under applicable federal securities laws. In addition, we may, in the future, issue additional shares of our common stock as compensation to our employees, directors or consultants, in connection with strategic alliances, collaborations, acquisitions or other transactions or to raise capital. Accordingly, sales of a substantial number of shares of our common stock in the public market could occur at any time.

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

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

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

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

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We lease approximately 18,300 square feet of office space in the building located at 100 North Main Street in Winston-Salem, North Carolina pursuant to a sublease. The term of our sublease expires December 30, 2015. The monthly payment under our sublease is approximately $23,000, subject to an annual escalation of approximately 3% during the term. We also lease approximately 4,100 square feet of storage space in the same building pursuant to a separate sublease. We believe our leased space is suitable for its intended purpose.

Item 3. Legal Proceedings.

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

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

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

Market Information

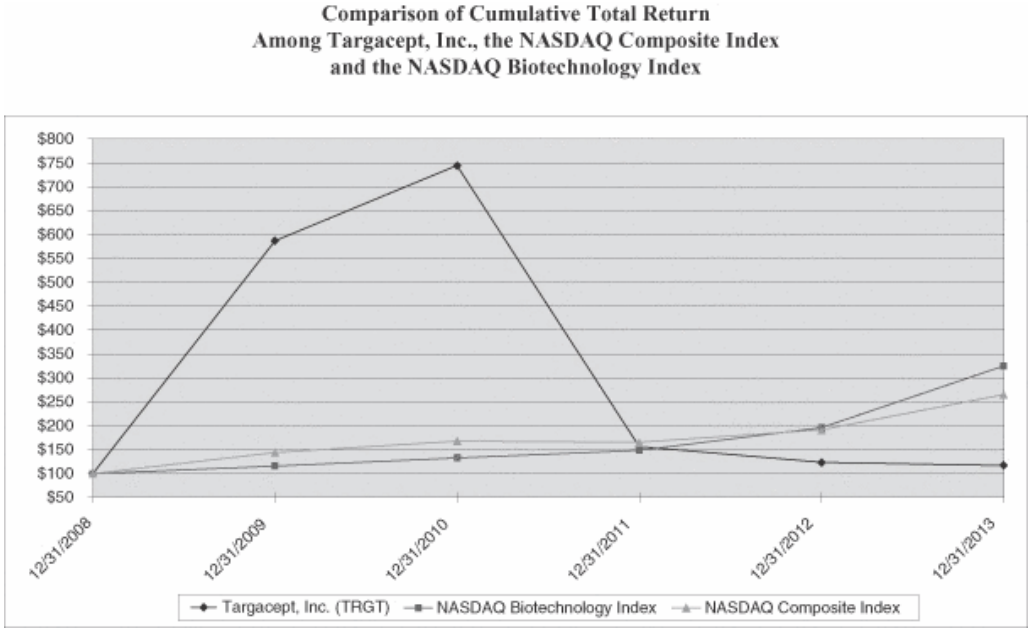
Our common stock currently trades on the NASDAQ Global Select Market under the symbol "TRGT." The following table sets forth, for the periods indicated, the high and low sales prices for our common stock:

	Common Stock	
	High	*Low*
2012:		
First Quarter	$7.70	$4.90
Second Quarter	$5.20	$4.04
Third Quarter	$5.17	$4.15
Fourth Quarter	$4.92	$3.85
2013:		
First Quarter	$4.83	$4.19
Second Quarter	$5.77	$4.06
Third Quarter	$5.84	$4.28
Fourth Quarter	$6.11	$3.75

Comparative Stock Performance Graph

The following graph and related information shall not be deemed "soliciting material" or to be "filed" with the SEC or subject to Regulation 14A or 14C, other than as provided in Item 201 of Regulation S-K, or to the liabilities of Section 18 of the Exchange Act, nor shall such information be incorporated by reference into any future filing under the Securities Act or the Exchange Act, except to the extent that we specifically incorporate it by reference into such a filing.

The following graph compares the cumulative total stockholder return for our common stock with the cumulative total stockholder return of the NASDAQ Composite Index and the NASDAQ Biotechnology Index. The comparison assumes the investment of $100.00 on December 31, 2008 in each of our common stock, the NASDAQ Composite Index and the NASDAQ Biotechnology Index and the reinvestment of any dividends. We have not paid any dividends on our common stock and do not include dividends in the representation of our performance. The performance shown for any prior period does not predict the performance to be expected for any future period.



Targacept, Inc.	100	587	744	156	123	117
NASDAQ Biotechnology Index	100	116	133	149	196	325
NASDAQ Composite Index	100	144	168	165	191	265

Stockholders

As of February 28, 2014, there were approximately 45 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 March 3, 2014, 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 3,455.

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.

Securities Authorized for Issuance Under Equity Compensation Plans

The response to this item is incorporated by reference from the discussion responsive thereto under the caption "Stock-Based Incentive Plans" in the notes to Financial Statements.

Calculation of Aggregate Market Value of Non-Affiliate Shares

For purposes of calculating the aggregate market value of shares of our common stock held by non-affiliates as set forth on the cover page of this annual report, we have assumed that all outstanding shares as of the determination date were held by non-affiliates, except for shares held by our executive officers, directors and their affiliated entities. In particular, we have assumed that any stockholder that held 10% or more of our outstanding common stock as of the determination date and is not affiliated with a director was a non-affiliate and expect that we would also make that assumption in the future unless there exists facts and circumstances that indicate that the 10% or greater stockholder exercises control over us. This assumption is not intended to constitute an admission that all executive officers and directors, and any 10% or greater stockholder treated as an affiliate for this purpose, are, in fact, our affiliates or that there are no 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 comprehensive income data for the years ended December 31, 2013, 2012 and 2011 and the balance sheet data as of December 31, 2013 and 2012 from our audited financial statements included in this annual report. We derived the statements of comprehensive income data for the years ended December 31, 2010 and 2009 and the balance sheet data as of December 31, 2011, 2010 and 2009 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,				
	2013	2012	2011	2010	2009
	(in thousands, except share and per share data)				
Statement of Operations Data:					
Net operating revenues	$ 3,629	$ 57,860	$ 97,637	$ 85,713	$ 25,062
Operating expenses:					
Research and development	38,840	49,087	95,215	64,546	40,179
General and administrative	12,005	13,193	12,167	8,052	8,167
Reduction in force	—	3,718	—	—	—
License fees and royalties	—	—	—	—	16,350
Cost of product sales	—	—	—	—	691
Total operating expenses	50,845	65,998	107,382	72,598	65,387
(Loss) income from operations	(47,216)	(8,138)	(9,745)	13,115	(40,325)
Interest income	784	1,070	1,348	1,463	1,050
(Loss) gain on sale of property and equipment	(213)	55	—	—	—
Interest expense	(53)	(86)	(132)	(153)	(217)
(Loss) income before income taxes	(46,698)	(7,099)	(8,529)	14,425	(39,492)
Income tax (expense) benefit	(7)	101	—	(3,526)	88
Net (loss) income	$ (46,705)	$ (6,998)	$ (8,529)	$ 10,899	$ (39,404)
Basic net (loss) income per share	$ (1.39)	$ (0.21)	$ (0.27)	$ 0.38	$ (1.54)
Diluted net (loss) income per share	$ (1.39)	$ (0.21)	$ (0.27)	$ 0.36	$ (1.54)
Weighted average common shares outstanding—basic	33,640,323	33,476,316	31,637,283	28,543,408	25,636,419
Weighted average common shares outstanding—diluted	33,640,323	33,476,316	31,637,283	30,150,324	25,636,419

	As of December 31,				
	2013	2012	2011	2010	2009
	(in thousands)				
Balance Sheet Data:					
Cash, cash equivalents and investments	$ 143,777	$ 184,927	$ 249,270	$ 252,509	$ 111,066
Working capital	82,627	116,394	119,606	119,422	213,269
Total assets	145,873	189,579	258,126	262,787	319,379
Long-term debt, net of current portion	283	1,136	1,986	1,349	1,966
Accumulated deficit	(280,633)	(233,928)	(226,930)	(218,401)	(229,300)
Total stockholders' equity	134,611	175,915	174,288	91,847	68,991

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

You should read the following discussion and analysis of our financial condition and results of operations together with our financial statements and the related notes included in this annual report. In addition to historical information, the following discussion contains forward-looking statements that involve risks, uncertainties and assumptions. Our actual results, performance or experience could differ materially from what is indicated by any forward-looking statement due to various important factors, risks and uncertainties, including, but not limited to, those set forth under "Cautionary Note Regarding Forward-Looking Statements," which precedes Part I of this annual report, and under "Risk Factors" in Item 1A of Part I of this annual report.

Overview

Background

We are a biopharmaceutical company engaged in the development of novel NNR Therapeutics to treat patients suffering from serious nervous system and gastrointestinal/ genitourinary diseases and disorders. 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-1734, TC-6499, AZD1446 (TC-6683), TC-5619 and TC-6987 and they are discussed under the caption "Business" in Item 1 of Part I of this annual report.

We have an ongoing collaboration agreement with AstraZeneca focused on compounds that act on the α4ß2 NNR, including AZD1446. Under our ongoing collaboration agreement with AstraZeneca:

- AstraZeneca has an exclusive license to AZD1446 and earlier-stage compounds that arose from the preclinical research collaboration conducted under the agreement described below;
- AstraZeneca is responsible for substantially all current and future development costs for AZD1446 and each other compound arising from the preclinical research collaboration described below that it elects to advance; 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 α4ß2 NNR as treatments for conditions characterized by cognitive impairment, under which AstraZeneca paid us research fees, based on a reimbursement rate specified under the agreement, for our research services.

Our ongoing collaboration agreement with AstraZeneca can be terminated by AstraZeneca for an uncured material breach by us or upon 90 days' notice given at any time.

Under a second collaboration agreement with AstraZeneca, which we refer to in this annual report as our "MDD agreement with AstraZeneca," we had been co-developing TC-5214 as a treatment for major depressive disorder, or MDD. Upon entering into the agreement, we received a $200.0 million upfront payment. Thereafter, AstraZeneca was responsible for 80%, and we were responsible for 20%, of the cost of the completed clinical program for TC-5214 in MDD, except that AstraZeneca was responsible for 100% of development costs that were required only for countries outside the United States and the European Union. Following completion of a Phase 3 clinical program for TC-5214 conducted under the agreement, we and AstraZeneca announced that a regulatory submission for TC-5214 as an adjunct therapy for MDD would not be pursued and the "switch" monotherapy trial was discontinued. AstraZeneca subsequently terminated the agreement, effective in May 2012. As a result of the termination, all rights and licenses for TC-5214 that we granted under the agreement to AstraZeneca terminated and reverted to us.

Since our inception, we have had limited revenue from product sales and have funded our operations principally through public and private offerings of equity securities, payments under collaboration and alliance agreements, grants and equipment financing. We have historically devoted substantially all of our resources to

the discovery and development of our product candidates and technologies, including the design, conduct and management of nonclinical and clinical studies and related manufacturing, regulatory and clinical affairs, as well as intellectual property prosecution.

In the second quarter of 2012, we completed a reduction in force as part of a plan to focus our resources on our more advanced programs. In October 2012, we announced a second reduction in force, as well as our plan to close our laboratory operations. We completed the second reduction in force and the laboratory closings in December 2012 and are no longer devoting resources to drug discovery or nonclinical research activities. We sold virtually all of our laboratory equipment after we closed our laboratories.

Except for a small number of periods in which we generated net income due primarily to the recognition into revenue of amounts received under collaboration agreements, we have not been profitable. As of December 31, 2013, we had an accumulated deficit of $280.6 million. We expect that we will incur losses in future periods as our product candidates advance into later-stage development and as we progress our programs and invest in additional product opportunities. Drug development, including clinical trials in particular, is time-consuming, expensive and may never yield a product that will generate revenue.

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

Revenue

In January 2010, we received the $200.0 million upfront payment under our MDD agreement with AstraZeneca, which we recorded as deferred revenue and began recognizing into revenue on a straight-line basis over the estimated period of our substantive performance obligations under the agreement.

In the first quarter of 2012, we and AstraZeneca announced that, based on the totality of the results of the Phase 3 program, a regulatory submission` for TC-5214 as an adjunct therapy for MDD would not be pursued and the "switch" monotherapy trial was discontinued. These events resulted in a change in the estimated period of our substantive performance obligations under our MDD agreement with AstraZeneca. Accordingly, we revised the revenue recognition period for the upfront payment and began recognizing the portion of the upfront payment not yet recognized into revenue on a straight-line basis over the remainder of the revised period. We had recognized the full amount of the upfront payment into revenue as of June 30, 2012.

