TorreyPines Therapeutics, Inc.
Form 10-K
March 29, 2007

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

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

For the fiscal year ended December 31, 2006

Or

o 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: 000-25571

TorreyPines Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

DELAWARE	**86-0883978**
State or other jurisdiction of incorporation or organization	(I.R.S. Employer Identification No.)
11085 North Torrey Pines Road, Suite 300 La Jolla, California	**92037**
(Address of principal executive offices)	(Zip Code)

Registrant s telephone number, including area code: (858) 623-5665

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

Common Stock, $0.001 par value

(Title of class)

The Nasdaq Stock Market LLC

(Name of Each Exchange on Which Registered)

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

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

Indicate by check mark if disclosure of delinquent filers pursuant to Item 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. x

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

Large accelerated filer o Accelerated filer o Non-accelerated filer x

Indicate by check mark where the registrant is a shell company (as defined in Rule 12b-2 of the Act). o Yes x No

The aggregate market value of the Common Stock of the registrant (the Common Stock) held by non-affiliates of the registrant, based on the last sale price of the Common Stock on June 30, 2006 (the last business day of the registrant s most recently completed second fiscal quarter) of $6.80 per share (as adjusted for a subsequent 8-for-1 reverse stock split) as reported by the Nasdaq National Market, was approximately $34,037,000. Shares of Common Stock held by each officer and director and by each person who is known by the registrant to own 5% or more of the outstanding Common Stock, if any, have been excluded in that such persons may be deemed to be affiliates of the registrant. Share ownership information of certain persons known by the registrant to own greater than 5% of the outstanding common stock for purposes of the preceding calculation is based solely on information on Schedules 13D and 13G, if any, filed with the Securities and Exchange Commission and is as of June 30, 2006. This determination of affiliate status is not necessarily a conclusive determination for any other purposes.

As of March 15, 2007 there were 15,700,039 shares of our Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the registrant s definitive Proxy Statement to be filed with the Securities and Exchange Commission by April 30, 2007 are incorporated by reference into Part III of this Annual Report on Form 10-K.

TORREYPINES THERAPEUTICS, INC.
FORM 10-K

For the Year Ended December 31, 2006

TABLE OF CONTENTS

PART I

Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements that involve a high degree of risk and uncertainty. Such statements include, but are not limited to, statements containing the words believes, anticipates, expects, estimates and words of similar import. Our actual results could differ materially from any forward-looking statements, which reflect management s opinions only as of the date of this report, as a result of risks and uncertainties that exist in our operations, development efforts and business environment. Unless required by law, we undertake no obligation to update or revise any forward-looking statements to reflect new information or future events or developments. Thus, you should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. You should carefully review the risks described in Risk Factors and elsewhere in this Annual Report on Form 10-K and the risk factors described in other documents that we file from time to time with the Securities and Exchange Commission, or SEC, including our Quarterly Reports on Form 10-Q.

TorreyPines Therapeutics and design, our tree logo and Posiphen are our trademarks or registered trademarks in the United States and certain other countries. We may also refer to trademarks of other corporations and organizations in this document.

Item 1. Business.

Overview

Prior to October 3, 2006, we were known as Axonyx Inc. On October 3, 2006, we completed a business combination, referred to as the Merger, with TorreyPines Therapeutics, Inc. (now known as TPTX, Inc.). For accounting purposes, we were deemed to be the acquired entity in the Merger. In connection with the Merger, we changed our name to TorreyPines Therapeutics, Inc. and effected an 8-for-1 reverse stock split of our Common Stock. All references to TorreyPines, we, us, our or the Company mean TorreyPines Therapeutics, Inc. and its subsidiaries, except where it is made clear that the term means only the parent company.

We are a biopharmaceutical company committed to the discovery, development and commercialization of novel small molecules to treat diseases and disorders of the central nervous system. Our therapeutic focus is in two areas: chronic pain, including migraine and neuropathic pain; and cognitive disorders, including cognitive impairment associated with schizophrenia and Alzheimer s disease. Through our in-house discovery programs and strategic in-licensing, we have built a robust pipeline of eight product candidates for these indications.

We currently have two product candidates in clinical trials for chronic pain. We initiated a Phase IIb clinical trial of tezampanel, our lead product candidate for chronic pain, in October 2006. This clinical trial will evaluate the use of tezampanel for the abortive treatment of migraine. We expect to have top line results from this clinical trial in the second half of 2007. We are currently conducting a Phase I clinical trial for our follow-on product candidate for chronic pain, NGX426.

We currently have one product candidate in clinical trials for cognitive disorders. NGX267 is our lead product candidate for the treatment of cognitive impairment associated with schizophrenia, or CIAS. We have completed two Phase I clinical trials of NGX267. We initiated an additional Phase I clinical trial of NGX267 in March 2007. Assuming favorable results, we intend to initiate a Phase II clinical trial in the second half of 2007. The Phase II clinical trial would evaluate NGX267 for the treatment of CIAS. We expect that NGX267 would be used as adjunctive therapy to current antipsychotic therapy to treat schizophrenia. Our second product candidate for the treatment of CIAS, NGX292, is currently in

preclinical development. In addition, although not the primary targeted indication, we may also evaluate NGX267 and NGX292 for the potential treatment of Alzheimer s disease.

We also have four product candidates in development and two programs in discovery focused on cognitive disorders. Phenserine, Posiphen, bisnorcymserine and NGX555 are in various stages of development for the treatment of Alzheimer s disease. We have completed Phase III clinical trials of phenserine and are currently pursuing out-licensing opportunities. Phase I clinical trials have been completed on Posiphen. Bisnorcymserine and NGX555 are currently in preclinical development. Our two drug discovery programs are focused on discovering and validating small molecules and novel molecular targets for Alzheimer s disease, and we are conducting both programs in collaboration with Eisai Co., Ltd., a leader in Alzheimer s disease research.

Our Product Development Programs

Our product development efforts focus on treatments for diseases and disorders of the central nervous system, or CNS. Within the broad CNS therapeutic category, we are currently concentrating on two main areas: chronic pain, including migraine and neuropathic pain; and cognitive disorders, including CIAS and Alzheimer s disease.

Our current product candidates, the lead indication associated with each candidate and the current development status of these candidates are illustrated in the following chart:

Product Candidate	**Lead Indication**	**Development Status**
Chronic Pain		
Tezampanel	Migraine	Phase IIb
NGX426	Migraine	Phase I
Cognitive Disorders		
NGX267	CIAS*	Phase I
NGX292	Alzheimer s disease	Preclinical
Phenserine	Alzheimer s disease	Phase III
Posiphen	Alzheimer s disease	Phase I
Bisnorcymserine (BNC)	Alzheimer s disease	Preclinical
NGX555	Alzheimer s disease	Preclinical

* Cognitive Impairment Associated with Schizophrenia

We currently have worldwide commercial rights to all of our product candidates, with the exception of phenserine. In January 2006, we granted to Daewoong Pharmaceutical Company, Ltd., or Daewoong, the commercialization rights for phenserine in South Korea.

Our Product Candidates for Chronic Pain

Tezampanel for the Treatment of Migraine

We in-licensed tezampanel from Eli Lilly & Company, or Eli Lilly, in 2003. Preclinical and clinical data suggest that tezampanel has the potential to be effective across a wide range of therapeutic applications both within and extending beyond the area of chronic pain. We believe that tezampanel has an opportunity to be a first-in-class treatment for various types of chronic pain, including migraine. We are currently developing tezampanel given by subcutaneous administration for the treatment of migraine.

Migraine

Despite being a common disorder, the biological cause of migraine is poorly understood. Until recently, the prevailing theory of the cause of migraine was dilation of the blood vessels in the brain which results in increased blood flow. Currently prescribed treatments for migraine, such as triptans, work by constricting blood vessels and thereby decrease blood flow. Treatments that decrease blood flow are only effective in relieving the pain and the accompanying symptoms of the current migraine attack. None of these products addresses other biological mechanisms that may initiate, aggravate, prolong or increase the frequency of migraines.

The 2005 American Migraine Prevalence and Prevention, or AMPP, study, sponsored by the National Headache Foundation, estimated that there are approximately 30 million people who suffer from migraines in the United States, with fewer than half that number seeking treatment. Since 1992 when Imitrex®, the current market leader, was introduced, a number of new products have entered the approximately $2 billion United States market for prescription medicines for migraine. However, there has been no treatment with a new mechanism of action introduced in the migraine market in over a decade. The AMPP study also confirmed that, despite the number of products available to treat migraines, large numbers of migraine sufferers are not getting adequate treatment or the relief they need.

Tezampanel

We believe that tezampanel has an opportunity to be a novel treatment for migraine. Tezampanel is an AMPA/kainate, or AK, receptor antagonist. AK receptors are part of the biological pathway that transmits pain signals to the brain. We believe that tezampanel works by selectively binding certain AK receptors to block the transmission of pain signals. For migraine sufferers, tezampanel may offer treatment of the pain associated with migraine as well as a reduction in the frequency or severity of subsequent migraines. We believe that tezampanel will potentially have the following product profile:

- comparable efficacy to triptans, morphine and other prescription pain relievers;
- improved safety relative to triptans, morphine therapies and other prescription pain relievers; and
- not cause physical dependence.

Additionally, unlike current treatment options, tezampanel does not constrict blood vessels. Theoretically, this may enable the use of tezampanel in patients who have been advised not to use triptans because they suffer from hypertension, peripheral vascular disease, coronary artery disease, or cerebrovascular disease. In addition, unlike current treatment options such as triptans, tezampanel does not work through binding to a serotonin receptor. This may enable tezampanel s use in patients who have been advised not to take a triptan if they are also taking antidepressant medication because of the potential of that combination to produce a serious side effect known as the serotonin syndrome .

Clinical Development Status

At the time we in-licensed tezampanel, it had been evaluated in five Phase IIa clinical trials using intravenous administration. In one of the Phase IIa clinical trials, tezampanel was evaluated for the treatment of migraine. The data from this clinical trial demonstrated that tezampanel was well-tolerated and more effective than placebo in relieving migraine pain. Additionally, tezampanel was found to be as effective as subcutaneous Imitrex® in relieving pain and in treating the typical symptoms of migraine, including nausea, vomiting, and sensitivity to light and sound. In this clinical trial tezampanel was better tolerated than Imitrex®, although the small number of patients in the trial provided limited data for this comparison. Based on this and other data we made the decision to move forward with the development of tezampanel for the treatment of migraine. To expand the potential market opportunity we are developing tezampanel given by subcutaneous administration.