Pursuant to a September 2010 amendment to our ongoing collaboration agreement with AstraZeneca related to a clinical trial of TC-1734 in mild to moderate Alzheimer's disease, we received a $500,000 payment in the fourth quarter of 2010 and cumulative payments of $5.5 million in the second half of 2011. We recorded all of these payments as deferred revenue and began recognizing them into revenue on a straight-line basis over the estimated period of our obligations with respect to the study. As a result of AstraZeneca's exercise of its right to terminate TC-1734 from the collaboration in March 2013, we recognized the remaining unrecognized deferred amount of $3.5 million into revenue during the first quarter of 2013.

As of December 31, 2013, we had received $61.6 million in aggregate upfront fees and milestone payments under our ongoing collaboration agreement with AstraZeneca and recognized an additional $26.5 million in collaboration research and development revenue for research services that we provided in the preclinical research collaboration conducted under that agreement. We immediately recognized an aggregate of $32.6 million of the amounts received under the agreement for achievement of milestone events, because each event met the conditions required for immediate recognition under our revenue recognition policy. We deferred recognition of an aggregate of $29.0 million received under the agreement and have fully recognized these deferred amounts into revenue over the respective periods discussed in Note 12 to our audited financial statements included in this annual report.

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

From time to time we seek and are awarded grants or perform work under grants awarded to third-party collaborators from which we derive revenue. During the third quarter of 2011, we were awarded a third grant from the Michael J. Fox Foundation for Parkinson's Research, or MJFF. Based on the terms of the grant, we received $250,000 upon inception of the grant term and an additional $250,000 in March 2012. In addition, we are a 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. Based on the terms of this arrangement, we received $191,000 in May 2012. 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 drug discovery and development programs. We record research and development expenses as they are incurred. Research and development expenses represented approximately 76%, 74% and 89% of our total operating expenses for the years ended December 31, 2013, 2012, and 2011, respectively. For 2012, reduction in force charges of $3.7 million, which are not included in research and development expenses, represented 6% of our total operating expenses. There were no reduction in force charges for 2013 or 2011.

Research and development expenses include costs associated with:

- clinical trials, including fees paid to contract research organizations to monitor and oversee some of our trials;
- the employment of personnel involved in clinical development, drug discovery, and research activities;
- research and development facilities, equipment and supplies;
- the screening, identification and optimization of product candidates;
- formulation and chemical development;
- production of clinical trial materials, including fees paid to contract manufacturers;
- nonclinical 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.

We utilize our research and development personnel and infrastructure resources across several programs, and many of our costs historically have not been specifically attributable to a single program. Accordingly, we cannot state precisely our total costs incurred on a program-by-program basis.

We have not received FDA or foreign regulatory marketing approval for any of our product candidates. Our current and future expenditures on development programs are subject to numerous uncertainties in timing and cost to completion. Our compounds are tested in numerous preclinical studies for safety, toxicology and efficacy. We then conduct 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 obtain 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 may take several years or more, and the length of time generally varies substantially according to the type, complexity, novelty and intended use of a product candidate. The cost of clinical trials for a particular product candidate may vary significantly as a result of a variety of factors, including:

- the number of subjects who participate in the trials;
- the number and locations of sites included in the trials;
- the length of time required to enroll trial subjects;
- the therapeutic areas being investigated;
- the duration of the trials and subject follow-up;
- the costs of producing supplies of the product candidate needed for trials and regulatory submissions;
- the efficacy and safety profile of the product candidate; and
- the costs and timing of, and the ability to secure, regulatory approvals.

In addition, our strategy includes entering into alliances and collaborations with third parties to participate in the development and commercialization of some of our product candidates. Where a third party has responsibility for or authority over any or all of the non-clinical or clinical development of a particular product candidate, the estimated completion date may be largely under control of that third party and not under our control. We cannot forecast with any degree of certainty whether any of our product candidates will be subject to future alliances or collaborations or how any such arrangement would affect our development plans or capital requirements. Because of this uncertainty, and because of the numerous uncertainties related to clinical trials and drug development generally, we are unable to determine the duration and completion costs of our development programs or whether or when we will generate revenue from the commercialization and sale of any of our product candidates.

General and Administrative Expenses

General and administrative expenses consist principally of salaries and other related costs for personnel in executive, finance, business development, legal, information technology 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.

Income Taxes

We have incurred cumulative net operating losses through December 31, 2013 and have not paid federal, state or foreign income taxes for any period since our inception. The application of U.S. generally accepted accounting principles, or GAAP, may for some periods result in non-cash income tax expense or benefit being

reflected in our Statement of Comprehensive Income (Loss). For the year ended December 31, 2012, we recognized $101,000 of income tax benefit as a result of the application of accounting guidance for intraperiod tax allocation, under which we are required to consider all items (including items recorded in other comprehensive income) in determining the amount of tax benefit that should be allocated to net loss. The non-cash income tax benefit for 2012 was offset in full by income tax expense recorded in other comprehensive income. For the tax year ended December 31, 2011, we did not recognize any income tax expense or benefit.

As of December 31, 2013, we had net operating loss carryforwards of $233.2 million for federal income tax purposes and $219.8 million for state income tax purposes, and we had research and development income tax credit carryforwards of $12.8 million for federal income tax purposes and $587,000 for state income tax purposes as of December 31, 2013. The federal net operating loss carryforwards begin to expire in 2024. The state net operating loss carryforwards begin to expire in 2019. The federal and state research and development tax credits begin to expire in 2021. As a result of various factors, including the subjectivity of measurements used in the calculation of particular tax positions taken or that may in the future be taken in our tax returns, it is uncertain whether or to what extent we will be eligible to use the tax credits.

Utilization of the net operating loss carryforwards and credits may be subject to a substantial annual limitation due to ownership change limitations provided by Section 382 of the Internal Revenue Code of 1986, as amended, and similar state provisions. When an ownership change, as defined by Section 382, occurs, an annual limitation is imposed on a company's use of net operating loss and credit carryforwards attributable to periods before the change. A series of stock issuances by us gave rise to such an ownership change in December 2004. 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 tax credits discussed above until it is more likely than not that we will realize any benefit from them.

Fair Value

The carrying amounts of our cash and cash equivalents, investments in marketable securities, accounts receivable, accounts payable and accrued expenses are considered to be representative of their respective fair values due to their short-term natures and, in the case of short-term investments, their market interest rates. Likewise, the carrying amounts of our long-term debts are considered to be representative of their fair value due to their market interest rates. Cash that we do not expect to use to fund our short-term liquidity requirements is invested in corporate debt securities and municipal bonds rated at least A quality or equivalent, U.S. Treasury notes and bonds, U.S. and state government agency-backed certificates and certificates of deposit. Our investments in marketable securities, which include marketable securities classified on our balance sheet as cash equivalents, are recorded at quoted market prices or observable market inputs and totaled $89.3 million at December 31, 2013.

Critical Accounting Policies and Estimates

Our management's discussion and analysis of financial condition and results of operations is 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, 2013 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 ongoing collaboration agreement with AstraZeneca and, if we enter into potential additional strategic alliances or collaborations, those additional strategic alliances or collaborations over at least the next several years.

Our collaboration and alliance agreements contain multiple elements, including: an upfront fee, which may include an initial payment upon commencement of the contractual relationship, payment representing a common stock purchase premium or payment to secure a right for a future license; research fees for ongoing research and development; payments associated with the achievement of discovery, development, regulatory and commercial milestone events; and royalties based on specified percentages of any net product sales. In determining the accounting for collaboration and alliance agreements, we first determine whether the agreement involves a single unit of accounting or separate units of accounting for revenue recognition purposes by evaluating each deliverable under the terms of the agreement. If a deliverable has value on a standalone basis, we treat the deliverable as a separate unit of accounting. We determine how to allocate amounts received under the agreement among the separate units, based on the respective selling price of each unit, and we determine the revenue recognition applicable to each unit. If an agreement does not have multiple deliverables that have standalone value, we consider the agreement to have one unit of accounting and we determine the revenue recognition applicable to the entire agreement.

We defer recognition of non-refundable upfront fees and recognize them into revenue on a straight-line basis over the estimated period of our substantive performance obligations. If we do not have substantive performance obligations, we recognize non-refundable upfront fees into revenue through the date the deliverable is satisfied. The period over which we recognize the revenue may be adjusted from time to time to take into account any delays or acceleration in the development of the applicable product candidate or any extension or shortening of the applicable performance period. Any such delay or acceleration in the development of a product candidate, or extension or shortening of a performance period, would result in decreases or increases to the recognition of deferred revenue from period to period. As of December 31, 2013, all amounts that we have recorded as deferred revenue are non-refundable.

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

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

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

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

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

Accrued Expenses

In the normal course of our business, we contract with research institutions and contract research organizations that conduct or manage clinical trials or other research and development activities on our behalf and with contract manufacturers that produce drug substance or clinical trial materials 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 clinical trial materials, 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. In the event a modification is made to a stock option after the grant date, we record additional stock-based compensation expense equal to the incremental fair value of the stock option immediately subsequent to the modification as compared to the fair value of the stock option immediately preceding the modification. During 2012, we modified some outstanding stock options held by executive and non-executive employees who departed Targacept to partially accelerate vesting and/or extend the permitted period for exercise. These modifications resulted in incremental compensation cost for the year ended December 31, 2012 of $1.4 million. We recorded stock-based compensation expense related to stock options granted to employees and directors of $5.2 million for

the year ended December 31, 2013, $7.8 million for the year ended December 31, 2012 (inclusive of expense resulting from stock option modifications) and $8.5 million for the year ended December 31, 2011. As of December 31, 2013, we had $5.5 million in total unrecognized compensation cost related to non-vested stock-based compensation arrangements, which we expect to record over a weighted average period of 2.83 years.

Results of Operations

Years ended December 31, 2013 and December 31, 2012

Net Operating Revenues

	Year ended December 31,		
	2013	2012	Change
	(in thousands)		
Operating revenues:			
License fees and milestones from collaborations	$3,536	$57,420	$(53,884)
Grant revenue	93	440	(347)
Net operating revenues	$3,629	$57,860	$(54,231)

Net operating revenues for the year ended December 31, 2013 decreased by $54.2 million as compared to the year ended December 31, 2012. The lower net operating revenues for 2013 were primarily attributable to a decrease of $53.9 million in license fees and milestones from collaborations. The lower license fees and milestones from collaborations principally resulted from the recognition of deferred revenue during 2012 of the remaining unrecognized portion of the upfront payment received under our MDD agreement with AstraZeneca, totaling $54.5 million, partially offset by $589,000 in increased recognition into revenue for 2013 of payments related to TC-1734 received under our ongoing collaboration agreement with AstraZeneca. We recognized into revenue during 2013 the remaining unrecognized portion of the payment related to TC-1734 received under our ongoing collaboration agreement with AstraZeneca, totaling $3.5 million.

We have recognized into revenue all amounts that had been previously deferred and, therefore, in future periods, will not recognize any additional revenue related to payments received under our current or previous collaboration agreements. We are eligible to receive additional milestone payments under our ongoing collaboration agreement with AstraZeneca. The amount of milestone payments will depend on whether AstraZeneca progresses the clinical development of AZD1446, and, if so, whether and when we achieve development, regulatory and commercial milestone events that are inherently uncertain. We expect that the amount of our milestone-based revenue, if any, will continue to vary from period to period.

Research and Development Expenses

	Year ended December 31,		
	2013	2012	Change
	(in thousands)		
Research and development expenses	$38,840	$49,087	$(10,247)

Research and development expenses for the year ended December 31, 2013 decreased by $10.2 million as compared to the year ended December 31, 2012. The lower research and development expenses for 2013 were principally attributable to decreases of:

- $14.9 million in other research and development-related operating costs, including infrastructure costs and stock-based compensation and other compensation-related expenses for research and development personnel, to $10.7 million for 2013, from $25.6 million for 2012; this decrease resulted primarily from the workforce reductions completed in the second and fourth quarters of 2012 discussed above;

- $2.2 million in costs incurred for the Phase 3 development program for TC-5214 as a treatment for MDD which completed in 2012; and
- $1.7 million in costs incurred for third-party research and development services in connection with nonclinical programs.

These decreases were partially offset by an increase of $8.6 million in costs incurred for third-party services associated with our clinical-stage product candidates (excluding costs for the completed program in MDD discussed above) to $28.1 million for 2013, from $19.5 million for 2012. This increase was principally due to costs related to the initiation and conduct of our Phase 2b study of TC-5214 in overactive bladder.

The costs that we incurred for the years ended December 31, 2013 and 2012 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,		
	2013	2012	Change
	(in thousands)		
TC-5214 overactive bladder	$14,235	$ 1,440	12,795
TC-5619	10,250	12,662	(2,412)
AZD3480	3,099	3,762	(663)
TC-6499	470	—	470
TC-6987	21	1,655	(1,634)
TC-5214 major depressive disorder	—	2,175	(2,175)
AZD1446	—	—	—

Based on our current clinical program related commitments, we expect our research and development expenses for the year ending December 31, 2014 to decrease as compared to 2013, principally as a result of our completion in December 2013 of a Phase 2b clinical trial of TC-5619 as a treatment for schizophrenia.

General and Administrative Expenses

	Year ended December 31,		
	2013	2012	Change
	(in thousands)		
General and administrative expenses	$12,005	$13,193	$(1,188)

General and administrative expenses for the year ended December 31, 2013 decreased by $1.2 million as compared to the year ended December 31, 2012. The lower general and administrative expenses were primarily attributable to a decrease of $825,000 in stock-based compensation expense, salary and other compensation-related expenses for general and administrative personnel, primarily due to $1.8 million in non-recurring severance and stock-based compensation expenses recorded for 2012; and partially offset by $573,000 in non-cash stock-based compensation charges resulting from the partial accelerated vesting of, and extended exercise periods for, some outstanding stock options held by two former executive officers who departed Targacept during 2013 and $306,000 in severance and other charges, resulting from the departure of one of the former executive officers.

Reductions in Force

	Year ended December 31,		
	2013	2012	Change
	(in thousands)		
Reductions in force	$—	$3,718	$(3,718)

As a result of the two reductions in force we completed during 2012 discussed above, we recorded as expense and paid $3.7 million in severance and other charges in 2012.

Years ended December 31, 2012 and December 31, 2011

Net Operating Revenues

	Year ended December 31,		
	2012	2011	Change
	(in thousands)		
Operating revenues:			
License fees and milestones from collaborations	$57,420	$96,979	$(39,559)
Grant revenue	440	658	(218)
Net operating revenues	$57,860	$97,637	$(39,777)

Net operating revenues for the year ended December 31, 2012 decreased by $39.8 million as compared to the year ended December 31, 2011. The lower net operating revenues for 2012 were primarily attributable to a decrease of $39.6 million in license fees and milestones from collaborations. The lower license fees and milestones from collaborations principally resulted from decreases in recognition of deferred revenue of:

- $18.4 million related to our now concluded strategic alliance with GlaxoSmithKline, as all remaining deferred revenue was recognized in the 2011 period in connection with termination of the alliance;
- $18.1 million associated with our now concluded MDD agreement with AstraZeneca due to the completion of our performance obligations in mid-2012; and
- $4.8 million related to the development of TC-5619 under our ongoing collaboration agreement with AstraZeneca, as the TC-5619-related payments became fully recognized in the second quarter of 2011.

These decreases were partially offset by an increase of $1.8 million in recognition of deferred revenue related to the development of TC-1734 under our ongoing collaboration agreement with AstraZeneca.

Research and Development Expenses

	Year ended December 31,		
	2012	2011	Change
	(in thousands)		
Research and development expenses	$49,087	$95,215	$(46,128)

Research and development expenses for the year ended December 31, 2012 decreased by $46.1 million as compared to the year ended December 31, 2011. The lower research and development expenses for 2012 were principally attributable to decreases of:

- $29.8 million in costs incurred related to our MDD agreement with AstraZeneca, to $2.2 million for 2012, from $32.0 million for 2011, as the development program conducted under the agreement wound down to completion;
- $7.5 million in other research and development-related operating costs, including infrastructure costs and stock-based compensation and other compensation-related expenses for research and development personnel, to $25.6 million for 2012, from $33.1 million for 2011; this decrease resulted primarily from the workforce reductions completed in the second and fourth quarters of 2012 discussed above;
- $5.4 million in costs incurred for third-party research and development services in connection with nonclinical programs to $1.7 million for 2012, from $7.1 million for 2011; and

- $3.4 million in costs incurred for third-party services associated with our clinical-stage product candidates (excluding costs for the completed program in major depressive disorder) to $19.5 million for 2012, from $22.9 million for 2011; this decrease, which was principally due to the completion of two exploratory clinical trials of TC-6987 during the first quarter of 2012, was partially offset by an increased level of activities for our Phase 2 clinical trials of TC-5619 ongoing during 2012 and costs related to our planned Phase 2b study of TC-5214 as a treatment for overactive bladder.

The costs that we incurred for the years ended December 31, 2012 and 2011 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,		
	2012	2011	Change
	(in thousands)		
TC-5619	$12,662	$ 9,847	2,815
AZD3480	3,762	4,110	(348)
TC-6987	1,655	8,858	(7,203)
TC-5214 overactive bladder	1,440	—	1,440
TC-5214 major depressive disorder	2,175	32,046	(29,871)
TC-6499	—	96	(96)
AZD1446	—	—	—

General and Administrative Expenses

	Year ended December 31,		
	2012	2011	Change
	(in thousands)		
General and administrative expenses	$13,193	$12,167	$1,026

General and administrative expenses for the year ended December 31, 2012 increased by $1.0 million as compared to the year ended December 31, 2011. The higher general and administrative expenses were principally attributable to $1.9 million in severance and stock-based compensation expense, including $1.3 million of non-cash charges, resulting from severance payable to our former chief executive officer, who departed Targacept in May 2012, and from the partial accelerated vesting of, and/or extended permitted exercise periods for, some outstanding stock options held by our former chief executive officer and two other executive officers who departed Targacept in the first half of 2012. These severance and stock-based compensation charges were partially offset by a decrease of $505,000 in patent-related charges. Exclusive of the increased stock-based compensation expense and decreased patent-related charges, general and administrative expenses decreased by $372,000 for 2012 as compared to 2011, primarily as a result of the two 2012 workforce reductions.

Reductions in Force

	Year ended December 31,		
	2012	2011	Change
	(in thousands)		
Reductions in force	$3,718	$—	$3,718

As a result of the two reductions in force we completed during 2012 discussed above, we recorded as expense and paid $3.7 million in severance and other charges.

Liquidity and Capital Resources

Sources of Liquidity

We have historically financed our operations and internal growth primarily through public and private offerings of our securities, payments received under collaboration and alliance agreements, including upfront fees, payments for research and development services and payments upon achievement of milestone events, grants and equipment financing.

Our cash, cash equivalents and investments in marketable securities were $143.8 million as of December 31, 2013 and $184.9 million as of December 31, 2012. As of December 31, 2013, we had $53.2 million of cash in bank depository accounts and institutional money market funds at Branch Banking and Trust Company, PNC Bank and Wells Fargo & Company. Substantially all of our remaining cash, cash equivalents and investments were invested as of December 31, 2013 in corporate debt securities and municipal bonds rated at lease A quality or equivalent, U.S. Treasury notes and bonds, U.S. and state government agency-backed securities and a certificate of deposit.

Stock Offerings

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

In November 2013, we filed a Form S-3 with the Securities and Exchange Commission which became effective December 11, 2013. Pursuant to this Form S-3, we may sell shares of common stock having an aggregate offering price of up to $200.0 million. Under an At-the-Market Issuance Sales Agreement, or ATM, with MLV & Co., LLC, filed concurrently with the Form S-3, we may offer and sell shares of common stock having an aggregate offering price of up to $40.0 million.

Strategic Alliances and Collaborations

As of December 31, 2013, we had received $61.6 million in aggregate upfront fees and milestone payments under our ongoing collaboration agreement with AstraZeneca and an additional $26.5 million in collaboration research and development revenue for research services that we provided in the preclinical research collaboration conducted under the agreement. Most recently, in September and December 2011, under an amendment to the agreement, we received cumulative payments of $5.5 million in connection with events associated with our ongoing Phase 2b study of TC-1734 as a treatment for mild to moderate Alzheimer's disease.

Since inception, we have received cumulative payments of $2.6 million upon achievement of milestone events under the agreement related to the development of AZD1446 and other product candidates arising under the preclinical research collaboration conducted under the agreement.

In addition, we are eligible under the agreement to receive contingent payments of up to $57.0 million, if development, regulatory and first commercial sale milestone events for AZD1446 are achieved for a specified indication under consideration for development and sales-related milestone events are then achieved for AZD1446, and up to $73.0 million, if development, regulatory and first commercial sale milestones are achieved for AZD1446 for any other indication. We are also eligible to receive stepped royalties on any future AZD1446 product sales for any indication. If AZD1446 is subsequently developed under the agreement for multiple indications, we would also be eligible to receive contingent payments of up to $35.0 million for each such

indication, if development, regulatory, first commercial sale and first detail milestone events are achieved. The likelihood that we will achieve any particular milestone event in any particular period is uncertain, and we may not ever achieve future milestone events with respect to AZD1446. We do not expect our ongoing collaboration agreement with AstraZeneca to be a significant source of future funds and we are not relying on the agreement as a source for any future funds.

In December 2009, we entered into our MDD agreement with AstraZeneca. We received a $200.0 million upfront payment from AstraZeneca in January 2010. Our MDD agreement with AstraZeneca was terminated effective in May 2012 and is no longer a potential source of future funds.

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

Loan Financing

In July 2010, we entered into a loan agreement with Branch Banking and Trust Company (the "Bank") that provided aggregate borrowing capacity of $4.0 million available to us at any time on or prior to June 30, 2011 to fund the purchase of equipment, furnishings, software and other fixed assets. In September 2010, we borrowed $1.2 million under the loan facility at a fixed interest rate of 3.4% per annum. We were obligated only to pay interest on the September 2010 borrowing through the remainder of 2010, and it is repayable in equal monthly installments of $28,000 that began January 1, 2011 and continue through the maturity date of December 1, 2014. In June 2011, we borrowed $2.1 million under the loan facility at a fixed interest rate of 3.471% per annum. The June 2011 borrowing is repayable in equal monthly installments of $48,000 that began July 1, 2011 and continue through the maturity date of June 1, 2015. Pursuant to the loan agreement, we granted a first priority security interest in favor of the Bank in the assets acquired with the proceeds of the loan facility. As of December 31, 2013, the outstanding principal balance under the loan facility was $1.1 million and there is no additional borrowing capacity remaining available to us.

In March 2008, we entered into a loan agreement with the Bank that provided borrowing capacity of $5.3 million to fund the purchase of equipment, furnishings, software and other fixed assets and enabled the refinancing of a previous loan facility that we had with R.J. Reynolds Tobacco Holdings, Inc. We borrowed $4.8 million upon entering into the loan agreement and borrowed the remaining $489,000 in September 2008. Pursuant to the loan agreement, we granted a first priority security interest in favor of the Bank in the assets acquired with the proceeds of the loan facility. The March 2008 loan bore interest at a fixed rate of 5.231% per annum and was repayable in equal monthly installments of $112,000 beginning April 1, 2008 and continuing through the maturity date of March 1, 2012 when it was repaid in full. The September 2008 loan bore interest at a fixed rate of 6.131% per annum and was repayable in equal monthly installments of $11,000 beginning October 1, 2008 and continuing through the maturity date of September 1, 2012 when it was repaid in full. There is no additional borrowing capacity remaining available to us under the loan agreement.

Cash Flows

	Year ended December 31,		
	2013	2012	Change
		(in thousands)	
Net cash used in operating activities	$(40,612)	$(64,239)	$ 23,627
Net cash provided by investing activities	13,409	39,822	(26,413)
Net cash used in financing activities	(552)	(626)	74
Net decrease in cash and cash equivalents	$(27,755)	$(25,043)	

	Year ended December 31,		
	2012	2011	Change
		(in thousands)	
Net cash used in operating activities	$(64,239)	$(83,718)	$ 19,479
Net cash provided by (used in) investing activities	39,822	(57,667)	97,489
Net cash (used in) provided by financing activities	(626)	82,814	(83,440)
Net decrease in cash and cash equivalents	$(25,043)	$(58,571)	

Net cash used in operating activities for the year ended December 31, 2013 decreased by $23.6 million as compared to the year ended December 31, 2012. For 2013, net cash used in operating activities was primarily attributable to aggregate payments of $42.5 million for research and development and general and administrative charges. These cash payments were partially offset by $1.7 million of interest-related adjustments to reconcile net loss to cash used in operating activities. For 2012, net cash used in operating activities was primarily attributable to aggregate payments of $61.8 million for research and development and general and administrative charges, as well as $3.7 million in payments made as a result of two workforce reductions. These cash payments were partially offset by $2.1 million of interest income and related amounts. The decrease of $19.3 million in payments made for research and development and general and administrative charges for 2013 as compared to 2012 was principally the result of the wind-down of the development program in major depressive disorder during 2012, our plan to focus our resources on our more advanced programs, the closing of our laboratories and the completion of two workforce reductions during 2012.