In November 2005, we initiated a Phase I single dose, placebo-controlled, dose-escalation clinical trial of tezampanel in healthy adult males. The goal of the clinical trial was to evaluate safety and tolerability, to identify the maximum tolerated single dose, and to characterize the pharmacokinetics of a dose of tezampanel given by subcutaneous injection. This clinical trial concluded in May 2006 with 110 healthy male adults enrolled, 88 of whom were exposed to tezampanel. The maximum tolerated single dose was determined to be 100 mg. At all doses up to and including 100 mg, tezampanel was well tolerated by the participants and no serious adverse events were reported.

In October 2006, we initiated a Phase IIb clinical trial of tezampanel, given subcutaneously, in patients who suffer a single acute migraine attack. The clinical trial is a randomized, double-blind, placebo-controlled, parallel-group, single dose, dose-ranging study to evaluate three doses of tezampanel, 40 mg, 70 mg, and 100 mg, compared to placebo. The total sample size is approximately 300 subjects or 75 subjects per treatment arm. We expect to report top line results from this clinical trial in the second half of 2007. A primary objective of this clinical trial is to identify one or more doses of tezampanel that are safe and effective and that can be evaluated in future Phase III clinical trials.

Other Indications

Preclinical and clinical data suggest that tezampanel has the potential to be effective across a wide range of therapeutic applications both within and extending beyond the area of chronic pain. Tezampanel was shown to be efficacious in validated preclinical models of epilepsy, cerebral neuroprotection, generalized anxiety disorder, and muscle spasticity and rigidity secondary to spinal cord injury as well as persistent pain.

In three separate double-blind, placebo-controlled, Phase IIa clinical trials, tezampanel was statistically superior to placebo in relieving lower back pain, pain from spinal cord trauma and post-operative pain. In another Phase IIa clinical trial, using a capsaician-induced pain model, tezampanel was shown to relieve the pain and hypersensitivity associated with central sensitization. The capsaicin model is a validated approach in humans to create a controlled, central sensitization effect by injecting capsaicin, an irritating substance, under the skin. In central sensitization, the body develops a memory for pain that abnormally alters subsequent responses to both painful and normally non-painful stimuli. Central sensitization is commonly seen in a number of chronic pain conditions. Collectively, these four Phase IIa clinical trials support the experimental premise that tezampanel relieves pain from a variety of sources. In the second half of 2007, we anticipate initiating a multiple dose clinical trial of tezampanel, given by subcutaneous administration.

NGX426 for the Treatment of Migraine.

NGX426, also in-licensed from Eli Lilly in 2003, is the oral prodrug of tezampanel. We are initially developing NGX426 as a treatment for migraine.

In June 2006, we filed an Investigational New Drug application, or IND, for NGX426 with the United States Food and Drug Administration, or FDA, Division of Neurology. In August 2006, we initiated a Phase I clinical trial of NGX426 designed as a randomized, double-blind, placebo-controlled, single dose dose-escalation study in 30 healthy adults. This clinical trial evaluated three doses of NGX426, 10 mg, 20 mg, and 30 mg, given orally. The primary objective of the clinical trial was to determine the rate and extent of conversion of NGX426, the prodrug, to tezampanel, the active compound. The clinical trial was completed in November 2006 and results indicated that NGX426 was well-tolerated and rapidly converted to tezampanel at the three doses tested with levels of NGX426 at or below the lower limit of detection.

In February 2007, we initiated a second Phase I clinical trial of NGX426 to identify the maximum tolerated single dose of NGX426 when given to healthy adults. This clinical trial is designed as a randomized, double-blind, placebo-controlled study in which healthy adults will receive placebo or an

escalating single dose of NGX426. A total of approximately 60 participants will be enrolled in cohorts of 10, with 8 subjects receiving NGX426 and 2 subjects receiving placebo. The doses to be tested range from 40 mg to 90 mg. The primary objective of this clinical trial is to determine the maximum safe and well-tolerated single dose of orally-administered NGX426. We expect to report results of this clinical trial in the second half of 2007.

Our Product Candidates for Cognitive Disorders

NGX267 and NGX292 for Treatment of CIAS and Alzheimer s Disease.

We in-licensed NGX267 and NGX292 from Life Science Research Israel, or LSRI, in May 2004. NGX267 is currently in Phase I clinical development for the treatment of CIAS. NGX292, a metabolite of NGX267, is a back-up compound in preclinical testing. NGX267 and NGX292 may also be developed for the treatment of Alzheimer s disease.

Cognitive Impairment Associated with Schizophrenia (CIAS)

Schizophrenia is a chronic and disabling mental illness that affects approximately 2.4 million adults in the United States. The illness is characterized by positive symptoms such as hallucinations and delusions as well as negative symptoms such as social isolation, withdrawal, and cognitive impairment. While there have been significant advances in the treatment of schizophrenia, the currently approved antipsychotic drugs primarily treat the positive symptoms. An emerging approach to improving the functional ability of patients with schizophrenia is to develop therapies that will improve their cognitive impairment. There are no current approved therapies for CIAS.

Market research conducted on our behalf supports our belief of the medical need and market opportunity for therapies to treat CIAS. According to this focus group research, more than half of adults diagnosed with schizophrenia have some form of cognitive impairment. In addition, physicians reported that a general assessment of cognitive function is routinely performed on approximately 80% of patients. Physicians cite poor working memory and reduced attention as the most common symptom of CIAS, and they confirm that the most significant unmet need in treating schizophrenia is improving work, school and social functionality for patients.

Alzheimer s Disease

Alzheimer s disease, the major cause of dementia in the elderly, is a chronic neurodegenerative disorder. According to the Alzheimer s Association, an estimated 5.0 million Americans have Alzheimer s disease, including 1 in 8 people over 65 and half of those over 85. Additionally, between 1980 and 2000, the number of people in the United States with Alzheimer s disease has more than doubled, and by 2050 the number of individuals with Alzheimer s disease could range from 11-16 million people in the United States. The characteristic signs and symptoms of Alzheimer s disease are gradual and characterized by a progressive decline in memory, problems with reasoning, difficulty in learning, and loss of language skills as well as secondary impairments that affect behavior and basic activities of daily living.

Alzheimer s disease is associated with a loss of nerve cells that release acetylcholine, a key substance involved in learning and working memory. The loss of these nerve cells, resulting in a depletion of acetylcholine, is progressive and results in profound memory disturbances and irreversible impairment of cognitive function. It has also long been hypothesized that the cause of Alzheimer s disease lies in the build up of protein deposits, referred to as amyloid plaques, in the brain. The plaques are largely comprised of aggregations of a peptide referred to as amyloid ß, or Aß, peptide. A specific Aß peptide, Aß42, is thought to play a significant role in the cause of Alzheimer s disease.

There are currently no approved products to treat the underlying cause of Alzheimer s disease or to modify the progression of the disease. All of the approved products, as well as many of the compounds under development for Alzheimer s disease, treat or intend to treat only the signs and symptoms of Alzheimer s disease. The most commonly prescribed products, acetlycholinesterase inhibitors, such as Aricept®, prevent the breakdown of intact acetylcholine leading to symptomatic improvement in memory, thinking, and activities of daily living. However, as the disease progresses, these drugs may lose their effectiveness and may be unable to slow the neurological decline.

NGX267 and NGX292

NGX267 is a partial muscarinic agonist with functionally specific M1 receptor activity. The pharmacological properties of NGX267 partially mimic the action of acetylcholine by stimulating the M1 receptors. Activation of the M1 receptor is thought to have the most potential for improving cognitive function because of the predominance of M1 receptors in areas of the brain involved in memory and cognition. NGX267 has been demonstrated in animal models to be effective in improving cognitive deficits in learning and memory.

In addition to improving cognition, a second mechanism of action, the reduction of Aß42, also supported by preclinical data, suggests that NGX267 may be effective as a treatment to delay the onset or to slow the progression of Alzheimer s disease. In transgenic mice, a specific animal model used in Alzheimer s disease studies, NGX267 has been shown to reduce Aß42 and to prevent the formation of amyloid plaques.

Because impairments in memory and learning have been demonstrated in both Alzheimer s disease patients and schizophrenic patients, we believe that we have a strong rationale to develop NGX267 as a treatment for Alzheimer s disease and CIAS. We have chosen CIAS as our initial indication for NGX267 because we believe we can generate proof of concept data for the treatment of CIAS more quickly than we can generate proof of concept data for the treatment of Alzheimer s disease. CIAS targets a younger and somewhat healthier population, potentially aiding clinical trial enrollment. In addition, we believe the design of a clinical trial for the treatment of CIAS may allow for a shorter clinical treatment duration than a clinical trial for the treatment of Alzheimer s disease. While we anticipate showing beneficial effects on memory and learning, it is unlikely that NGX267 would be effective in controlling symptoms such as hallucinations or delusions that are associated with schizophrenia. Therefore, our clinical program will evaluate NGX267 as adjunctive, or add-on, therapy with commonly used antipsychotics.

NGX292, the major metabolite of NGX267, has demonstrated a biological profile similar to the profile of NGX267. NGX292, also in-licensed from LSRI in 2004, is currently in preclinical development.

Clinical Development Status

In July 2005, we initiated a Phase I, first-in-human clinical trial of NGX267. The clinical trial was designed as a double-blind, placebo-controlled, ascending dose study. The goal of the clinical trial was to identify the maximum tolerated single dose of NGX267 in healthy young adult males and to evaluate the safety and tolerance of single doses of NGX267 given to healthy young adult males. The clinical trial, completed in October 2005, enrolled a total of 34 subjects and identified the maximum tolerated single dose of NGX267 as 35 mg. All doses up to and including 35 mg were well tolerated by the participants and there were no reports of serious adverse events.

In January 2006, we initiated a second Phase I clinical trial of NGX267 of similar design in a population of healthy elderly males and females. We anticipated that healthy elderly individuals would be more sensitive to NGX267. The clinical trial, completed in July 2006, enrolled a total of 26 subjects and identified 15 mg as the maximum tolerated dose. The clinical trial confirmed the safety and tolerability of a

single dose of NGX267 up to 15 mg in a healthy elderly population. There were no reports of serious adverse events in the clinical trial.

In March 2007, we initiated a multiple dose Phase I clinical trial of NGX267. We anticipate data from this clinical trial will be available in the second half of 2007. Assuming favorable results from this multiple dose clinical trial, we plan to initiate a Phase II clinical trial in the second half of 2007 evaluating NGX267 as a potential treatment for CIAS. We do not intend to initiate any clinical trials of NGX267 in 2007 for the treatment of Alzheimer s disease.

Phenserine for Alzheimer s Disease

Phenserine, an acetylcholinesterase inhibitor, has the potential to both provide symptomatic improvement and treat disease progression in patients with mild to moderate Alzheimer s disease. A total of three Phase III clinical trials were initiated in 2003 and 2004 to evaluate phenserine in patients with Alzheimer s disease. In the first completed clinical trial, phenserine failed to demonstrate efficacy on the primary outcome measures, the Alzheimer s Disease Assessment Scale-cognitive subscale, or ADAS-cog, and the Clinical Interview Based Impression of Change, or CIBIC+, when compared to placebo. Given these results, enrollment in the two identically designed ongoing clinical trials, was halted. The data from the two halted clinical trials, analyzed as a single clinical trial, did not demonstrate a statistically significant benefit for phenserine compared to placebo in either the ADAS-cog or CIBIC+ primary outcome measures evaluated after 3 months of treatment. Further analysis of the data from these clinical trials, conducted as part of our strategy to identify a development partner for phenserine, demonstrated a statistically significant benefit of phenserine over placebo as measured by the ADAS-cog and a positive trend towards improvement in the CIBIC+ in the prospectively randomized group of patients who were dosed at the highest dose, 15 mg, for more than 12 weeks. At this time, there are no ongoing clinical trials of phenserine and we do not intend to initiate any additional clinical trials.

In January 2006, we announced that we granted to Daewoong an exclusive license for the use of phenserine in the South Korean market. Under the terms of the agreement Daewoong, at its own cost, agreed to pursue the product development and regulatory work necessary for a new drug application, or NDA, or its equivalent in South Korea. We are continuing our efforts to look for additional development partners for phenserine.

Posiphen for Alzheimer s Disease

Posiphen, the positive isomer of phenserine, has potential application as a disease modifying agent to slow or delay the progression of Alzheimer s disease. Posiphen has been shown to lower beta-amyloid precursor protein and beta-amyloid levels in preclinical studies. Two Phase I clinical trials have been completed for Posiphen. The first Phase I single ascending dose clinical trial was completed in January 2006. The data from this double-blind, placebo controlled clinical trial in healthy men and women demonstrated that Posiphen appears to be well tolerated at single doses up to and including 80mg with no serious adverse events being reported.

In May 2006, we announced the completion of a multiple dose Phase I clinical trial with Posiphen in healthy volunteers. This multiple ascending-dose clinical trial examined the effects of 20, 40 and 60 mg doses of Posiphen given four times daily, for a period of 7, 7 and 10 days, respectively. Participants were enrolled in groups of 16, with 12 subjects receiving Posiphen and 4 subjects receiving placebo. The clinical adverse event data from this clinical trial appears to be generally consistent with the results of the earlier single ascending dose Phase I clinical trial that suggested that Posiphen was well tolerated with no serious adverse events reported. There are currently no plans to conduct additional clinical trials with Posiphen in patients with Alzheimer s disease in 2007.

Bisnorcymserine for Alzheimer s Disease

Bisnorcymserine, or BNC, is a potential treatment to improve the symptoms of patients with severe Alzheimer s disease. A butyrylcholinesterase inhibitor, BNC selectively inhibits butyrylcholinesterase, an enzyme similar to acetylcholinesterase. Normally these two enzymes coexist throughout the body, with acetylcholinesterase predominating in degrading acetylcholine. In the brain of Alzheimer s disease patients, as acetylcholinesterase levels gradually fall, there appears to be a concomitant increase in butyrylcholinesterase levels in specific nerve pathways within areas of the brain associated with Alzheimer s disease. Like acetylcholinesterase, butyrylcholinesterase degrades acetylcholine, decreasing the availability of this key neurotransmitter. BNC, by blocking the action of butyrylcholinesterase, should increase the availability of acetylcholine, potentially improving memory and cognition. We plan to complete the current on-going preclinical studies and seek development partners for BNC.

NGX555 for Alzheimer s Disease

NGX555, a gamma-secretase modulator, was discovered through our internal research. NGX555 is in early preclinical testing and we believe it may represent a new generation of disease modifying therapies that target the mechanism underlying Alzheimer s disease. Preclinical data suggests that NGX555 may be effective in lowering levels of Aß42 in animals.

Our Drug Discovery Programs

We have two drug discovery programs, a gamma-secretase modulator program and an Alzheimer s disease genetics program, both undertaken in collaboration with Eisai, a leader in Alzheimer s disease research. These programs are focused on discovering and validating novel small molecules and molecular targets for Alzheimer s disease.

Gamma-secretase Modulator Program

Our approach to Alzheimer s disease drug discovery is firmly rooted in the amyloid hypothesis. First generation approaches to lowering Aß42 focused on inhibiting, as opposed to modulating, the activity of a large, complex and essential enzyme called gamma-secretase that is involved in the production of Aß42. Gamma-secretase inhibitors have been associated with side effects presumably because they completely block the functioning of the enzyme.

We have identified two distinct series of second generation compounds that modulate, or influence, the gamma-secretase enzyme as opposed to inhibiting it. These gamma-secretase modulators, or GSMs, reduce the brain levels of Aß42 while maintaining the critical overall balance of Aß in the brain. They do this by influencing the enzyme to make shorter, less toxic Aß peptides at the expense of the longer, toxic Aß42 peptide. Because GSM compounds allow the gamma-secretase enzyme to perform its normal functions, they appear to have addressed some of the side effects associated with the first generation compounds that fully inhibited enzyme functioning.

Our GSM compounds are oral, small molecules that have been shown to penetrate the blood brain barrier upon chronic oral dosing in rodents. In the brain, they appear to preferentially lower A 42 levels by modulation of gamma-secretase.

Alzheimer s Disease Genetics Program

Since its inception in 2001, our Alzheimer s disease genetics program has been a shared research effort between us and Dr. Rudolph E. Tanzi, a founder of TPTX and Director, Genetics and Aging Research Unit at Massachusetts General Hospital. Our genetics research program integrates human genetic mapping, genomics, and bioinformatics. Dr. Tanzi, a leading geneticist, has been involved in the

discovery of all three early-onset familial Alzheimer s disease genes. The goals of our genetics research program are two-fold: to provide new targets for drug discovery, and to facilitate methods for reliably predicting and diagnosing Alzheimer s disease.

Recent data suggests that up to 80% of cases of Alzheimer s disease have a genetic component. In 2005, the scope of our Alzheimer s disease genetics program was significantly expanded to include a comprehensive and state-of-the-art screening of over 400 families, comprising more than 1,600 participants with late-onset Alzheimer s disease. The resulting whole-genome family-based association screen is expected to identify up to 95% of the genetic variants and mutations conferring risk or protection for Alzheimer s disease. Once completed, this screening may enhance our ability to identify novel pathways involved in the cause and course of Alzheimer s disease and to strengthen our pipeline with new targets for drug discovery.

Our Business Strategy

Our goal is to discover, develop and commercialize important new therapies to treat patients suffering from CNS diseases and disorders. Key aspects of our strategy include the following:

Maintain a balanced and diversified CNS portfolio with respect to development time and risk

We intend to maintain a balanced portfolio of CNS product candidates, taking into account overall development time and risk. Our product candidates for chronic pain have demonstrated Phase IIa proof of concept clinical trial results and have a shorter development timeline when compared to our product candidates for the treatment of cognitive disorders such as CIAS and Alzheimer s disease, which represent longer term opportunities. We believe that this diversified approach to development, potentially supplemented by in-house discovery and strategic product acquisitions, will provide us an opportunity to build a stable and sustainable CNS company.

Access new product candidates through in-house discovery efforts and strategic product acquisitions

We believe that our in-house discovery operation is an important component in fulfilling our goal of delivering important new CNS therapies to patients. In addition to internally growing our product candidate pipeline, our discovery operations reinforce a corporate culture of innovation and leading-edge science that we believe will attract highly accomplished scientists. Supplementing these discovery operations, we may pursue additional product candidate acquisitions and in-licenses.

Attract, retain, and develop world-class scientists, drug developers, and management

We believe that our employees and the culture in which they operate provide the platform for building and sustaining our competitive advantage. We have assembled a management team and scientists with significant industry experience to lead the discovery, development, and commercialization of our product candidates. Members of our management team have contributed to the discovery, development, and approval of multiple drug candidates to treat CNS diseases and disorders, and have been directly involved in the development of Exelon® for Alzheimer s disease, Maxalt® for migraine, and Stadol® for pain.

Establish strategic alliances to maximize the commercial potential of our product candidates

In order to be successful and deliver meaningful new treatments to patients, we intend to advance our product candidates to key milestones, such as early proof of concept, and then, if appropriate, enter into strategic alliances. These alliances are intended to fund expensive, late stage development programs in chronic pain and cognitive disorders and in some cases to provide the large sales forces needed for commercialization.

Strategic Alliance, License and Other Commercial Agreements

We understand that drug development is long and costly and we may need strategic partners to maximize the potential of one or more of our product candidates. Our goal is to strike a balance between advancing product development at our expense and partnering with third parties at key points along the development path to advance our product candidates. Overall, our strategy is to reach key milestones, such as early proof of concept data, with our product candidates before entering into strategic alliances. We believe that, in this way, significant commercial value in the product candidates can be retained while obtaining strategic and financial assistance to advance our programs. We speak to prospective partners on a regular basis, understanding that discussions and ultimately mutually beneficial strategic alliances are the result of ongoing relationship building.

In addition to strategic development alliances, our alliance strategy also includes entering into agreements or partnerships that provide pharmaceutical drug developers with access to our drug discovery technologies. To date, we have entered into two such strategic alliances with Eisai, one for our gamma-secretase modulator program and one for our Alzheimer s disease genetics research program.

Since inception, our revenue has been derived from our strategic alliances. For the fiscal year ended December 31, 2006, 100% of our revenue was derived from our agreement with Eisai.

Eisai

Since March 2001, we have had an ongoing relationship with Eisai with respect to our Alzheimer s disease drug and target discovery programs.

2005 Collaboration Agreement

In February 2005, we entered into a collaboration agreement with Eisai regarding our program for discovery of novel, small molecule compounds designed to delay the onset or slow the progression of Alzheimer s disease. Under the agreement, Eisai has exclusive, time-limited rights of first negotiation and refusal for compounds discovered in the course of the program.

We received an initial $10.0 million cash payment from Eisai in consideration of the rights granted to Eisai under the agreement. The agreement had an initial two-year term that Eisai elected to extend for an additional 12 months for an additional fee of $5.0 million.

2005 Alzheimer s Disease Genetics Research Program Cooperation Agreement

In October 2005, we entered into a cooperation agreement with Eisai to continue to work together on our Alzheimer s disease genetics research program that focuses on the discovery of genes responsible for late onset Alzheimer s disease. The agreement has a two-year term and may be extended by Eisai for up to an additional 12 months. Under the agreement, Eisai is funding our work regarding the genetics program and Eisai has exclusive time-limited rights of first negotiation and refusal for gene targets discovered and validated in the course of the genetics program. The total payments we may receive under this agreement are approximately $15.0 million, which includes research support and a cash payment for the right of first negotiation and refusal, and an extension fee if Eisai chooses to extend the agreement.