Net cash used in operating activities for the year ended December 31, 2012 decreased by $19.5 million as compared to the year ended December 31, 2011. For 2011, net cash used in operating activities was primarily attributable to aggregate payments of $92.2 million for research and development and general and administrative charges, partially offset by $5.5 million received from AstraZeneca in 2011 in connection with events associated with our ongoing Phase 2b clinical trial of TC-1734 as a treatment for mild to moderate Alzheimer's disease and $2.1 million of interest income and related amounts. The decrease of $30.4 million in payments made for third-party research and development services and personnel and infrastructure costs for 2012 as compared to 2011 was principally the result of the wind-down of the development program in major depressive disorder during 2012, our completion of two exploratory studies of TC-6987 during 2012, our plan to focus our resources on our more advanced programs, the closing of our laboratories and the completion of two workforce reductions during 2012.

Based on our current clinical program related commitments, we expect payments for operating activities for the year ending December 31, 2014 to decrease as compared to 2013, principally as a result of the completion in December 2013 of the clinical trial of TC-5619 as a treatment for schizophrenia.

Net cash provided by investing activities for the year ended December 31, 2013 decreased by $26.4 million as compared to the year ended December 31, 2012. 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 sales of investments in marketable securities for 2013 were $12.3 million as compared to $38.6 million for 2012. The net sales of investment in marketable securities for both periods occurred as funds were transferred to cash for working capital. Net cash provided by investing activities for the year ended December 31, 2012 was $39.8 million and net cash used in investing activities for the year ended December 31, 2011 was $57.7 million, a change of $97.5 million. Our net purchases of investments in marketable securities for 2011 were $56.2 million and occurred primarily as a result of our receipt of proceeds from our common stock offering in May and June 2011.

Net cash used in financing activities for the year ended December 31, 2013 decreased by $74,000 as compared to the year ended December 31, 2012. Net cash used in financing activities for the year ended

December 31, 2012 was $626,000 and net cash provided by financing activities for the year ended December 31, 2011 was $82.8 million, a change of $83.4 million. The difference for 2012 as compared to 2011 was primarily attributable to net proceeds of $80.8 million in May and June 2011 from our common stock offering.

Funding Requirements

As of December 31, 2013, we had an accumulated deficit of $280.6 million. We may require additional capital in future periods as our product candidates advance into later-stage development and as we progress our programs and invest in additional product development opportunities. Our future capital requirements are difficult to forecast and will depend on many factors, including:

- the scope, progress, duration, results and cost of clinical trials, as well as non-clinical studies and assessments, of our product candidates and programs;
- whether we establish additional strategic alliances, collaborations and licensing or other comparable arrangements, or whether we pursue and complete any merger, acquisition or other significant corporate transaction, and, if we do, the associated terms in each case;
- the costs to satisfy our obligations under potential future alliances, collaborations or licensing or other comparable arrangements;
- whether and to what extent we in-license, acquire or risk-share in developing product candidates from external sources, and the terms and scope of any related agreements;
- the extent to which we retain development or commercialization rights or responsibilities for our product candidates and incur associated development costs, manufacturing costs or costs to establish sales and marketing functions;
- whether and to what extent milestone events are achieved for AZD1446 under our ongoing collaboration agreement with AstraZeneca;
- the costs of preparing, filing and prosecuting patent applications and maintaining, enforcing and defending patents and other intellectual property rights;
- the number and characteristics of product candidates that we pursue and programs that we conduct;
- the costs of manufacturing-related services for our product candidates in development;
- the costs, timing and outcomes of regulatory reviews or other regulatory actions;
- the timing, receipt and amount of sales or royalties, if any, from our potential products;
- the extent of our general and administrative expenses; and
- the rate of technological advancements for the indications that we target.

Our existing capital resources may not be sufficient to enable us to fund the completion of the development of any of our product candidates. We currently expect our existing capital resources to be sufficient to fund our operations through at least the end of 2015. However, our operating plan may change as a result of many factors, including those described above, and we may need additional funds sooner than planned to meet operational needs and capital requirements.

To the extent our capital resources are insufficient to meet future capital requirements or to the extent the conditions for raising capital are favorable, we may seek to finance future cash needs through public or private equity or debt offerings or other financings (whether utilizing our currently effective Registration Statement on Form S-3 and our ATM, or otherwise). Our access in the future to additional equity or debt financing, on acceptable terms or at all, is uncertain. We may also seek to finance future cash needs through alliances, collaborations or licensing or other comparable arrangements. Strategic alliances, collaborations or licensing or other comparable arrangements may not be available on acceptable terms or at all. If adequate funds are not

available, we may be required to delay, reduce the scope of or eliminate our development programs or obtain funds through arrangements with collaborators or others that may require us to relinquish rights to certain product candidates that we might otherwise seek to develop or commercialize independently. Additionally, any future equity funding may significantly dilute the ownership of our stockholders.

We cannot determine precisely the completion dates and related costs of our 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 development programs or establish strategic alliances, collaborations or licensing or other arrangements for our product candidates. Our failure, or the failure of any of our present or future licensees or collaborators, to complete research and development programs for our product candidates could have a material adverse effect on our financial position or results of operations.

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

Contractual Obligations

The following table summarizes our fixed contractual obligations as of December 31, 2013:

	Payments Due by Period (in thousands)				
Contractual Obligation	Total	Less Than 1 Year	1 - 3 Years	3 - 5 Years	More Than 5 Years
Long-term debt obligations	$ 1,164	$ 879	$285	$—	$ —
Operating lease obligations	819	492	327	—	—
Purchase obligations	18,655	18,508	147	—	—
	$20,638	$19,879	$759	$—	$ —

The amounts of purchase obligations reflected in the above table include obligations to purchase drug substance or clinical trial materials, to compensate clinical investigators, clinical trial sites and contract research organizations contingent on the performance of services in connection with clinical trials and to compensate contract research organizations contingent on the performance of non-clinical research and development services. The 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, 2013.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

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

The primary objectives of our investment activities are to preserve our capital and meet our liquidity needs to fund operations. We also seek to generate competitive rates of return from our investments without assuming significant risk. To achieve our objectives, we maintain a portfolio of cash equivalents and investments in a variety of securities that are of high credit quality based on ratings from commonly relied upon rating agencies. As of December 31, 2013, we had cash, cash equivalents and investments in marketable securities of $143.8 million. Our cash, cash equivalents and investments in marketable securities may be subject to interest rate risk and could fall in value if market interest rates increase. However, because our cash is invested in accounts with market interest rates and because our cash equivalents and 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, 2013 would not have a material impact on the total fair value of our portfolio.

We sometimes contract for the conduct of clinical trials or other research and development and manufacturing activities with contract research organizations, clinical trial sites and contract manufacturers in Europe or elsewhere outside of the United States. We may be subject to exposure to fluctuations in foreign currency exchange rates in connection with these agreements. If the average exchange rate between the currency of our payment obligations under any of these agreements and the U.S. dollar were to strengthen or weaken by 10% against the corresponding exchange rate as of December 31, 2013, 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, 2013 and 2012, and the related statements of comprehensive income (loss), stockholders' equity and cash flows for each of the three years in the period ended December 31, 2013. 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, 2013 and 2012, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2013, 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, 2013, based on criteria established in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 framework) and our report dated March 14, 2014 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Raleigh, North Carolina
March 14, 2014

TARGACEPT, INC.

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

	December 31, 2013	December 31, 2012
ASSETS		
Current assets:		
Cash and cash equivalents	$ 54,485	$ 82,240
Investments in marketable securities—short term	37,844	42,721
Current receivables	278	1,380
Prepaid expenses	999	1,402
Total current assets	93,606	127,743
Investments in marketable securities—long term	51,448	59,966
Property and equipment, net	682	1,639
Intangible assets	97	115
Other assets	40	116
Total assets	$ 145,873	$ 189,579
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,296	$ 2,056
Accrued expenses	8,830	6,085
Current portion of long-term debt	853	851
Current portion of deferred revenue	—	2,357
Total current liabilities	10,979	11,349
Long-term debt, net of current portion	283	1,136
Deferred revenue, net of current portion	—	1,179
Total liabilities	11,262	13,664
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.001 par value, 100,000,000 shares authorized; 33,718,179 and 33,615,081 shares issued and outstanding at December 31, 2013 and December 31 2012, respectively	34	34
Preferred stock, $0.001 par value, 5,000,000 shares authorized; 0 shares issued and outstanding at December 31, 2013 and 2012	—	—
Capital in excess of par value	415,123	409,608
Accumulated other comprehensive income	87	201
Accumulated deficit	(280,633)	(233,928)
Total stockholders' equity	134,611	175,915
Total liabilities and stockholders' equity	$ 145,873	$ 189,579

See accompanying notes.

TARGACEPT, INC.

STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
(in thousands, except share and per share amounts)

	Year ended December 31,		
	2013	2012	2011
Operating revenues:			
License fees and milestones from collaborations	$ 3,536	$ 57,420	$ 96,979
Grant revenue	93	440	658
Net operating revenues	3,629	57,860	97,637
Operating expenses:			
Research and development (including stock-based compensation of $2,497, $3,792 and $4,885 in 2013, 2012 and 2011, respectively)	38,840	49,087	95,215
General and administrative (including stock-based compensation of $2,719, $3,956 and $3,628 in 2013, 2012 and 2011, respectively)	12,005	13,193	12,167
Reductions in force (including stock-based compensation of $98 in 2012)	—	3,718	—
Total operating expenses	50,845	65,998	107,382
Loss from operations	(47,216)	(8,138)	(9,745)
Other income (expense):			
Interest income	784	1,070	1,348
(Loss) gain on sale of property and equipment	(213)	55	—
Interest expense	(53)	(86)	(132)
Total other income (expense)	518	1,039	1,216
Loss before income taxes	(46,698)	(7,099)	(8,529)
Income tax (expense) benefit	(7)	101	—
Net loss	$ (46,705)	$ (6,998)	$ (8,529)
Basic and diluted net loss per share	$ (1.39)	$ (0.21)	$ (0.27)
Weighted average common shares outstanding—basic and diluted	33,640,323	33,476,316	31,637,283
Net loss	$ (46,705)	$ (6,998)	$ (8,529)
Unrealized (loss) gain on available-for-sale securities, net	(114)	165	(189)
Comprehensive loss	$ (46,819)	$ (6,833)	$ (8,718)

See accompanying notes.

TARGACEPT, INC.

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

	Common Stock		Capital in Excess of Par Value	Other Comprehensive Income	Accumulated Deficit	Total Stockholders' Equity
	Shares	Amount				
Balances at January 1, 2011	28,870,691	$ 29	$309,994	$ 225	$(218,401)	$ 91,847
Issuance of common stock related to exercise of stock options	305,395	—	1,802	—	—	1,802
Stock-based compensation	—	—	8,513	—	—	8,513
Net proceeds from public stock offering	4,207,317	4	80,840	—	—	80,844
Net change in unrealized holding gain on available-for-sale marketable securities	—	—	—	(189)	—	(189)
Net loss	—	—	—	—	(8,529)	(8,529)
Comprehensive loss	—	—	—	—	—	(8,718)
Balances at December 31, 2011	33,383,403	33	401,149	36	(226,930)	174,288
Issuance of common stock related to exercise of stock options	231,678	1	613	—	—	614
Stock-based compensation	—	—	7,846	—	—	7,846
Net change in unrealized holding gain on available-for-sale marketable securities, net of taxes	—	—	—	165	—	165
Net loss	—	—	—	—	(6,998)	(6,998)
Comprehensive loss	—	—	—	—	—	(6,833)
Balances at December 31, 2012	33,615,081	34	409,608	201	(233,928)	175,915
Issuance of common stock related to exercise of stock options	103,098	—	299	—	—	299
Stock-based compensation	—	—	5,216	—	—	5,216
Net change in unrealized holding gain on available-for-sale marketable securities, net of taxes	—	—	—	(114)	—	(114)
Net loss	—	—	—	—	(46,705)	(46,705)
Comprehensive loss	—	—	—	—	—	(46,819)
Balances at December 31, 2013	33,718,179	$ 34	$415,123	$ 87	$(280,633)	$ 134,611

See accompanying notes.

TARGACEPT, INC.