Eli Lilly

In April 2003, we entered into a development and licensing agreement with Eli Lilly to obtain an exclusive license to Eli Lilly s AK antagonist assets including tezampanel, and its prodrug NGX426. We paid Eli Lilly an up-front license fee of $6.0 million under the agreement. If specified development, regulatory and commercial milestones are achieved, we will be obligated to make milestone payments to Eli Lilly. We are also obligated to pay royalties to Eli Lilly on any sales of tezampanel and NGX426. We

are required to use commercially reasonable efforts to develop and commercialize the product candidates subject to the agreement, including use of commercially reasonable efforts to achieve specified development events within specified timeframes.

The term of the development and licensing agreement will continue until all royalty payment obligations have expired on a country-by-country basis, unless the agreement is earlier terminated. Under certain termination circumstances, all of the rights granted to us under the agreement will revert to Eli Lilly.

Life Science Research Israel (LSRI)

In May 2004, we entered into an agreement with LSRI to obtain an exclusive license to their muscarinic agonist assets including NGX267 and NGX292. No up-front license fee was paid. For the first two years of the agreement, we provided specified amounts of research funding to LSRI. Through December 31, 2006 we paid LSRI total milestone payments of approximately $2.2 million. If additional specified development, regulatory and commercial milestones are achieved, we will be obligated to make milestone payments to LSRI which may total up to an additional $18.3 million. We are also obligated to pay royalties to LSRI on sales of NGX267 and NGX292 and to pay LSRI a percentage of specified payments we receive upon sublicensing rights to either compound, subject to a minimum amount payable to LSRI for the first sublicense. If we sublicense rights to a compound after a specified point in development of the compound, LSRI will select the level of royalty and sublicense payments from among the alternatives provided in the agreement. We are required to use commercially reasonable efforts to develop and commercialize the product candidates subject to the agreement, including use of commercially reasonable efforts to achieve specified development events within specified timeframes.

The term of the agreement will continue on a country-by-country basis until the later of a specified number of years from the date of first commercial sale of a product in such country or the expiration in such country of the last-to-expire patent covering a product candidate licensed under the agreement, provided, however, that in the event that generic competition occurs in such country and results in a loss of a certain percentage of the market share for such product then the royalty payments will terminate in such country.

CURE, LLC, Public Health Service/National Institutes of Health

On February 27, 1997, we acquired the worldwide exclusive patent rights to phenserine and certain additional compounds via a sublicense with CURE, LLC, referred to as CURE, from the Public Health Service, parent agency of the National Institutes of Health/National Institute on Aging.

Under the license agreement, we agreed to pay royalties to CURE of up to 3% of the first $100 million and 1% thereafter, of net product sales of, and sub-licensed royalties on, products developed from the patented technologies. We also agreed to pay an upfront fee in the amount of $25,000, milestone payments aggregating $600,000 when certain clinical and regulatory milestones are reached, and patent filing and prosecution costs. We have been paying minimum annual royalty payments of $10,000 since January 31, 2000, which will increase to $25,000 per year on commencement of sales of a product until the expiration or termination of the agreement.

Pursuant to the agreement, we are obligated to achieve certain development deadlines or the acquired patent rights may revert to CURE. On May 27, 2002, we signed an amendment letter with CURE that amends the reversionary rights provision of the license agreement extending the deadlines by which we are to achieve certain development milestones.

The general terms of this agreement continue until the last to expire of the licensed patents. We may also terminate this agreement without cause with 60 days notice.

University of Iowa Research Foundation

We have a license agreement with the University of Iowa Research Foundation, or UIRF, pursuant to which UIRF has granted us an exclusive United States license to certain patents and patent applications relating to spinal administration of tezampanel. Under the terms of the agreement we have the right to sublicense our license.

If we achieve specified regulatory and patent-related milestones, we will be obligated to make milestone payments to UIRF which may total up to $0.4 million. We must also pay UIRF an annual license maintenance fee which may be reduced by the amount of other payments made by TorreyPines to UIRF under the agreement. We are also obligated to pay royalties to UIRF on any sales of tezampanel using the licensed patent rights and to pay UIRF a percentage of specified payments we receive upon sublicensing rights to the licensed patent rights. We are required to use commercially reasonable efforts to commercialize products using the licensed patent rights.

This agreement will continue until the expiration of the last-to-expire of the licensed patents and patent applications unless earlier terminated.

Johnson & Johnson Development Corporation

We have an agreement with Johnson & Johnson Development Corporation, or JJDC, regarding our development work into the effects of using M1 agonists, such as NGX267 and NGX292, in the treatment of CNS diseases and disorders. Upon completion of a specified level of development of our lead M1 agonist, we are obligated to provide results for the compound to JJDC. For a specified period of time following receipt of the results, or at an earlier time as agreed to by both parties, JJDC has the exclusive right of first negotiation with us regarding rights or products related to our M1 agonist program.

Competition

We and our strategic alliance partners face intense competition. We are in competition with fully integrated pharmaceutical companies, smaller companies that may be collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have prescription products for chronic pain, migraine, neuropathic pain and Alzheimer s disease already approved by the FDA or they are pursuing the same or similar approaches to those which constitute our discovery and development platforms and operate larger research and development programs in these fields than ours. In addition, while there are no approved therapies for CIAS, this is an emerging focus for many CNS companies, creating future competition in development and commercialization. Lastly, many of these competitors, either alone or together with their collaborative partners, have substantially greater financial resources than us, as well as greater experience in developing pharmaceutical products, undertaking preclinical testing and human clinical trials, obtaining FDA and other regulatory approvals of products, formulating and manufacturing pharmaceutical products, and launching, marketing, distributing and selling products.

We believe that competition for the chronic pain, migraine, CIAS and Alzheimer s disease products that we and any future strategic alliance partners may develop will come from companies that are conducting research, engaging in clinical development, or currently marketing and selling therapeutics to treat these conditions. These competitors include the industry s leading CNS companies.

Migraine and Chronic Pain

Current Treatments for Migraine

Triptans are the most commonly prescribed drugs for the treatment of moderate to severe migraine. There are seven triptans approved for use and Imitrex®, marketed by GlaxoSmithKline, dominates the market. Other triptans are: Zomig®, Maxalt®, Amerge®, Frova , Axert®, and Relpax®. Patients who suffer from a mild migraine, or are unaware that their headache is a migraine, generally treat themselves with an over-the-counter analgesic such as aspirin or ibuprofen.

Potential Treatments for Migraine and Chronic Pain

According to PhRMA s 2006 report, *Medicines in Development for Neurologic Disorders,* there are more than 30 companies seeking to develop compounds to treat migraine and pain disorders or to obtain additional indications to broaden the use of currently approved pain relieving prescription medications. This list includes most of the large pharmaceutical companies such as Abbott Laboratories, AstraZeneca, Eisai, Elan, Eli Lilly, GlaxoSmithKline, Merck, Pfizer, and Wyeth Pharmaceuticals as well as small and mid-sized biotechnology companies.

Cognitive Impairment Associated with Schizophrenia and Alzheimer s Disease

Current Treatments for Cognitive Impairment Associated with Schizophrenia

There are no FDA approved drugs for the treatment of CIAS. In research that we commissioned in November 2006, physicians consistently noted the large unmet treatment need given the lack of effective therapy options currently available for CIAS. Physician interviews conducted as part of the research revealed that a range of treatments for CIAS are tried including products approved for the treatment of Alzheimer s disease such as Aricept, Namenda, and Exelon, stimulants, such as Provigil and Ritalin, that are used to treat Attention Deficit Hyperactivity Disorder, and antidepressants. Only 55% of the physicians interviewed in connection with our research have tried using pharmaceutical products approved for other uses to treat CIAS and of those prescribers, fewer than 10% of their patients are successfully treated.

Potential Treatments for Cognitive Impairment Associated with Schizophrenia

Through various market reports and company announcements, we believe that there are more than 20 companies seeking to develop compounds to treat cognitive disorders in general, often without any specific reference to CIAS. This list includes most of the large pharmaceutical companies such as Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Novartis, and Roche as well as small and mid-sized biotechnology companies.

Current Treatments for Alzheimer s Disease

Despite limited effectiveness, acetylcholinesterase inhibitors are the mainstay treatment option for Alzheimer s disease. Four acetylcholinesterase inhibitors are approved for the symptomatic improvement of mild to moderate Alzheimer s disease: Aricept, the market leader, Exelon, Razadyne (formally Reminyl), and Cognex. One additional product, Namenda, a compound with a different mechanism of action, is approved for symptomatic improvement in patients with moderate to severe Alzheimer s disease.

Potential Treatments for Alzheimer s Disease

According to PhRMA s 2006 report, *Medicines in Development for Neurologic Disorders,* there are more than 25 companies, among others, seeking to develop compounds to treat Alzheimer s disease or to obtain additional indications to broaden the use of currently approved treatments for Alzheimer s disease. This list includes most of the large pharmaceutical companies such as Abbott Laboratories, AstraZeneca, Eisai, Elan, Eli Lilly, GlaxoSmithKline, Johnson & Johnson, Merck, Novartis, Pfizer, and Wyeth Pharmaceuticals as well as small and mid-sized biotechnology companies.

In each of these areas, it is also possible that other companies, including large pharmaceutical companies, may be working on competitive projects of which we are not aware.

We intend to compete with these companies on the basis of our intellectual property portfolio, the expertise of our scientific personnel and our relationships with key academic thought leaders in the areas of our focus, the effectiveness of our business strategies when compared to our competitors, the depth and breadth of our strategic alliances, our expertise in small molecule drug discovery technology and the availability of working capital to fund operations and advance programs under development.

Our success will depend, in part, upon our ability to achieve market share at the expense of existing and established as well as future products in the relevant target markets. Existing and future products, both branded and generic, as well as technological approaches or delivery systems, will compete directly with our products. Many of the companies competing against us have financial and other resources substantially greater than ours. In addition, many of our competitors have significantly greater experience in developing, marketing and selling pharmaceutical products, including products to treat migraine, chronic pain and Alzheimer s disease, testing pharmaceutical and other therapeutic products, and obtaining FDA and other regulatory approvals of products for use in health care.

Proprietary Rights

Patent Applications

Our policy is to pursue patents, both those generated internally and those licensed from third parties, pursue trademarks, maintain trade secrets and use other means to protect our technology, inventions and improvements that are commercially important to the development of our business.

Our success will depend significantly on our ability to:

- obtain and maintain patent and other proprietary protection for the technology, inventions and improvements we considers important to our business;
- defend our patents;
- preserve the confidentiality of our trade secrets; and
- operate without infringing the patents and proprietary rights of third parties.

As of December 31, 2006, we controlled approximately 317 patents and patent applications worldwide. Of these, 55 pertain to tezampanel and/or NGX426 (including 12 issued U.S. patents), 51 pertain to NGX267 and/or NGX292 (including 3 issued U.S. patents), 87 pertain to phenserine and/or Posiphen (including 3 issued U.S. patents), 40 pertain to BNC (including 2 issued U.S. patents), and 14 pertain to NGX555 (including 1 allowed U.S. patent application). Issued patents, and patents that may issue from these pending applications, would expire between 2010 and 2025. In accordance with the Hatch-Waxman Act in the United States, and corresponding legislation in certain foreign countries, patents covering our drug products may be eligible for up to five years of patent term restoration.

Trademarks, Trade Secrets and Other Proprietary Information

We own the TORREYPINES THERAPEUTICS & Design trademark, which is registered in the U.S. and in Japan, Canada, and the European Community. We also own our Tree Logo trademark, which is registered in the U.S. Additionally, we own the POSIPHEN trademark, which is registered or pending in approximately 25 countries.

To protect our trade secrets and proprietary information, we require our employees, scientific advisors, consultants and collaborators to execute confidentiality agreements when they begin to work with us. Additionally, we require our employees, scientific advisors and consultants to assign any inventions developed as a result of their relationship with us to TorreyPines. While these agreements provide a certain degree of protection of our proprietary information and internally developed technologies, they do not provide protection in the event of unauthorized disclosure of such information.

Manufacturing and Supply

We currently have no manufacturing capabilities and rely, or will rely, on third parties for the preclinical or clinical supplies of each of our product candidates. We do not currently have relationships for redundant supply or a second source for any of our product candidates. However, we believe that there are alternate sources of supply that can satisfy our preclinical and clinical trial requirements without significant delay or material additional costs.

Since our product candidates are all in an early stage of development, there is no commercial process developed for the synthesis of active pharmaceutical ingredient, or API, for any of our compounds. In addition, we have not identified final market formulations and delivery systems for any of our product candidates. We must rely upon third party vendors to achieve a final commercial process for API and to obtain FDA approval for both the API process and the drug product. Our reliance on third party vendors may result in delays, significant and unanticipated costs, or yield lower than anticipated amounts of product.

Commercial quantities of any products we seek to develop will have to be manufactured in facilities and by processes that comply with the FDA and other regulations for Good Manufacturing Practices. We plan to rely on third parties to manufacture commercial quantities of any products we successfully develop. We believe that there are several manufacturing sources available to us on commercially reasonable terms to meet our clinical requirements as well as any commercial production requirements.

Sales and Marketing

We currently have no marketing, sales or distribution capabilities. We may establish a small, specialty sales and marketing capability in the United States if and when we obtain regulatory approval for tezampanel for the treatment of migraine.

To market tezampanel outside of the United States, or if and when the oral migraine treatment, NGX426, obtains regulatory approval, or in situations or markets where a more favorable return may be realized through licensing commercial rights to a third party, we may license a portion or all of our commercial rights in a territory to a third party in exchange for one or more of the following: up-front payments, research funding, development funding, milestone payments and royalties on product sales.

Given the early stage of development, we do not have a sales and marketing plan for our CIAS and Alzheimer s disease product candidates. In order to participate in the commercialization of any of our products, we must develop these capabilities on our own or in collaboration with third parties. Alternatively, we may also choose to hire a third party to provide sales personnel instead of developing our own staff.

Government Regulation

FDA Requirements for New Drug Compounds

The research, testing, manufacture and marketing of pharmaceutical products are extensively regulated by numerous governmental authorities in the United States and other countries. In the United States, pharmaceutical products are subject to rigorous regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, labeling, promotion and marketing and distribution of pharmaceutical products. Failure to comply with applicable regulatory requirements may subject a company to a variety of administrative or judicial sanctions, including:

- suspension of review or refusal to approve pending applications;
- product seizures;
- recalls;
- withdrawal of product approvals;
- restrictions on, or prohibitions against, marketing its products;
- fines;
- restrictions on importation of its products;
- injunctions;
- debarment; and
- civil and criminal penalties.

The steps ordinarily required before a new pharmaceutical product may be marketed in the United States include:

- preclinical laboratory tests, animal studies and formulation studies according to good laboratory practices, or GLPs;
- submission to the FDA of an IND which must become effective before clinical, or human, testing may commence;
- adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each indication for which FDA approval is sought according to good clinical practices;
- submission to the FDA of an NDA;
- satisfactory completion of an FDA Advisory Committee review, if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with current good manufacturing practices, or cGMP; and
- FDA review and approval of the NDA.

Satisfaction of FDA pre-market approval requirements typically takes several years, and the actual time required may vary substantially based upon the type, complexity and novelty of the product or disease. Government regulation may delay or prevent marketing of potential candidates for a considerable period of time and impose costly procedures upon a manufacturer s activities. Success in early stage clinical trials does not assure success in later stage clinical trials. Data obtained from clinical activities is not always conclusive and may be susceptible to varying interpretations that could delay, limit or prevent regulatory approval. Even if a product receives regulatory approval, 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.

Preclinical tests include laboratory evaluation of product chemistry and formulation, as well as toxicology studies to assess the safety of the product. The conduct of the preclinical tests and formulation of compounds for testing must comply with federal regulations and requirements. The results of preclinical testing are then submitted to the FDA as part of an IND application.

An IND, which must be approved before human clinical trials may begin, will automatically become effective 30 days after the FDA receives it, unless the FDA raises concerns or questions about the IND. If the FDA has questions or concerns, they must be resolved to the satisfaction of the FDA before initial clinical testing can begin. In addition, the FDA may, at any time, impose a clinical hold on ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. In some instances, the IND process can result in substantial delay and expense.

Clinical trials involve the administration of the investigational drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted in compliance with federal regulations and requirements, under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated, among other things. Each protocol involving testing in the United States must be submitted to the FDA as part of the IND. In addition, an institutional review board, or IRB, at each site at which the clinical trial is conducted must approve the protocols, protocol amendments and informed consent documents for patients. All clinical trial participants must provide their informed consent in writing.

Clinical trials to support a new drug application for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase I clinical trials, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess safety, including side effects associated with increasing doses, metabolism, pharmacokinetics and pharmacological actions. Phase II clinical trials usually involves trials in a limited patient population, usually several hundred people, to determine dosage tolerance and optimum dosage, identify possible adverse effects and safety risks, and provide preliminary support for the efficacy of the drug in the indication being studied. In certain patient populations, accelerated approval is available based on Phase II clinical trial data. A Phase IIa clinical trial is typically designed to obtain proof-of-concept data and determine if the product candidate has an effect on a limited number of patients. A clinical trial designed to generate efficacy data but that is not expected to satisfy FDA criteria for NDA approval is sometimes referred to as a Phase IIb clinical trial. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase II clinical trials, Phase III clinical trials are undertaken to further evaluate clinical efficacy and safety within an expanded patient population, usually several hundred to several thousand subjects, typically at geographically dispersed clinical trial sites. Phase I, Phase II or Phase III clinical trials of any product candidate may not be completed successfully within any specified time period, if at all.

After successful completion of the required clinical testing, generally an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the United States. The NDA must include the results of extensive preclinical studies and clinical trials and other detailed information, including, information relating to the product s pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA is substantial. Under federal law, the submission of NDAs are generally subject to substantial application user fees, currently exceeding $750,000, and the sponsor and/or manufacturer under an approved application are also subject to annual product and establishment user fees, currently exceeding $40,000 per product and $250,000 per establishment. Additional user fees exceeding $300,000 apply for NDA supplements containing clinical

data. Fees are waived for the first pre-market application from companies with gross sales of less than $30 million. These fees are typically increased annually.

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 the NDA is sufficiently complete to permit substantive review. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under federal law, the FDA has agreed to certain performance goals in the review of most NDAs. Applications for non-priority drug products are generally reviewed within 12 months. Applications for priority drugs, such as those that address an unmet medical need, are generally reviewed within 6 months. The review process can be significantly extended by FDA requests for additional information or clarification regarding 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. Also, before approving an NDA, the FDA will inspect the facility or the facilities at which the product is manufactured to assure that the facilities, methods and controls are adequate to preserve the product s identity, strength, quality and purity.

If FDA evaluations of the NDA and the manufacturing facilities are favorable, the FDA may issue an approval letter, or, in some cases, an approvable letter followed by an approval letter. An approvable letter generally contains a statement of specific conditions that must be met in order to secure final approval of the NDA. If and when those conditions have been met to the FDA s satisfaction, the FDA will typically issue an approval letter. An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. If the FDA s evaluation of the NDA submission is not favorable, the FDA may refuse to approve the NDA or issue a not approvable letter. A not approvable letter outlines the deficiencies in the submission and may require additional testing or information in order for the FDA to reconsider the application. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. With limited exceptions, the FDA may withhold approval of an NDA regardless of prior advice it may have provided or commitments it may have made to the sponsor.

As a condition of NDA approval, the FDA may require post-approval testing and surveillance to monitor the drug s safety or efficacy and may impose other conditions, including labeling restrictions which can materially impact the potential market and profitability of the drug. In addition, a product approval may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

The FDA has various programs, including FastTrack designation, accelerated approval and priority review that are intended to expedite or simplify the process for reviewing certain drugs. Specifically, drug products that are intended for the treatment of serious or life-threatening conditions and demonstrate the potential to address unmet medical needs may be eligible for FastTrack designation and/or accelerated approval. Products may qualify for accelerated approval based on adequate and well-controlled Phase II clinical trial results that establish that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. As a condition of approval, the FDA may require that a sponsor of a drug product receiving FastTrack or accelerated approval perform post-marketing clinical trials. In addition, if a drug product would provide a significant improvement compared to marketed products, it may be eligible to receive priority review, which shortens the time in which the FDA acts on the sponsor s application. Even if a drug product qualifies for one or more of these programs, the FDA may later decide that the drug no longer meets the conditions for qualification or the time period for FDA review or approval will not be shortened.

After an NDA is approved, the approved drug will be subject to certain post-approval requirements, including a requirement to report adverse events and to submit annual reports. In addition, a supplemental NDA may be required for approval of changes to the originally approved indication, prescribing information, product formulation, and manufacturing and testing requirements. Following approval, drug products are required to be manufactured and tested for compliance with NDA and/or compendia specifications prior to release for commercial distributions. The manufacture and testing must be performed in approved manufacturing and testing sites that comply with cGMP requirements and are subject to FDA inspection authority.