STATEMENTS OF CASH FLOWS
(in thousands)

	Year ended December 31,		
	2013	2012	2011
Operating activities			
Net loss	$(46,705)	$ (6,998)	$ (8,529)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:			
Recognition of deferred revenue	(3,536)	(57,860)	(97,439)
Amortization of premium on marketable securities, net	908	937	911
Depreciation and amortization	547	2,212	2,480
Stock-based compensation expense	5,216	7,846	8,513
Loss (gain) on disposal of property and equipment	213	(55)	—
Income tax expense (benefit) from other comprehensive income	7	(101)	—
Changes in operating assets and liabilities:			
Current receivable	226	(1,162)	620
Other assets	527	2,017	(443)
Accounts payable, license fees payable and accrued expenses	1,985	(11,515)	4,419
Deferred license fee revenue	—	440	5,750
Net cash used in operating activities	(40,612)	(64,239)	(83,718)
Investing activities			
Purchase of investments in marketable securities	(57,551)	(120,972)	(156,253)
Proceeds from sale of investments in marketable securities	69,882	159,538	100,012
Purchase of property and equipment	(92)	(333)	(1,431)
Proceeds from sale of property and equipment	1,170	1,589	5
Net cash provided by (used in) investing activities	13,409	39,822	(57,667)
Financing activities			
Proceeds from issuance of long-term debt	—	—	2,132
Principal payments on long-term debt	(851)	(1,240)	(1,964)
Proceeds from issuance of common stock, net	299	614	82,646
Net cash (used in) provided by financing activities	(552)	(626)	82,814
Net decrease in cash and cash equivalents	(27,755)	(25,043)	(58,571)
Cash and cash equivalents at beginning of year	82,240	107,283	165,854
Cash and cash equivalents at end of year	$ 54,485	$ 82,240	$ 107,283

See accompanying notes.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS
DECEMBER 31, 2013

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 development of novel NNR Therapeutics™ to treat patients suffering from serious nervous system and gastrointestinal/genitourinary diseases and disorders. 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

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.

Cash and Cash Equivalents

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

Investments in Marketable Securities

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

The Company determines the appropriate classification of marketable securities at the time of purchase and reevaluates its classification as of each balance sheet date. All marketable securities owned during 2013 and 2012 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 comprehensive income (loss).

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 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 comprehensive income (loss) and establishes a new cost basis in the investment.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

2. Summary of Significant Accounting Policies (continued)

Receivables

The Company's current receivables at December 31, 2013 and 2012 are related to the Company's collaboration agreement with AstraZeneca AB and the sale of equipment as a result of the Company closing its laboratory operations. During 2013, 2012, and 2011, the Company recognized revenue of $3,536,000, $57,420,000, and $96,979,000, respectively, or 97%, 99% and 99% of net operating revenues, respectively, from the collaboration and alliance agreements discussed in Note 12. During 2013 and 2012, the Company sold equipment with a book value of $519,000 and $1,534,000, respectively, of which $183,000 and $1,046,000 was receivable at December 31, 2013 and 2012, respectively.

Long-lived Assets

Property and equipment consists primarily of laboratory equipment, office furniture and fixtures and, prior to December 31, 2013, leasehold improvements and is recorded at historical cost, net of accumulated depreciation. Depreciation is computed using the straight-line method over the estimated useful lives of the assets. Equipment is typically depreciated over 3 to 5 years, office furniture and fixtures are typically depreciated over 7 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 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 research or development of the Company's product candidates, salaries of, and stock-based compensation for, personnel involved in research and development activities, contractor fees, administrative expenses and allocations of research and development-related overhead costs. Administrative expenses and research and development-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.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

2. Summary of Significant Accounting Policies (continued)

Accrued Expenses

The Company records accruals based on estimates of the services received, efforts expended and amounts owed pursuant to contracts with clinical trial 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 clinical trial materials, 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, 2013 and 2012, the Company had deposits in excess of federally insured limits of $57,485,000 and $87,081,000, 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 into separate units of accounting for revenue recognition purposes and, if division is required, how the arrangement consideration should be allocated among the separate units of accounting. If the arrangement constitutes separate units of accounting according to the separation criteria of ASC 605-25, the consideration received is allocated among the separate units of accounting and the applicable revenue recognition criteria must be applied to each unit. If the arrangement constitutes a single unit of accounting, the revenue recognition policy must be determined for the entire arrangement and the consideration received is recognized over the period of inception through the date on which the last deliverable within the single unit of accounting is expected to be delivered. Revisions to the estimated period of recognition are reflected in revenue prospectively.

Collaboration research and development revenue is earned and recognized as research or development is performed and related expenses are incurred. Non-refundable upfront fees, which may include, for example, an initial payment upon effectiveness of the contractual relationship, payment representing a common stock purchase premium or payment to secure a right for a future license, are recorded as deferred revenue and recognized into revenue as license fees and milestones from collaborations on a straight-line basis over the

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

2. Summary of Significant Accounting Policies (continued)

estimated period of the Company's substantive performance obligations. If the Company does not have substantive performance obligations, it recognizes non-refundable upfront fees into revenue through the date the deliverable is satisfied.

Revenue for non-refundable payments based on the achievement of milestone events under collaboration agreements is recognized in accordance with ASC 605, Subtopic 28, *Milestone Method*, or ASC 605-28. Milestone events under the Company's collaboration agreements may include research, development, regulatory, commercialization or sales events. Under ASC 605-28, a milestone payment is recognized as revenue when the applicable event is achieved if the event meets the definition of a milestone and the milestone is determined to be substantive. ASC 605-28 defines a milestone event as an event having all of the following characteristics: (1) there is substantive uncertainty regarding achievement of the milestone event at the inception of the arrangement; (2) the event can only be achieved based, in whole or in part, on either the company's performance or a specific outcome resulting from the company's performance; and (3) if achieved, the event would result in additional payment due to the company. The Company also treats events that can only be achieved based, in whole or in part, on either a third party's performance or a specific outcome resulting from a third party's performance as milestone events if the criteria of ASC 605-28 are otherwise satisfied. A milestone is considered substantive if it meets all of the following criteria: (A) the payment is commensurate with either the Company's performance to achieve the milestone or with the enhancement of the value of the delivered item; (B) the payment relates solely to past performance; and (C) the payment is reasonable relative to all of the deliverables and payment terms within the arrangement. If any of these conditions is not met, the milestone payment is deferred and recognized on a straight-line basis over a period determined as discussed above.

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

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 qualifying costs.

Income Taxes

The Company uses the liability method in accounting for income taxes as required by ASC Topic 740, *Income Taxes*, or ASC 740. Under ASC 740, deferred tax assets and liabilities are recorded for operating loss and tax credit carryforwards and for the future tax consequences attributable to the differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect of a change in tax rates on deferred tax assets and liabilities is recognized in the results of operations in the period that includes the enactment date. A valuation allowance is recorded to reduce the carrying amounts of deferred tax assets unless it is more likely than not that the assets will be realized. ASC 740 prescribes a recognition threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. ASC 740 also provides guidance on de-recognition, classification, interest and penalties, accounting in interim periods, disclosures and transition. The Company's policy is to classify any interest recognized in accordance with ASC 740 as interest expense and to classify any penalties recognized in accordance with ASC 740 as an expense other than income tax expense.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

2. Summary of Significant Accounting Policies (continued)

Net Income or Loss Per Share

The Company computes net income or loss per share in accordance with ASC Topic 260, *Earnings Per Share*, or ASC 260. Under the provisions of ASC 260, basic net income or loss per share, or Basic EPS, is computed by dividing net income or loss by the weighted average number of common shares outstanding. Diluted net income or loss per share, or Diluted EPS, is computed by dividing net income or loss by the weighted average number of common shares outstanding plus, in the case of diluted net income per share, dilutive common share equivalents outstanding.

The calculations of Basic EPS and Diluted EPS are set forth in the table below (in thousands, except share and per share amounts):

	Year Ended December 31,		
	2013	2012	2011
Basic and diluted:			
Net loss	$ (46,705)	$ (6,998)	$ (8,529)
Weighted average common shares—basic and diluted	33,640,323	33,476,316	31,637,283
Basic and diluted EPS	$ (1.39)	$ (0.21)	$ (0.27)

Common share equivalents consist of the incremental common shares that would be outstanding upon the exercise of stock options, calculated using the treasury stock method. For each of the years ended December 31, 2013, 2012 and 2011, the Company excluded all common share equivalents from the calculation of Diluted EPS because the Company had a net loss. As a result, Diluted EPS is identical to Basic EPS for those years. If the Company had been in a net income position for the years ended December 31, 2013, 2012 and 2011, 4,364,064, 4,250,964 and 3,597,530 shares, respectively, subject to outstanding stock options may have been included in the calculation of common share equivalents using the treasury stock method.

Public Offerings of Common Stock

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

Stock-Based Compensation

The Company has two stock-based incentive plans, the 2000 Equity Incentive Plan of Targacept, Inc., as amended and restated through March 15, 2006, or the 2000 Plan, and the Targacept, Inc. 2006 Stock Incentive Plan, as amended and restated through March 9, 2011 and further amended on December 7, 2012, March 13, 2013 and April 10, 2013, or the 2006 Plan. The 2000 Plan and the 2006 Plan, or the Plans, are described more fully in Note 9.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

2. Summary of Significant Accounting Policies (continued)

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

ASC 718 also requires the benefits of tax deductions in excess of recognized compensation expense to be reported as a financing cash flow, rather than as an operating cash flow. This requirement reduces net operating cash flows and increases net financing cash flows for periods after adoption. The Company cannot estimate the future effect of excess tax deductions or shortfalls on cash flows because they depend on, among other things, when employees exercise stock options and the tax deductions available to the Company at those times.

Prepaid Expenses

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

Fair Value

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

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

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

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

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

Level 3 Inputs—unobservable inputs for the assets.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

2. Summary of Significant Accounting Policies (continued)

The following tables present the Company's investments in marketable securities (including, if applicable, those classified on the Company's balance sheet as cash equivalents) that are measured at fair value on a recurring basis as of December 31, 2013 and 2012, respectively:

December 31, 2013	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
		(in thousands)	
U.S. Treasury and U.S. or state government agency-backed securities	$37,029	$ —	$ —
Corporate debt securities	—	43,347	—
Municipal bonds	—	3,509	—
Certificates of deposit	5,000	—	—
Accrued interest	407	—	—
Total cash equivalents and marketable securities	$42,436	$ 46,856	$ —

December 31, 2012	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)
		(in thousands)	
U.S. Treasury and U.S. or state government agency-backed securities	$46,371	$ —	$ —
Corporate debt securities	—	47,173	—
Municipal bonds	—	2,700	—
Certificates of deposit	10,000	—	—
Accrued interest	443	—	—
Total cash equivalents and marketable securities	$56,814	$ 49,873	$ —

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

Accumulated Other Comprehensive Income or Loss

Accumulated other comprehensive income or loss, as presented in stockholders' equity on the Company's balance sheet, reflects the cumulative net unrealized gains or losses on available-for-sale securities for all periods. The table below reflects changes in accumulated other comprehensive income for the year ended December 31, 2013, in thousands.

Accumulated other comprehensive income, January 1, 2013	$201
Unrealized loss on available-for-sale securities, net	(34)
Net realized gains on available-for sale securities reclassified out of other comprehensive income	(87)
Income taxes	7
Accumulated other comprehensive income, December 31, 2013	$ 87

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

3. Investments in Marketable Securities

The following is a reconciliation of amortized cost to fair value of available-for-sale marketable securities (including those classified on the Company's balance sheet as cash equivalents) held at December 31, 2013 and 2012:

December 31, 2013	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
		(in thousands)		
Security type				
Cash Equivalents				
Corporate debt securities	$ —	$ —	$ —	$ —
Marketable Securities—Short term				
U.S. Treasury and U.S. or state government agency-backed securities	16,352	39	—	16,391
Corporate debt securities	14,307	35	—	14,342
Municipal Bonds	1,910	3	—	1,913
Certificates of deposit	5,000	—	—	5,000
Accrued interest	198	—	—	198
Marketable Securities—Long term				
U.S. Treasury and U.S. or state government agency-backed securities	20,628	14	(4)	20,638
Corporate debt securities—long term	28,909	101	(5)	29,005
Municipal Bonds	1,598	4	(6)	1,596
Accrued interest	209	—	—	209
Total available-for-sale marketable securities	$89,111	$ 196	$ (15)	$89,292

December 31, 2012	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Fair Value
		(in thousands)		
Security type				
Cash Equivalents				
Corporate debt securities	$ 4,000	$ —	$ —	$ 4,000
Marketable Securities—Short term				
U.S. Treasury and U.S. or state government agency-backed securities	25,412	27	—	25,439
Corporate debt securities	7,193	16	—	7,209
Certificates of deposit	10,000	—	—	10,000
Accrued interest	73	—	—	73
Marketable Securities—Long term				
U.S. Treasury and U.S. or state government agency-backed securities	20,846	86	—	20,932
Corporate debt securities—long term	35,802	177	(15)	35,964
Municipal Bonds	2,689	11	—	2,700
Accrued interest	370	—	—	370
Total available-for-sale marketable securities	$106,385	$ 317	$ (15)	$106,687

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

3. Investments in Marketable Securities (continued)

As of December 31, 2013, the Company held investments in marketable securities with unrealized gains of $196,000 and unrealized losses of $15,000. For the investments in an unrealized loss position, the duration of the loss was less than 12 months, and the investments are not considered to be other-than-temporarily impaired.