Approved drugs must be promoted in a manner that is consistent with their terms and conditions of approval, and that is not false or misleading. In addition, the FDA requires substantiation of any claims of superiority of one product over another, generally through adequate and well-controlled head-to-head clinical trials. To the extent that market acceptance of our product candidates may depend on their superiority over existing therapies, any restriction on our ability to advertise or otherwise promote claims of superiority, or requirements to conduct additional expensive clinical trials to provide proof of such claims, could negatively affect the sales of our products and/or our expenses.

Once an NDA is approved, the product covered thereby becomes a listed drug which 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 has the same active ingredients, strength, dosage form, route of administration and conditions of use, and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Generally, an ANDA applicant is required only to conduct bioequivalence testing, and is not required to conduct or submit results of preclinical or clinical tests to prove the safety or efficacy of its drug product. Drugs approved in this way, commonly referred to as generic equivalents to the listed drug, are listed in the FDA s Approved Drug Products with Therapeutic Equivalence Evaluations, which is referred to as the Orange Book, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

Federal law provides for a period of three years of exclusivity following approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage, dosage form, indication or route of administration or combination, if one of the clinical trials conducted was essential to the approval of the application and was conducted or sponsored by the applicant. During this three year period, the FDA cannot grant effective approval of an ANDA based on that listed drug. Federal law also provides a period of exclusivity for five years following the approval of a drug containing a new chemical entity, except that an ANDA may be submitted after four years following the approval of the original product if the ANDA challenges a listed patent as invalid or not infringed.

Applicants submitting an ANDA are required to make a certification with regard to any patents listed for an innovative drug, stating that either there are no patents listed in the Orange Book for the innovative drug, any patents listed have expired, the date on which the patents will expire, or that the patents listed are invalid, unenforceable, or will not be infringed by the manufacture, use, or sale of the drug for which the ANDA is submitted. If an ANDA applicant certifies that it believes all listed patents are invalid or not infringed, it is required to provide notice of its ANDA submission and certification to the NDA sponsor and the patent owner. If the patent owner, its representatives, or the approved application holder, who is an exclusive patent licensee, then initiates a suit for patent infringement against the ANDA sponsor within 45 days of receipt of the notice, the FDA cannot grant effective approval of the ANDA until either 30 months have passed or there has been a court decision holding that the patents in question are invalid or not infringed. On the other hand, if a suit for patent infringement is not initiated within the 45 days, the ANDA applicant may bring a declaratory judgment action.

If the ANDA applicant certifies that it does not intend to market its generic product before some or all listed patents on the listed drug expire, then the FDA cannot grant effective approval of the ANDA

until those patents expire. The first ANDA submitting a substantially complete application certifying that all listed patents for a particular product are invalid or not infringed may qualify for a period of 180 days of exclusivity against other generics, which begins to run after a final court decision of invalidity or non-infringement or after the applicant begins marketing its product, whichever occurs first, during which time subsequently submitted ANDAs cannot be granted effective approval. If more than one applicant files a substantially complete ANDA on the same day, each such first applicant will be entitled to share the 180-day exclusivity period, but there will only be one such period, beginning on the date of the first marketing by any of the first applicants.

From time to time, legislation is drafted and introduced in Congress that could significantly change the statutory provisions governing the approval, manufacturing and marketing of drug products. In addition, FDA regulations and guidance are often revised or reinterpreted by the agency or the courts in ways that may significantly affect our business and products candidates. It is impossible to predict whether legislative changes will be enacted, or FDA regulations, guidance or interpretations changed, or what the impact of such changes, if any, may be.

Foreign Regulation of New Drug Compounds

Approval of a product by comparable regulatory authorities may be necessary in foreign countries prior to the commencement of marketing of the product in those countries, whether or not FDA approval has been obtained. In general, each country has its own procedures and requirements, many of which are time consuming, expensive, and may require additional studies prior to marketing the product. Also, the time required may differ from that required for FDA approval. Thus, there can be substantial delays in obtaining required approvals from foreign regulatory authorities after the relevant applications are filed.

In Europe, marketing authorizations may be granted at a centralized level, a decentralized level or a national level. The centralized procedure provides a single marketing authorization valid in all European Union member states, and is mandatory for the approval of most medicinal products, including certain biotechnology products. The decentralized procedure allows an applicant to seek market authorizations in several designated member states at once, and a national market authorization provides an authorization valid in only one member state. All medicinal products that are not subject to the centralized procedure and which have received at least one marketing authorization in another member state may receive additional marketing authorizations from other member states through a mutual recognition procedure.

Hazardous Materials

Our research and development processes involve the controlled use of hazardous materials, chemicals and radioactive materials and the production of waste products. We are subject to federal, state and local laws and regulations governing the use, manufacture, storage, handling and disposal of hazardous materials and waste products. We do not expect the cost of complying with these laws and regulations to be material.

Employees

As of December 31, 2006, we had 43 full-time employees, 32 of whom were engaged in research and development and 11 of whom were engaged in management, administration and finance. Of our employees, more than half hold advanced degrees. None of our employees are represented by a labor union or covered by a collective bargaining agreement, nor have we experienced work stoppages. We believe that relations with our employees are good.

Company Website

We maintain a website at *www.torreypinestherapeutics.com*. We make available free of charge on our website our periodic and current reports as soon as reasonably practicable after such reports are filed with the Securities and Exchange Commission, or SEC. Information contained on, or accessible through, our website is not part of this report or our other filings with the SEC.

We were initially incorporated in Nevada on July 29, 1997 as Axonyx Inc. In October 2006, we were reincorporated in Delaware and changed our name to TorreyPines Therapeutics, Inc. Our principal executive offices are located at 11085 North Torrey Pines Road, Suite 300, La Jolla, CA 92037, and our telephone number is (858) 623-5665.

Item 1A. Risk Factors.

You should consider carefully the following information about the risks described below, together with the other information contained in this annual report on Form 10-K and in our other filings with the Securities and Exchange Commission, before you decide to buy or maintain an investment in our common stock. We believe the risks described below are the risks that are material to us as of the date of this annual report. If any of the following risks actually occur, our business financial condition, results of operations and future growth prospects would likely be materially and adversely affected. In these circumstances, the market price of our common stock could decline, and you may lose all or part of the money you paid to buy our common stock.

Risks Related to Our Business

We expect to continue to incur net operating losses for the next several years and may never achieve profitability.

We have incurred net operating losses every year since our inception. As of December 31, 2006, we had an accumulated deficit of approximately $73.0 million. Over the next several years we expect a significant increase in our operating losses as we conduct additional research, development, clinical testing and regulatory compliance activities. All of our revenue to date has been payments received in connection with our collaboration and licensing agreements. We cannot be certain that we will generate additional revenue through licensing activities or that we will receive any of the milestone or royalty payments associated with our current collaboration and licensing agreements. Given the risks associated with discovery, development, clinical testing, manufacturing and marketing of drug products, we may never be successful in commercializing a drug product that will enable us to be profitable. Our ability to generate significant continuing revenue depends on a number of factors, including:

- successful completion of ongoing and future clinical trials for our product candidates;
- achievement of regulatory approval for our product candidates;
- successful completion of current and future strategic collaborations; and
- successful manufacturing, sales, distribution and marketing of our products.

We do not anticipate that we will generate significant continuing revenue for several years. Even if we do achieve profitability, we may not be able to sustain or increase profitability.

Substantially all of our product candidates are at an early stage of development and only a portion of these are in clinical development. We cannot be certain that any of our product candidates will be successfully developed, receive regulatory approval, or be commercialized.

Our product candidates, other than phenserine, are at an early stage of development and we do not have any products that are commercially available. Our product candidates, tezampanel and NGX426 for migraine, phenserine and Posiphen for Alzheimer s disease, and NGX267 for CIAS are currently in clinical development. Our other product candidates, NGX292, a muscarinic agonist, BNC, a butyrylcholinesterase inhibitor and NGX555, a gamma-secretase modulator, are in preclinical development. We will need to perform additional development work and conduct further clinical trials for all of our product candidates before we can seek the regulatory approvals necessary to begin commercial sales.

Success in preclinical testing and early clinical trials does not mean that later clinical trials will be successful. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have shown promising results. In future clinical trials with larger or somewhat different populations, results from early clinical trials may not be reproduced and analysis of new or additional data may not demonstrate sufficient safety and efficacy to support regulatory approval of a product candidate.

Additionally, preclinical studies and clinical trials are expensive, can take many years, and have an uncertain outcome. Product candidates may not be successful in clinical trials for a number of reasons, including, but not limited to, the failure of a product candidate to be safe and efficacious, the results of later stage clinical trials not confirming earlier clinical results, or clinical trial results not being acceptable the FDA or other regulatory agencies.

We do not anticipate that any of our current product candidates will be eligible to receive regulatory approval and begin commercialization for a number of years, if at all. Even if we were to ultimately receive regulatory approval for one or more of our product candidates, we may be unable to successfully commercialize them for a variety of reasons including:

- the availability of alternative treatments;
- the product not being cost effective to manufacture and sell;
- limited acceptance in the marketplace; and
- the effect of competition with other marketed products.

The success of our product candidates may also be limited by the prevalence and severity of any adverse side effects. Additionally, any regulatory approval to market a product may be subject to the imposition by such regulatory agency of limitations on the indicated uses. These limitations may reduce the size of the market for the product. If we fail to commercialize one or more of our current product candidates, our business, results of operations, financial condition, and prospects for future growth will be materially and adversely affected.

Delays in the commencement or completion of clinical testing of our product candidates could result in increased costs to us and delay our ability to generate significant revenues.

We cannot predict whether we will encounter problems with any of our planned clinical trials that will cause us or regulatory authorities to delay or suspend our clinical trials, or delay the analysis of data from our ongoing clinical trials. Any of the following factors could delay the clinical development of our product candidates:

- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of one or more clinical trials;

- delays in receiving, or the inability to obtain, required approvals from institutional review boards or other reviewing entities at clinical trial sites selected for participation in a clinical trial;

- delays or slower than anticipated enrollment of participants into clinical trials;

- lower than anticipated retention rate of participants in clinical trials;

- need to repeat clinical trials as a result of inconclusive or negative results or unforeseen complications in testing;

- inadequate supply or deficient quality of product candidate materials or other materials necessary to conduct our clinical trials;

- unfavorable FDA inspection and review of a clinical trial site or records of any clinical or preclinical investigation;

- serious, unexpected or undesirable side effects experienced by participants in the clinical trials that delay or preclude regulatory approval or limit the commercial use or market acceptance if approved;

- findings that the clinical trial participants are being exposed to unacceptable health risks;

- placement by the FDA of a clinical hold on a clinical trial;

- restrictions on or post-approval commitments with regard to any regulatory approval we ultimately obtain that renders a product candidate not commercially viable; and

- unanticipated cost overruns in preclinical and clinical trials.

In addition, once a clinical trial has started, it may be suspended or terminated by us or the FDA or other regulatory authorities due to a number of factors, including:

- failure to conduct the clinical trial in accordance with regulatory requirements;

- inspection of the clinical trial operations or clinical trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;

- negative clinical trial results;

- adverse events or negative side-effects experienced by the clinical trial participants; or

- lack of adequate funding to continue the clinical trial.

We will need to reach agreement with the FDA on the targeted endpoints for our clinical trials. In some cases, the FDA may not have validated endpoints established, and we may work with the FDA to potentially design and validate one or more endpoints. The FDA may not approve any or all of the endpoints and they may ultimately decide that the endpoints are inadequate to demonstrate the safety and efficacy levels required for regulatory approval. Our failure to adequately demonstrate the safety and efficacy of our product candidates would jeopardize our ability to achieve regulatory approval for, and ultimately to commercialize, the product candidates.

Clinical trials require sufficient participant enrollment, which is a function of many factors, including the size of the target population, the nature of the clinical trial protocol, the proximity of participants to clinical trial sites, the availability of effective treatments for the relevant disorder or disease, the eligibility criteria for our clinical trials and competing clinical trials. Delays in enrollment can result in increased costs and longer development times. Failure to enroll participants in our clinical trials could delay the completion of the clinical trials beyond current

expectations. In addition, the FDA could require us to conduct clinical trials with a larger number of participants than we may project for any of our product

candidates. As a result of these factors, we may not be able to enroll a sufficient number of participants in a timely or cost-effective manner.

Additionally, enrolled participants may drop out of clinical trials, which could impair the validity or statistical significance of the clinical trials. A number of factors can lead participants in a clinical trial to discontinue participating in the clinical trial, including, but not limited to: the inclusion of a placebo arm in the clinical trial; possible lack of effect of the product candidate being tested at one or more of the dose levels being tested; adverse side effects experienced by the participant, whether or not related to the product candidate; and the availability of alternative treatment options.

We, the FDA or other applicable regulatory authorities may suspend clinical trials of a product candidate at any time if we or they believe the participants in such clinical trials, or in independent third-party clinical trials for product candidates based on similar technologies, are being exposed to unacceptable health risks or for other reasons. In addition, it is impossible to predict whether legislative changes will be enacted, or whether FDA regulations, guidance or interpretations will be changed, or what the impact of such changes, if any, may be.

If we experience any such problems, we may not have the financial resources to continue development of the product candidate that is affected or the development of any of our other product candidates. If we experience significant delays in the commencement or completion of clinical testing, financial results and the commercial prospects for the product candidates will be harmed, costs will increase and our ability to generate revenue will be delayed.

We expect to complete a Phase IIb clinical trial of tezampanel in 2007, and our stock price could decline significantly if the results are not favorable or are not viewed favorably.

In the second half 2007, we expect to complete a Phase IIb clinical trial currently in progress for tezampanel. The results of this clinical trial may not be favorable or viewed favorably by us or third parties, including investors and analysts. Biopharmaceutical company stock prices have declined significantly in certain instances where clinical results were not favorable, were perceived negatively or otherwise did not meet expectations. Unfavorable results or negative perceptions regarding the results of our clinical trials of tezampanel, or any of our other product candidates, could cause our stock price to decline significantly.

We rely on third parties to assist us in conducting clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may not be able to obtain regulatory approval for or commercialize our product candidates.

We rely on, and intend to continue to rely on, third parties, such as contract research organizations, medical institutions, clinical investigators and contract laboratories, to conduct clinical trials of our product candidates. Our reliance on these third parties for development activities reduces our control over these activities. If these third parties do not successfully carry out their contractual duties or obligations or meet expected deadlines, or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or for other reasons, our clinical trials may be extended, delayed or terminated. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, we may be required to replace them. Although we believe there are a number of third-party contractors we could engage to continue these activities, replacing a third-party contractor may result in a delay of the affected trial. Accordingly, we may not be able to obtain regulatory approval for or successfully commercialize our product candidates.

We have licensed rights to product candidates tezampanel and NGX426 from Eli Lilly. Eli Lilly has rights of termination under the license agreement, which if exercised would adversely affect our business.

In April 2003, we entered into an agreement with Eli Lilly to obtain an exclusive license from Eli Lilly to their AK antagonist assets including tezampanel, as well as NGX426. Pursuant to the license agreement we have obligations to make payments to Eli Lilly under the agreement and to use commercially reasonable efforts to develop and commercialize the product candidates, including achievement of specified development events within specified timeframes. Eli Lilly may terminate the agreement for uncured material breach of the agreement by us, including any breach of our diligence obligations. If Eli Lilly were to terminate the agreement, we would lose rights to the AK antagonist product candidates, and our business would be adversely affected.

We have licensed rights to product candidates NGX267 and NGX292 from LSRI and LSRI has rights of termination under the license agreement, which if exercised would adversely affect our business.

In May 2004, we entered into an agreement with LSRI to obtain an exclusive license from LSRI to their muscarinic agonist assets NGX267 and NGX292. We have obligations to make payments to LSRI under the agreement and to use commercially reasonable efforts to develop and commercialize the product candidates subject to the agreement, including achievement of specified development events within specified timeframes. LSRI may terminate the agreement for uncured material breach of the agreement by us, including any breach of our diligence obligations. If LSRI were to terminate the agreement, we would lose rights to the muscarinic agonist product candidates, and our business would be adversely affected.

We depend on Eisai for funding for our gamma-secretase modulator program and Alzheimer s disease genetics research program. Eisai has the first right to obtain rights to gene targets and compounds resulting from these programs, which could delay or limit our ability to develop and commercialize these gene targets and compounds.

In February 2005, we entered into an agreement with Eisai to discover small molecule gamma-secretase modulator compounds useful in the treating Alzheimer s disease in humans. The agreement had an initial two-year term which Eisai elected to extend for an additional 12 months. In October 2005, we entered into an agreement with Eisai to discover gene targets useful in treating or preventing Alzheimer s disease in humans. This agreement also has a two-year term and may be extended by Eisai for up to an additional 12 months. We depend upon Eisai to provide funding for the research we conduct under each of these agreements. If Eisai were to cease funding these programs for any reason, we would need to provide our own funding for the programs, seek a strategic partner for further work on the programs, raise additional funding, or curtail or abandon the programs.

During the term of the respective agreements, Eisai has exclusive first rights of negotiation and refusal with regard to a license, collaboration or other arrangement regarding compounds discovered and validated in the course of the gamma-secretase modulator program or gene targets discovered and validated in the course of the Alzheimer s disease genetics research program, as applicable. These rights held by Eisai may delay or limit our ability to enter into a license, collaboration or other arrangement with a third party for any compounds resulting from the gamma-secretase modulator program or gene targets resulting from the Alzheimer s disease genetic research program.

We have an agreement providing Johnson & Johnson Development Corporation the first right to obtain rights to our M1 agonist program, which could delay or limit our ability to develop and commercialize these product candidates.

We have an agreement with Johnson & Johnson Development Corporation, or JJDC, regarding our research and development work into the effects of using M1 agonists, such as NGX267 and NGX292, in

the treatment of CNS diseases and disorders. Upon completion of a specified level of development of our lead M1 agonist, we are obligated to provide results for the compound to JJDC.

For a specified period following receipt of the results, or at an earlier time as agreed to by both parties, JJDC has the exclusive right of first negotiation with us regarding our intellectual property rights or products related to our M1 agonist program. These rights held by JJDC may delay or limit our ability to enter into a transaction with a third party for our M1 agonist product candidates.

If we fail to enter into and maintain collaborations for our product candidates, we may have to reduce or delay product development or increase expenditures.

Our strategy for developing, manufacturing, and commercializing potential products includes establishing and maintaining collaborations with pharmaceutical and biotechnology companies to advance some of our programs and share expenditures with partners on those programs. We may not be able to negotiate future collaborations on acceptable terms, if at all. If we are not able to establish and maintain collaborative arrangements, we may have to reduce or delay further development of some programs or undertake the development activities at our own expense. If we elect to increase capital expenditures to fund development programs on our own, we will need to obtain additional capital, which may not be available on acceptable terms or at all. Even if we do succeed in securing such collaborations, we may not be able to maintain them if, for example, objectives under the agreement are not met, the agreement is terminated or not renewed, development or approval of a product candidate is delayed or sales of an approved drug are disappointing. Furthermore, any delay in entering into collaborations could delay the development and commercialization of our product candidates and reduce their competitiveness, even if they reach the market. Any such delay related to our collaborations could adversely affect our business.

If our strategic partners do not devote adequate resources to the development and commercialization of our product candidates, we may not be able to commercialize our products and achieve revenues.

We may enter into collaborations with other strategic partners with respect to our product candidates. If we enter into any such collaborations, we may have limited or no control over the amount and timing of resources that our partners dedicate to the development of our product candidates. Our ability to commercialize products we develop with our partners and generate royalties from product sales will depend on the partner s ability to assist us in establishing the safety and efficacy of our product candidates, obtaining regulatory approvals and achieving market acceptance of products. Our partners may elect to delay or terminate development of a product candidate, independently develop products that could compete with our products, or not commit sufficient resources to the marketing and distribution of products under the collaboration. If our partners fail to perform as expected under the collaborative agreements, our potential for revenue from the related product candidates will be dramatically reduced. In addition, revenue from our future collaborations may consist of contingent payments, such as payments for achieving development and commercialization milestones and royalties payable on sales of any successfully developed drugs. The milestone, royalty or other revenue that we may receive under these collaborations will depend upon both our ability and our partner s ability to successfully develop, introduce, market and sell new products. In some cases, we will not be involved in these processes and, accordingly, will depend entirely on our partners.

We will need substantial additional funding and may be unable to raise capital when needed, which would force us to delay, reduce or eliminate our research and development programs or commercialization efforts.

We will need to raise substantial additional capital in the future and additional funding requirements will depend on, and could increase significantly as a result of, many factors, including:

- the rate of progress and cost of clinical trials;

- the scope of our clinical trials and other research and development activities;
- the prioritization and number of clinical development and research programs we pursue;
- the terms and timing of any collaborative, licensing and other arrangements that we may establish;
- the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;
- the costs and timing of regulatory approvals;
- the costs of goods and manufacturing expenses; and
- the costs of establishing or contracting for sales and marketing capabilities.

We do not anticipate that we will generate significant continuing revenue for several years, if at all. Until we can generate significant continuing revenue, if ever, we expect to satisfy our future cash needs through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements, as well as through interest income earned on cash balances. We cannot be certain that additional funding will 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 one or more of its research and development programs or commercialization efforts.