As of December 31, 2013, the Company's investments in marketable securities reach maturity between January 23, 2014 and December 12, 2016, with a weighted average maturity date of approximately January 29, 2015.

4. Property and Equipment

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

	December 31,	
	2013	2012
	(in thousands)	
Equipment	$ 165	$ 2,628
Office furniture and fixtures	2,373	2,880
Leasehold improvements	22	—
	2,560	5,508
Less: accumulated depreciation	(1,878)	(3,869)
Property and equipment, net	$ 682	$ 1,639

The Company recorded $505,000, $2,195,000, and $2,463,000 of depreciation expense for the years ended December 31, 2013, 2012 and 2011, respectively. During the year ended December 31, 2012, the Company closed its laboratory operations and completed two reductions in force (see Note 13). In connection with the reductions in force, the Company sold laboratory equipment and office furniture and fixtures with a book value of $519,000 and $1,534,000 for the year ended December 31, 2013 and 2012, respectively, which resulted in a cumulative loss of $213,000 and a cumulative gain of $55,000 for the year ended December 31, 2013 and 2012, respectively.

5. Intangible Assets

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

	December 31,	
	2013	2012
	(in thousands)	
Patents	$ 296	$ 296
Less: accumulated amortization	(199)	(181)
Total	$ 97	$ 115

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.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

5. Intangible Assets (continued)

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

6. Accrued Expenses

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

	December 31,	
	2013	2012
	(in thousands)	
Clinical trial and nonclinical study costs	$7,578	$5,232
Employee compensation	1,200	797
Other	52	56
Total	$8,830	$6,085

7. Long-term Debt

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

In March 2008, the Company entered into a loan agreement with a bank that provided borrowing capacity of $5,300,000 to fund the purchase of equipment, furnishings, software and other fixed assets and enable the refinancing of an existing loan facility with another lender. The Company borrowed $4,811,000 upon entering into the loan agreement and borrowed the remaining $489,000 in September 2008. The Company's March 2008 borrowing bore interest at a fixed rate of 5.231% per annum and was repayable in equal monthly installments of $112,000 beginning April 1, 2008 through the maturity date of March 1, 2012. The March 2008 borrowing was paid and satisfied in full on March 1, 2012. The Company used $1,679,000 of the proceeds from the March 2008 borrowing to pay and satisfy in full the principal and interest outstanding on two tranches of the existing loan facility with another lender. The Company's September 2008 borrowing bore interest at a fixed rate of 6.131% per annum and was repayable in equal monthly installments of $11,000 beginning October 1, 2008 through the maturity date of September 1, 2012. The September 2008 borrowing was paid and satisfied in full on August 31, 2012.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

7. Long-term Debt (continued)

The Company paid $56,000, $91,000 and $134,000 in interest under notes payable during the years ended December 31, 2013, 2012 and 2011, respectively. Future scheduled maturities of long-term debt were as follows at December 31, 2013 (in thousands):

2014	$ 853
2015	283
2016 and thereafter	—
	$1,136

8. Income Taxes

For the year ended December 31, 2012, the Company recognized $101,000 of income tax benefit as a result of the application of intraperiod tax allocation provisions of ASC 740, under which the Company is required to consider all items (including items recorded in other comprehensive income) in determining the amount of tax benefit that should be allocated to net loss. The non-cash income tax benefit was offset in full by income tax expense recorded in other comprehensive income. For the year ended December 31, 2013, the Company recorded $7,000 income tax expense, and a corresponding $7,000 income tax benefit in other comprehensive income, as the available-for-sale securities began to be sold. For the year ended December 31, 2011, the Company did not recognize any income tax expense or benefit. For the years shown, components of the Company's income tax expense (benefit) were as follows:

	Year Ended December 31,		
	2013	2012	2011
	(in thousands)		
Current:			
Federal	$ —	$ —	$ —
State	—	—	—
Net current income tax (benefit) expense	—	—	—
Deferred:			
Federal	(18,076)	(1,128)	(6,147)
State	1,010	(718)	(1,095)
Valuation allowance	17,073	1,745	7,242
Net deferred income tax expense (benefit)	7	(101)	—
Net income tax expense (benefit)	$ 7	$ (101)	$ —

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

8. Income Taxes (continued)

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

	Year Ended December 31,		
	2013	2012	2011
Expected federal income tax benefit/expense at statutory rate	35%	35%	35%
Increase (decrease) resulting from:			
Research and development credits	4	—	19
Stock-based compensation	(1)	(15)	(13)
State income tax expense, net of federal benefit	4	2	3
Change in state rates	(6)	—	—
Change in unrecognized tax benefit reserves	—	—	—
Change in valuation allowance	(37)	(25)	(85)
Other	—	4	41
	(1)%	1%	— %

At December 31, 2013, 2012 and 2011, the Company had net operating loss carryforwards for federal income tax purposes of $233,170,000, $187,752,000, and $135,860,000, respectively, and for state income tax purposes of $219,792,000, $176,296,000 and $134,470,000, respectively. At December 31, 2013, 2012 and 2011, the Company had research and development income tax credit carryforwards for federal income tax purposes of $12,773,000, $10,762,000 and $10,778,000, respectively. The Company had research and development income tax credit carryforwards for state income tax purposes of $587,000 at December 31, 2013, 2012 and 2011. The federal net operating loss carryforwards begin to expire in 2024. The state net operating loss carryforwards begin to expire in 2019. The federal and state research and development tax credits begin to expire in 2021.

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 gave rise to such an ownership change in December 2004. 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 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. The valuation allowance increased by $17,110,000, $1,745,000, and $7,242,000 for the years ended December 31, 2013, 2012 and 2011, respectively.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

8. Income Taxes (continued)

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

	December 31,	
	2013	2012
	(in thousands)	
Deferred tax assets:		
Net operating loss carryforward	$ 81,183	$ 65,935
Research and development tax credit	12,044	10,033
Stock-based compensation	6,498	5,260
Patents	1,641	1,798
Collaboration revenue	—	1,341
Other	36	94
Total gross deferred tax assets	101,402	84,461
Valuation allowance	(101,211)	(84,101)
Net deferred tax asset	191	360
Deferred tax liabilities		
Equipment and other	(191)	(360)
Net deferred tax asset	$ —	$ —

As of December 31, 2013, the Company had cumulative tax deductions from exercises of stock options in excess of expense recorded for the stock options under GAAP. The $7,551,000 benefit of these excess tax deductions had not begun to be realized as of December 31, 2013 because the Company incurred operating losses in the years the respective stock options were exercised and has incurred cumulative net operating losses since inception. Accordingly, the tax benefit will not be recognized as an increase to capital in excess of par value unless and until the excess deductions reduce income taxes payable.

The Company follows the provisions of ASC 740, which prescribes a threshold and measurement attribute for the financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return and also provides guidance on de-recognition, classification, interest and penalties, accounting in interim periods and disclosures. There was no cumulative effect adjustment upon adoption.

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

Balance at January 1, 2011	$1,474
Additions (decreases) based on tax positions related to current and prior years	—
Balance at December 31, 2011	1,474
Additions (decreases) based on tax positions related to current and prior years	—
Balance at December 31, 2012	1,474
Additions (decreases) based on tax positions related to current and prior years	2
Balance at December 31, 2013	$1,476

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

8. Income Taxes (continued)

has no tax positions for which it is reasonably possible that the total amount of unrecognized tax benefits will significantly increase or decrease during 2014. No interest or penalties with respect to unrecognized tax positions are recognized in the statement of comprehensive income (loss) for any of the years ended December 31, 2013, 2012 or 2011.

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. The Company's 2010 federal income tax return is currently under examination.

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, 2013, the number of shares authorized for issuance under the Plans was 7,821,554, of which 3,281,926 shares remained available for grant.

Awards may be made with respect to the 2006 Plan, or may have been made with respect to both Plans, to participants under the Plans in the form of incentive and nonqualified stock options, restricted stock, stock appreciation rights, stock awards, and performance awards. Eligible participants under the Plans include employees, directors and certain independent contractors, consultants or advisors of the Company or a related corporation. Awards made under the Plans have vesting periods that are determined at the discretion of the administrator and range from 0 to 5 years and most commonly have 10-year contractual terms or, in some cases, shorter terms designed to comply with Section 409A of the Internal Revenue Code. The exercise price of stock 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.

In addition to awards made under the Plans, on December 3, 2012, the Company granted a nonqualified option to purchase 400,000 shares of its common stock pursuant to an employment agreement entered into by the Company in connection with the hire of its president and chief executive officer. The option, which was not granted pursuant to a Plan, has similar terms to nonqualified stock options granted under the 2006 Plan.

Under ASC 718, the Company recognizes the grant date fair value of stock options issued to employees and non-employee directors over the requisite service periods, which are typically the vesting periods. The Company uses the Black-Scholes-Merton formula to estimate the fair value of its stock-based payments. The volatility assumption used in the Black-Scholes-Merton formula is primarily based on the Company's implied volatility, the calculated historical volatility of twelve to sixteen benchmark companies in the Company's industry that have been identified as comparable public entities, the Company's historical volatility and the implied volatility of the same benchmark companies. The expected term for stock options granted during 2013, 2012 and 2011 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.

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

9. Stock-Based Incentive Plans (continued)

The following table illustrates the weighted average assumptions for the Black-Scholes-Merton model used in determining the fair value of stock options granted as of the respective dates shown:

	Year ended December 31,		
	2013	2012	2011
Dividend yield	—	—	—
Risk-free interest rate	1.1%	1.0%	2.5%
Volatility	82%	69%	67%
Expected term	5.73 years	6.16 years	6.00 years

During 2013 and 2012, the Company partially accelerated the vesting of, and/or extended the permitted period for exercise for, some outstanding stock options held by several employees who departed the Company. These modifications resulted in incremental compensation cost recorded by the Company for the year ended December 31, 2013 and 2012 of $573,000 and $1,397,000.

A summary of option activity and changes during the year ended December 31, 2013 appears below.

	Shares Subject to Options	Weighted Average Exercise Price Per Share	Weighted Average Remaining Contractual Term	Aggregate Intrinsic Value
			(in thousands)	
Outstanding at January 1, 2013	4,369,804	$ 10.84		
Granted	926,650	4.95		
Forfeited	(653,728)	10.12		
Exercised	(103,098)	2.89		
Outstanding at December 31, 2013	4,539,628	$ 9.93	5.48	$372,288
Vested and exercisable at December 31, 2013	3,181,974	$ 11.54	4.05 years	$372,288

The weighted average grant date fair value of options granted during the years ended December 31, 2013, 2012, and 2011 was $3.38, $2.98 and $15.87, respectively. The total intrinsic value of options exercised during the years ended December 31, 2013, 2012, and 2011 was $200,000, $472,000, and $6,082,000, respectively. During 2013, 176,102 shares subject to options expired upon reaching the 10-year contractual term, and are included in the "Forfeited" amount in the table above.

A summary of the status of non-vested stock options outstanding as of December 31, 2013 and changes during the year ended December 31, 2013 appears below.

	Shares Subject to Options	Weighted Average Grant-Date Fair Value Per Share
Non-vested at January 1, 2013	1,567,570	$ 5.84
Granted	926,650	3.38
Vested	(803,484)	6.45
Forfeited	(333,082)	4.92
Non-vested at December 31, 2013	1,357,654	$ 4.04

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

9. Stock-Based Incentive Plans (continued)

As of December 31, 2013, there was $5,491,000 of total unrecognized compensation expense related to non-vested stock-based compensation arrangements, before considering forfeitures. That cost is expected to be recorded over a weighted average period of 2.83 years. The total fair value of shares subject to stock-based compensation arrangements that vested during the years ended December 31, 2013, 2012, and 2011 was $5,140,000, $7,836,000 and $8,481,000, respectively.

The Company had 4,539,337 and 4,369,804 shares of common stock reserved for future issuance upon the exercise of outstanding stock options at December 31, 2013 and 2012, respectively.

On January 23, 2014, the Company granted 834,618 stock options to employees. The stock options will vest over 16 quarters, beginning March 31, 2014.

10. Commitments and Contingencies

Leases

On December 4, 2012, the Company entered into an agreement with B/E Aerospace, Inc. to sublease approximately 18,282 square feet of office space in Winston-Salem, North Carolina. The term of the sublease began on January 1, 2013 and ends on December 30, 2015. The monthly rent payable by the Company under the sublease is approximately $22,000 for the first year, subject to escalation of approximately 3% for each subsequent year of the term. The sublease is subject to the terms and conditions of the prime lease covering the subleased space between B/E Aerospace and its landlord, SL Winston-Salem LLC.