We do not have internal manufacturing capabilities. If we fail to develop and maintain supply relationships with collaborators or other third-party manufacturers, we may be unable to develop or commercialize our products.

Our ability to develop and commercialize our products depends in part on our ability to manufacture, or arrange for future collaborators or other third parties to manufacture, our products at a competitive cost, in accordance with regulatory requirements and in sufficient quantities for clinical testing and eventual commercialization. None of our current product candidates have been manufactured on a commercial scale. We and our third-party manufacturers may encounter difficulties with the small- and large-scale formulation and manufacturing processes required to manufacture our product candidates, resulting in delays in clinical trials and regulatory submissions, in the commercialization of product candidates or, if any product candidate is approved, in the recall or withdrawal of the product from the market. Our inability to enter into or maintain agreements with capable third-party manufacturers on acceptable terms could delay or prevent the commercialization of our products, which would adversely affect our ability to generate revenue and could prevent us from achieving profitability.

We have supplies of tezampanel, NGX426 and NGX267 that we expect to need for current clinical trials. We will need to identify and reach agreement with third parties for the supply of our product candidates for future clinical trials. We do not have long-term supply agreements with third parties, and we may not be able to enter into supply agreements with them in a timely manner or on acceptable terms, if at all. These third parties may also be subject to capacity constraints that would cause them to limit the amount of our product candidates they can produce or the chemicals that we can purchase. Any interruption or delay we experience in the supply of our product candidates or the chemicals may impede or delay such product candidates clinical development and cause us to incur increased expenses associated with identifying and qualifying one or more alternate suppliers.

In addition, we, our future collaborators or other third-party manufacturers of our products must comply with cGMP requirements enforced by the FDA through its facilities inspection program. These requirements include quality control, quality assurance and the maintenance of records and documentation. In addition, product manufacturing facilities in California are subject to licensing requirements of the California Department of Health Services and may be inspected by the California Department of Health Services at any time. We, our collaborators or other third-party manufacturers of our products may be unable to comply with these cGMP requirements and with other FDA, state and

foreign regulatory requirements. A failure to comply with these requirements may result in fines and civil penalties, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval.

We currently have no marketing or sales staff. If we are unable to enter into or maintain collaborations with marketing partners or if we are unable to develop our own sales and marketing capabilities, we may not be successful in commercializing our potential products and we may be unable to generate significant revenues.

We may elect to commercialize some of the products we are developing on our own, with or without a partner, where those products can be effectively marketed and sold in concentrated markets that do not require a large sales force to be competitive. We currently have no sales, marketing or distribution capabilities. To be able to commercialize our own products, we will need to establish our own specialized sales force and marketing organization with technical expertise and with supporting distribution capabilities. Developing such an organization is expensive and time consuming and could delay or limit our ability to commercialize products.

To commercialize any product candidate that we decide not to market on our own, we will depend on collaborations with third parties that have established distribution systems and direct sales forces. If we are unable to enter into such collaborations on acceptable terms, we may not be able to successfully commercialize those products.

To the extent that we enter into arrangements with collaborators or other third parties to perform sales and marketing services, our product revenue is likely to be lower than if we directly marketed and sold our product candidates. If we are unable to establish adequate sales and marketing capabilities, independently or with others, we may not be able to generate significant revenue and may not become profitable and the price of our common stock may be negatively affected.

Many of our product candidates are new therapies for chronic pain, CIAS and Alzheimer s disease, and we do not know whether these product candidates will yield commercially viable products or receive regulatory approval.

Tezampanel and NGX426 are antagonists of the AK receptors. They are part of a new class of compounds that block the AK receptors and, in turn, stop the transmission of pain signals. These product candidates may represent a novel approach to the management of chronic pain, including migraine and neuropathic pain. There are currently no approved products for chronic pain that are AK antagonists. As a result, we cannot be certain that our product candidates will result in commercially viable drugs that safely and effectively treat chronic pain indications such as migraine or neuropathic pain.

NGX267 and NGX292 are muscarinic agonists with functionally specific M1 receptor activity that we intend to develop for the treatment of CIAS. There are currently no approved therapies for the treatment of CIAS. Therefore, in order to successfully commercialize our product candidates, we will need to agree with the FDA and other applicable regulatory agencies on clinical trial endpoints regarding safety and efficacy. Given the lack of current treatments for CIAS, we may be unable to agree on the endpoints or successfully complete clinic trials that demonstrate that such endpoints, if agreed to, have been met. Any delay in agreeing to clinical trial endpoints or in achieving those endpoints will prevent us from commercializing our product candidates.

NGX267 and NGX292 as well as NGX555, a gamma-secretase modulator, are product candidates for Alzheimer s disease. These product candidates belong to classes of compounds that have been or are being studied as a treatment for Alzheimer s disease, but there are no approved muscarinic agonist products or gamma-secretase modulator products for Alzheimer s disease. As a result, we cannot be certain that our product candidates will safely and effectively improve the symptoms of Alzheimer s disease or modify the progression of the disease or result in commercially viable drugs.

If our product candidates do not achieve market acceptance among physicians, patients, health care payors and the medical community, they will not be commercially successful and our business will be adversely affected.

The degree of market acceptance of any of our approved product candidates among physicians, patients, health care payors and the medical community will depend on a number of factors, including:

- acceptable evidence of safety and efficacy;
- relative convenience and ease of administration:
- the prevalence and severity of any adverse side effects;
- availability of alternative treatments;
- pricing and cost effectiveness;
- effectiveness of sales and marketing strategies; and
- ability to obtain sufficient third-party coverage or reimbursement.

If we are unable to achieve market acceptance for our product candidates, then such product candidates will not be commercially successful and our business will be adversely affected.

If our efforts to discover new product candidates do not succeed, and product candidates that we recommend for clinical development do not actually begin clinical trials, our business will suffer.

We intend to use our proprietary technologies and expertise in Alzheimer s disease and related neurodegenerative diseases and disorders to discover, develop and commercialize new products for the treatment and prevention of these diseases and disorders. Once recommended for development, a product candidate undergoes drug substance scale up, preclinical testing, including toxicology tests, and formulation development. If this work is successful, an IND would need to be prepared, filed, and approved by the FDA and the product candidate would then be ready for human clinical testing.

The process of researching, discovering, and conducting preclinical testing on product candidates is expensive, time-consuming and unpredictable. If we are unable to advance our product candidates to clinical trials our business will be adversely affected.

If we fail to attract and keep key management and scientific personnel, we may be unable to develop or commercialize our product candidates successfully.

Our success depends on our continued ability to attract, retain and motivate highly qualified management and scientific personnel. The loss of the services of any principal member of our senior management could delay or prevent the commercialization of our product candidates. We employ these individuals on an at-will basis and their employment can be terminated by us or them at any time, for any reason and with or without notice, subject to the terms contained in their respective employment agreements and offer letters.

Competition for qualified personnel in the biotechnology field is intense. We may not be able to attract and retain quality personnel on acceptable terms given the competition for such personnel among biotechnology, pharmaceutical and other companies.

Companies and universities that have licensed product candidates to us for research, clinical development and marketing are sophisticated competitors that could develop similar products to compete with our products.

Licensing our product candidates from other companies, universities or individuals does not always prevent them from developing non-identical but competitive products for their own commercial purposes, nor from pursuing patent protection in areas that are competitive with us. Our partners who created these

technologies are sophisticated scientists and business people who may continue to do research and development and seek patent protection in the same areas that led to the discovery of the product candidates that they licensed to us. The development and commercialization of successful new drug products from our research program is likely to attract additional research by our licensors in addition to other investigators who have experience in developing products for the CNS market. By virtue of the previous research that led to the discovery of the drugs or product candidates that they licensed to us, these companies, universities, or individuals may be able to develop and market competitive products in less time than might be required to develop a product with which they have no prior experience.

Changes in, or interpretations of, accounting rules and regulations could result in unfavorable accounting charges or require us to change our compensation policies.

Accounting methods and policies for biopharmaceutical companies, including policies governing revenue recognition, expenses, accounting for stock options and in-process research and development costs are subject to further review, interpretation and guidance from relevant accounting authorities, including the SEC. Changes to, or interpretations of, accounting methods or policies in the future may result in unfavorable accounting charges or may require us to change our compensation policies to avoid such charges.

Our management will be required to devote substantial time to comply with public company regulations.

As a public company, we will incur significant legal, accounting and other expenses. In addition, the Sarbanes-Oxley Act of 2002, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and the Nasdaq Global Market, impose various requirements on public companies, including corporate governance practices. Our management and other personnel will have to meet these requirements. Moreover, these rules and regulations will increase our legal and financial compliance costs and will make some activities more time-consuming and costly.

In addition, the Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we must perform system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of its internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act. Our compliance with Section 404 will require that we incur substantial accounting and related expense and expend significant management efforts. We will need to hire additional accounting and financial staff to satisfy the ongoing requirements of Section 404. Moreover, if we are not able to comply with the requirements of Section 404, or if we or our independent registered public accounting firm identifies deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our stock could decline and we could be subject to sanctions or investigations by the Nasdaq Global Market, SEC or other regulatory authorities.

We are a defendant in a class action lawsuit and a stockholder derivative lawsuit which, if determined adversely, could have a material adverse affect on us.

A class action securities lawsuit and a stockholder derivative lawsuit was filed against us prior to the Merger, as described under Part I, Item 3 Legal Proceedings. We are defending against these actions vigorously; however, we do not know what the outcome of these proceedings will be and, if we do not prevail, we may be required to pay substantial damages or settlement amounts. Furthermore, regardless of the outcome, we may incur significant defense costs, and the time and attention of our management may be diverted from normal business operations. If we are ultimately required to pay significant defense costs, damages or settlement amounts, such payments could materially and adversely affect our operations and results. We have purchased liability insurance, however, if any costs or expenses associated with the litigation exceed the insurance coverage, we may be forced to bear some or all of these costs and expenses

directly, which could be substantial and may have an adverse effect on our business, financial condition, results of operations and cash flows. In any event, publicity surrounding the lawsuits and/or any outcome unfavorable to us could adversely affect our reputation and share price. The uncertainty associated with substantial unresolved lawsuits could harm our business, financial condition and reputation.

We have certain obligations to indemnify our officers and directors and to advance expenses to such officers and directors. Although we have purchased liability insurance for our directors and officers, if our insurance carriers should deny coverage, or if the indemnification costs exceed the insurance coverage, we may be forced to bear some or all of these indemnification costs directly, which could be substantial and may have an adverse effect on our business, financial condition, results of operations and cash flows. If the cost of our liability insurance increases significantly, or if this insurance becomes unavailable, we may not be able to maintain or increase our levels of insurance coverage for our directors and officers, which could make it difficult to attract or retain qualified directors and officers.

Fluctuations in c