The Company has entered into various other lease agreements, primarily for storage space and equipment. The Company's previous office lease expired on December 31, 2012. Rent expense incurred by the Company under the office leases and other operating leases was $582,000, $2,819,000 and $2,575,000 for the years ended December 31, 2013, 2012 and 2011, respectively.

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

2014	$492
2015	327
2016	
2017 and thereafter	—
	$819

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 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 current base salary for from up to nine to 18 months following termination, depending on the executive and the circumstances of termination. The executive officer would also be entitled to continuation of the health and life insurance benefits coverage provided 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 $275,000, $454,000, and $535,000 to the plan for the years ended December 31, 2013, 2012 and 2011, respectively. The Company matched employee contributions to the plan, on a per employee basis, up to 4% of each employee's wages, subject to statutory limits, for the years ended December 31, 2013, 2012 and 2011.

12. Strategic Alliance and Collaboration Agreements

AstraZeneca AB

In December 2005, the Company entered into a collaborative research and license agreement with AstraZeneca AB that was initially focused in cognitive disorders. In March 2013, the Company and AstraZeneca amended the agreement. As amended, the agreement permits AstraZeneca to pursue development and commercialization of compounds that it has licensed from the Company in any therapeutic area. The Company is eligible to receive license fees and milestone payments under the agreement. The amount of license fees and milestone payments depends on the timing and achievement of specified milestone events.

AstraZeneca paid the Company an initial fee of $10,000,000 in February 2006. Based on the agreement terms, the Company allocated $5,000,000 of the initial fee to a nonclinical research collaboration that the Company conducted with AstraZeneca under the agreement, 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 grants of licenses to develop and commercialize the Company's product candidate TC-1734 (formerly known as AZD3480), until December 2006, when AstraZeneca made a determination to proceed with further development of TC-1734. As a result, in the first quarter of 2007, the Company began recognizing the $5,000,000 of the initial fee that it had previously deferred as revenue on a straight-line basis over the estimated development period for TC-1734. In September 2010, the Company and AstraZeneca amended the agreement to enable the Company to conduct a clinical trial of TC-1734 in mild to moderate Alzheimer's disease and to provide for respective roles and responsibilities and associated financial terms for such a study. Under the 2010 amendment, the Company received from AstraZeneca $500,000 in October 2010, $2,000,000 in September 2011 and $3,500,000 in December 2011.

In March 2013, AstraZeneca exercised its right to terminate TC-1734 from the collaboration. At that time, the Company was recognizing both the portion of the $5,000,000 of the initial fee attributable to TC-1734 license grants not yet recognized and the payments received under the 2010 amendment into revenue on a straight-line basis over the period of the Company's substantive performance obligations under the agreement, as amended. As a result of AstraZeneca's exercise of its termination right for TC-1734, the Company recognized into revenue during the first quarter of 2013 all of the initial fee and payments received under the 2010 amendment that had not yet been recognized as of the date of AstraZeneca's action, totaling $3,142,000. The Company recognized an aggregate of $3,536,000, $2,946,000, and $1,192,000 of the initial fee and the payments received under the 2010 amendment into revenue during the years ended December 31, 2013, 2012, and 2011, respectively.

The Company is eligible to receive additional payments from AstraZeneca if specified milestone events under the agreement are achieved for the Company's product candidate AZD1446 (TC-6683). The amounts of the contingent milestone payments vary depending on the applicable indication pursued and range from an additional $7,000,000 to $14,000,000 if development milestone events are achieved, an additional $8,000,000 to $10,000,000 if a regulatory milestone event is achieved, up to an additional $12,000,000 to $49,000,000 if first

12. Strategic Alliance and Collaboration Agreements (continued)

commercial sale milestone events are achieved and, in specified circumstances, up to an additional $30,000,000 if sales-related milestone events are achieved. If regulatory approval is achieved for AZD1446 for any indication, the Company is also eligible to receive stepped royalties on any sales of AZD1446. If AZD1446 is subsequently developed under the agreement for other indications, the Company would also be eligible to receive contingent milestone payments of up to $35,000,000 for each successive indication, if development, regulatory and first detail milestone events are achieved.

Based solely on projected activities and timelines, the Company expects that the earliest a contingent milestone payment could conceivably be earned under the agreement with respect to AZD1446 is in the second half of 2014, in the amount of $2,000,000, if a development milestone event is achieved. The likelihood that the Company will earn that milestone amount or achieve any particular milestone event with respect to AZD1446 in 2014 or in any future period is uncertain, and the Company may not earn any milestone amount or achieve any milestone event with respect to AZD1446 in 2014 or ever. The Company considers that each of the potential milestone events under the agreement with respect to AZD1446 would be substantive because the applicable criteria of its revenue recognition policy (see Note 2) would be satisfied.

AstraZeneca has paid the Company an aggregate of $88,120,000 under the agreement since its inception, including the initial fee and payments upon the achievement of milestone events, to maintain option rights and for research services rendered in the completed preclinical research collaboration. As of December 31, 2013, this entire amount had been fully recognized into revenue.

Prior Collaboration Agreement

In December 2009, the Company entered into a collaboration and license agreement with AstraZeneca AB for the global development and commercialization of TC-5214 as a treatment for major depressive disorder. Under the agreement, AstraZeneca made an upfront payment to the Company of $200,000,000. The Company recorded the upfront payment made by AstraZeneca as deferred revenue and began recognizing the payment as revenue on a straight-line basis over the estimated period of the Company's substantive performance obligations under the agreement, or approximately 33 months after the agreement date. The Company recognized $54,473,000 of the upfront payment as revenue for the year ended December 31, 2012 and $72,565,000 for each of the years ended December 31, 2011 and 2010. Under the terms of an existing license agreement, the Company paid $16,000,000 to University of South Florida Research Foundation, in February 2011 based on the Company's receipt of the upfront payment from AstraZeneca.

Under the agreement, AstraZeneca was responsible for 80% and the Company was responsible for 20% of the costs of the global development program for TC-5214 in major depressive disorder, except that AstraZeneca was responsible for 100% of development costs that were required only for countries outside the United States and the European Union. In addition, for each of the Company and AstraZeneca, costs that were not contemplated at execution to be part of the program were in some cases excluded from the cost-sharing arrangement.

The Company's portion of the costs of the TC-5214 development program was $2,175,000 and $32,046,000 for the years ended December 31, 2012 and 2011, respectively. AstraZeneca's allocable portion of the program costs paid by the Company was $127,000 and $336,000 for the years ended December 31, 2012 and 2011, respectively. AstraZeneca's allocable portion of the program costs paid by the Company is reflected in the Company's financial statements as a reduction to research and development expense.

12. Strategic Alliance and Collaboration Agreements (continued)

In the first quarter of 2012, the Company and AstraZeneca announced that, based on the totality of the results of the Phase 3 development program for TC-5214, a regulatory submission for TC-5214 as an adjunct therapy for major depressive disorder would not be pursued. Also in the first quarter of 2012, the Company reported that the Company and AstraZeneca determined to discontinue a Phase 2b clinical trial of TC-5214 as a "switch" monotherapy. These determinations resulted in a change in the estimated period of the Company's substantive performance obligations under the agreement, and the Company revised the revenue recognition period for the upfront payment accordingly. As a result, the entire upfront payment was recognized into revenue by June 30, 2012. In April 2012, the Company received notice of termination of the agreement from AstraZeneca. By the terms of the agreement, the termination became effective in May 2012.

GlaxoSmithKline

On July 27, 2007, the Company entered into a product development and commercialization agreement with SmithKline Beecham Corporation, doing business as GlaxoSmithKline, and Glaxo Group Limited, which are referred to together as GlaxoSmithKline, that set forth the terms of an alliance designed to discover, develop and market product candidates that selectively target specified NNR subtypes for specified therapeutic focus areas. In February 2011, the Company received notice of termination of the agreement from GlaxoSmithKline. By the terms of the agreement, the termination became effective in May 2011.

Under the agreement and a related stock purchase agreement, GlaxoSmithKline made an initial payment to the Company of $20,000,000 and purchased 1,275,502 shares of the Company's common stock for an aggregate purchase price of $15,000,000 on July 27, 2007. The purchase price paid by GlaxoSmithKline reflected an aggregate deemed premium of $3,521,000, based on the closing price of the Company's common stock on the trading day immediately preceding the date that the agreements were signed and announced. The Company deferred recognition of both the initial payment made by GlaxoSmithKline and the deemed premium paid for the shares of the Company's common stock purchased by GlaxoSmithKline and began recognizing both amounts into revenue on a straight-line basis over the nine-year period of the Company's research and early development obligations estimated at inception of the agreement.

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 as of inception of the agreement of the product candidate to which the payment related, there was not substantive uncertainty regarding achievement of the milestone event within the meaning of the Company's revenue recognition policy. Accordingly, the Company recorded the payment as deferred revenue and began recognizing it into revenue on a straight-line basis over the remaining portion of the nine-year period of the Company's research and early development obligations estimated at inception of the agreement.

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

TARGACEPT, INC.

NOTES TO FINANCIAL STATEMENTS (continued)
DECEMBER 31, 2013

13. Reductions In Force

On April 25, 2012, the Company announced a reduction in force as part of a plan to focus its resources on its more advanced programs. The restructuring was completed in the second quarter of 2012. The Company recorded $2,312,000 in severance and other charges related to the reduction in force in the year ended December 31, 2012. Upon the completion of the restructuring, the Company's workforce was reduced by 65 employees, or approximately 46%.

On October 8, 2012, the Company announced a further reduction in force and the closing of its laboratory operations. Both of these actions were completed in the fourth quarter of 2012. The Company recorded $1,406,000 in severance and other charges related to the reduction in force in the year ended December 31, 2012. Upon the completion of the restructuring, the Company's workforce was further reduced by 27 employees, or approximately 38%.

14. Selected Quarterly Financial Data (unaudited)

	2013 Quarter			
	First	Second	Third	Fourth
	(in thousands, except share and per share amounts)			
Net operating revenues	$ 3,536	$ —	$ —	$ 93
Loss from operations	(8,274)	(12,488)	(13,146)	(13,308)
Net loss	(8,066)	(12,371)	(12,902)	(13,366)
Basic net loss per share(1)	$ (0.24)	$ (0.37)	$ (0.38)	$ (0.40)
Weighted average common shares outstanding—basic and diluted(2)	33,616,342	33,626,980	33,644,256	33,673,047

	2012 Quarter			
	First	Second	Third	Fourth
	(in thousands, except share and per share amounts)			
Net operating revenues	$ 22,857	$ 33,645	$ 768	$ 590
Income (loss) from operations	1,986	14,234	(8,098)	(16,260)
Net income (loss)	2,259	14,492	(7,879)	(15,870)
Basic net income (loss) per share(1)	$ 0.07	$ 0.43	$ (0.24)	$ (0.47)
Diluted net income (loss) per share(1)	$ 0.07	$ 0.43	$ (0.24)	$ (0.47)
Weighted average common shares outstanding—basic	33,390,286	33,409,341	33,494,106	33,609,867
Weighted average common shares outstanding—diluted(2)	33,822,010	33,638,629	33,494,106	33,609,867

(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 each quarter of 2013 and for the third and fourth quarters of 2012 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, 2013 using the criteria established in a report entitled "Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission" (1992 framework) 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, 2013, 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, 2013. 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, 2013, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (1992 framework) (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, 2013, 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, 2013 and 2012, and the related statements of comprehensive income (loss), stockholders' equity and cash flows for each of the three years in the period ended December 31, 2013 and our report dated March 14, 2014 expressed an unqualified opinion thereon.

/s/ Ernst & Young LLP

Raleigh, North Carolina
March 14, 2014

(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, 2013 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 2014 Annual Meeting of Stockholders to be filed with the SEC under the captions "Board of Directors and Management," "Corporate Governance" and "Section 16(a) Beneficial Ownership Reporting Compliance" and is incorporated by reference in this Item 10.

Code of Business Conduct and Ethics

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

Item 11. Executive Compensation.

Information called for by this Item may be found in our definitive Proxy Statement in connection with our 2014 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 2014 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 2014 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 2014 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 .

(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 14, 2014

Targacept, Inc.

By: /S/ STEPHEN A. HILL
Stephen A. Hill
Chief Executive Officer and President

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/S/ STEPHEN A. HILL **Stephen A. Hill**	Chief Executive Officer, President and Director (principal executive officer)	March 14, 2014
/S/ ALAN A. MUSSO **Alan A. Musso**	Senior Vice President, Finance and Administration, Chief Financial Officer and Treasurer (principal financial officer and principal accounting officer)	March 14, 2014
/S/ JOHN P. RICHARD **John P. Richard**	Chairman of the Board of Directors	March 14, 2014
/S/ CHARLES A. BLIXT **Charles A. Blixt**	Director	March 14, 2014
/S/ JULIA R. BROWN **Julia R. Brown**	Director	March 14, 2014
/S/ ERROL B. DE SOUZA **Errol B. De Souza**	Director	March 14, 2014
/S/ ALAN W. DUNTON **Alan W. Dunton**	Director	March 14, 2014

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 members of executive management (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	Sublease, dated December 4, 2012, by and between the Company and B/E Aerospace, Inc. (incorporated by reference to Exhibit 10.2 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2012)
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 and further amended on December 7, 2012, March 13, 2013 and April 10, 2013 (incorporated by reference to Exhibit 99 to the Company's Registration Statement on Form S-8, as filed with the SEC on June 6, 2013 (Registration No. 333-189143))
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))

Exhibit Number	Description
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*	Separation Agreement and Release, dated June 21, 2012, 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 June 30, 2012)
10.6(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))
10.6(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)
10.7*	Separation Agreement and Release, dated as of March 29, 2013, by and between the Company and Jeffrey P. Brennan (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2013)
10.8*	Transition Services Agreement, effective as of August 13, 2013, by and between the Company and Peter A. Zorn (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on August 13, 2013)
10.9*	Employment Agreement, effective as of November 14, 2012, by and between the Company and Stephen A. Hill (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on November 16, 2012)
10.10*	Nonqualified Stock Option Agreement, dated December 3, 2012, by and between the Company and Stephen A. Hill (incorporated by reference to Exhibit 99.1 to the Company's Registration Statement on Form S-8, as filed with the SEC on January 4, 2013 (Registration No. 333-185888))
10.11*	Form of Retention Award Agreement by and between the Company and its executive officers and certain other personnel (incorporated by reference to Exhibit 10.11 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2012)
10.12(a)+	Amended and Restated License Agreement, dated as of March 9, 2004, by and between the Company and University of South Florida Research Foundation, Inc. (incorporated by reference to Exhibit 10.16 to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))
10.12(b)+	Amendment No. 1, effective September 21, 2009, to Amended and Restated License Agreement dated March 9, 2004, by and between the Company and University of South Florida Research Foundation, Inc. (incorporated by reference to Exhibit 10.2 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2009)
10.13(a)+	License Agreement, dated May 26, 1999, by and between the Company and University of Kentucky Research Foundation (incorporated by reference to Exhibit 10.18(a) to the Company's Registration Statement on Form S-1, as filed with the SEC on January 17, 2006 (Registration No. 333-131050))

Exhibit Number	Description
10.13(b)+	Amendment No. 1, dated August 16, 2005, to License Agreement, dated May 26, 1999, by and between the Company and University of Kentucky Research Foundation (incorporated by reference to Exhibit 10.18(b) to Amendment No. 5 to the Company's Registration Statement on Form S-1, as filed with the SEC on April 6, 2006 (Registration No. 333-131050))
10.14(a)+	Collaborative Research and License Agreement, dated as of December 27, 2005, by and between the Company and AstraZeneca AB (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2006)
10.14(b)	Amendment No. 1 dated November 10, 2006 to Collaborative Research and License Agreement between the Company and AstraZeneca AB dated December 27, 2005 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2006)
10.14(c)+	Amendment No. 2 dated July 8, 2009 to Collaborative Research and License Agreement between the Company and AstraZeneca AB dated December 27, 2005 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2009)
10.14(d)+	Amendment No. 3, effective as of April 30, 2010, to Collaborative Research and License Agreement between the Company and AstraZeneca AB dated December 27, 2005 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended June 30, 2010)
10.14(e)+	Amendment No. 4, effective as of September 28, 2010, to Collaborative Research and License Agreement between the Company and AstraZeneca AB dated December 27, 2005 (incorporated by reference to Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2010)
10.14(f)+	Amendment No. 5, effective as of March 5, 2013, to Collaborative Research and License Agreement between the Company and AstraZeneca AB dated December 27, 2005 (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended March 31, 2013)
10.14(g)++	Amendment No. 6, effective as of February 7, 2014, to Collaborative Research and License Agreement between the Company and AstraZeneca AB dated December 27, 2005
10.15+	Amended and Restated Supply Agreement, effective December 3, 2009, by and among the Company, Interchem Corporation and Euticals S.p.A. (as successor to Poli Industria Chimica, SPA) (incorporated by reference to Exhibit 10.19 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2009)
10.16*	Description of Annual Cash Incentive Program (incorporated by reference to Exhibit 10.16 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2012)
10.17*	Description of Non-Employee Director Compensation Program (incorporated by reference to Exhibit 10.17 to the Company's Annual Report on Form 10-K for the Year Ended December 31, 2012)
10.18*	Employment Agreement, effective as of August 26, 2013 by and between the Company and Patrick C. Rock (incorporated by reference in Exhibit 10.1 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2013)
10.19*	Form of Non-employee Director Nonqualified Stock Option Agreement under Targacept, Inc. 2006 Stock Incentive Plan (incorporated by reference in Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended September 30, 2013)
10.20	At-the-Market Issuance Sales Agreement, dated November 26, 2013 (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on November 26, 2013)

Exhibit Number	Description
10.21*	Employment Agreement, effective as of June 28, 2013, by and between the Company and Steven M. Toler, Ph.D. (incorporated by reference to Exhibit 10.3 to the Company's Quarterly Report on Form 10-Q for the Quarter Ended June 30, 2013)
10.22*	Employment Agreement, effective as of June 28, 2013, by and between the Company and David A. Hosford, M.D. (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on June 28, 2013)
10.23*	Amendment No. 1 to Employment Agreement, dated January 24, 2014, by and between the Company and Stephen A. Hill (incorporated by reference to Exhibit 10.1 to the Company's Current Report on Form 8-K, as filed with the SEC on January 28, 2014)
10.24*	Amended and Restated Employment Agreement, dated January 24, 2014, by and between the Company and Alan A. Musso (incorporated by reference to Exhibit 10.2 to the Company's Current Report on Form 8-K, as filed with the SEC on January 28, 2014)
23.1	Consent of Ernst & Young LLP
31.1	Certification of the Chief Executive Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification of the Chief Financial Officer pursuant to Rule 13a-14(a) and 15d-14(a) of the Securities Exchange Act of 1934, as adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1	Certification of the Chief Executive Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
32.2	Certification of the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
101	The following materials from the Company's Annual Report on Form 10-K for the year ended December 31, 2013, formatted in XBRL (eXtensible Business Reporting Language): (i) the Balance Sheets, (ii) the Statements of Operations, (iii) the Statements of Stockholders' Equity, (iv) the Statements of Cash Flows, and (v) Notes to Financial Statements, tagged as blocks of text.

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

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

* Denotes management contract, compensatory plan or arrangement.

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

Exhibit 10.14(g)

CERTAIN CONFIDENTIAL MATERIAL APPEARING IN THIS DOCUMENT, MARKED BY [********], 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.

AMENDMENT NO. 6 TO COLLABORATIVE RESEARCH AND LICENSE AGREEMENT

This Amendment No. 6 to Collaborative Research and License Agreement (this "**Amendment**"), effective as of the date of signature of the last Party to sign below, amends the Collaborative Research and License Agreement entered into as of December 27, 2005 by and between AstraZeneca AB, a company limited by shares organized and existing under the laws of Sweden ("**AstraZeneca**"), and Targacept, Inc., a Delaware (USA) corporation ("**Targacept**"), as amended by Amendment No. 1 dated November 10, 2006, Amendment No. 2 effective July 8, 2009, Amendment No. 3 effective April 30, 2010, Amendment No. 4 effective September 28, 2010 and Amendment No. 5 effective March 5, 2013 (the "**Agreement**"). Capitalized terms used herein and not otherwise defined shall have the meanings ascribed to them in the Agreement.

WHEREAS AstraZeneca and Targacept desire to (a) amend, in accordance with Section 17.6 of the Agreement, the Agreement to modify the compounds that constitute Basket Compounds and (b) memorialize the termination of certain compounds from the Agreement and the agreement of the parties regarding such compounds after termination.

NOW, THEREFORE, in consideration of the mutual covenants contained herein and for other good and valuable consideration, AstraZeneca and Targacept, intending to be legally bound, hereby agree that, as of the effective date of this Amendment:

1. Section 1.52A of the Agreement is hereby deleted in its entirety and replaced with the following:

"1.52A **"Basket Compound"** means each of AZD1446 (TC-6683) [********], in each case identified by the chemical structure acknowledged by the Parties as such compound as of the Amendment No. 5 Date, any enantiomer, metabolite or prodrug of any of the aforementioned compounds, and, in each case, any salt form, polymorph, crystalline form, hydrate, solvate or formulation thereof."

2. Except as expressly amended by this Amendment, all of the terms and conditions of the Agreement shall remain in full force and effect.

3. Termination of Returned Compounds.

(a) With effect on the date of this Amendment, the Agreement shall be terminated with respect to each of [********], [********], [********], [********], [********] (collectively, the "**Returned Compounds**") pursuant to Section 11.2.3 of the Agreement, notwithstanding any prior written notice from AstraZeneca to Targacept otherwise required for such termination pursuant to Section 11.2.3 of the Agreement.

(b) The Parties hereby acknowledge and agree that: (i) as of the effective date of this Amendment, each Returned Compound shall be deemed to be a Terminated Compound and a Terminated AZ Compound; and (ii) no Returned Compound and no metabolite of a Returned Compound shall be, notwithstanding anything in the Agreement to the contrary, an Additional Compound or Excluded Zone Compound, it being the intent of Targacept and AstraZeneca that, notwithstanding anything in the Agreement to the contrary, Targacept and its Affiliates and licensees (and sublicensees, through multiple tiers) shall have (A) the exclusive and unrestricted worldwide right to Exploit Returned Compounds, or any of them, including any salt form, polymorph, crystalline form, prodrug, pharmacologically active metabolite, hydrate, solvate or formulation thereof, in all respects and (B) the non-exclusive and unrestricted worldwide right to Exploit pharmacologically inactive metabolites of Returned Compounds, or any such metabolite, in all respects; provided that Targacept does not by the foregoing clause (B) grant to AstraZeneca any such rights.

[remainder of page intentionally left blank]

IN WITNESS WHEREOF AstraZeneca and Targacept have executed this Amendment as of the respective dates set forth below.

TARGACEPT, INC.		ASTRAZENECA AB (publ.)	
By:	/s/ Stephen A. Hill	By:	/s/ Jan-Olof Jacke
Name:	Stephen A. Hill	Name:	Jan-Olof Jacke
Title:	Chief Executive Officer	Title:	President
Date:	Feb. 7, 2014	Date:	Feb. 6, 2014

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 Nos. 333-189143, 333-133881 and 333-160331) pertaining to the Targacept, Inc. 2006 Stock Incentive Plan,
- Registration Statement (Form S-8 No. 333-185888) of Targacept, Inc. pertaining to the Nonqualified Stock Option Agreement between Targacept, Inc. and Dr. Stephen A. Hill dated December 3, 2012; and
- Registration Statement (Form S-3 No. 333-192552) of Targacept, Inc.;

of our reports dated March 14, 2014, 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, 2013.

/s/ Ernst & Young LLP

Raleigh, North Carolina
March 14, 2014

EXHIBIT 31.1

CERTIFICATION PURSUANT TO RULE 13a-14(a) AND 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Stephen A. Hill, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: March 14, 2014

By: /s/ Stephen A. Hill
Stephen A. Hill
Chief Executive Officer and President
(Principal Executive Officer)

EXHIBIT 31.2

CERTIFICATION PURSUANT TO RULE 13a-14(a) AND 15d-14(a) OF THE SECURITIES EXCHANGE ACT OF 1934, AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Alan A. Musso, certify that:

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

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

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

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

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

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

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

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

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

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

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

Date: March 14, 2014

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

EXHIBIT 32.1

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

In connection with the Annual Report on Form 10-K of Targacept, Inc. (the "Company") for the year ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Stephen A. Hill, President and Chief Executive Officer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

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

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

Date: March 14, 2014

By: /s/ Stephen A. Hill
Stephen A. Hill
Chief Executive Officer and President
(Principal Executive Officer)

EXHIBIT 32.2

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

In connection with the Annual Report on Form 10-K of Targacept, Inc. (the "Company") for the year ended December 31, 2013 as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I, Alan A. Musso, Senior Vice President, Finance and Administration, Chief Financial Officer and Treasurer of the Company, hereby certify, pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, that, to my knowledge:

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

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

Date: March 14, 2014

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