TorreyPines Therapeutics, Inc.
Form 10-K
March 27, 2009
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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, 2008

Or

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the transition period from to

Commission File Number: 000-25571

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 405 of the Securities Act. Yes ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes ¨ No x

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 ¨

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, a non-accelerated filer, or a smaller reporting company. See definition of large accelerated filer, accelerated filer and smaller reporting company in Rule 12b-2 of the Exchange Act. (Check one):

Large accelerated filer ¨	Accelerated filer ¨	Non-accelerated filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company x

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

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, 2008 (the last business day of the registrant s most recently completed second fiscal quarter) of $1.24 per share as reported by the Nasdaq Global Market, was approximately $12,087,000. 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, 2008. This determination of affiliate status is not necessarily a conclusive determination for any other purposes.

As of March 18, 2009 there were 15,974,058 shares of our Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

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TORREYPINES THERAPEUTICS, INC.

FORM 10-K

For the Year Ended December 31, 2008

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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

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 providing patients with better alternatives to existing therapies through the development and commercialization of small molecule compounds. Our goal is to develop versatile product candidates each capable of treating a number of acute and chronic diseases and disorders such as migraine, acute and chronic pain, and xerostomia. Due to the Company s current financial condition as described further in this report, we have been and are continuing to explore financing and strategic alternatives, including a possible project financing, equity financing, or a partnership in order to continue the development of our three product candidates, two ionotropic glutamate receptor antagonists and one muscarinic receptor agonists. Additionally, we have been and are continuing to explore other strategic alternatives, including a possible asset out-licensing, asset sale or sale of the Company. If we are unable to complete a financing or strategic transaction during the first half of 2009, we will be unable to continue as a going concern and may be forced to cease operations, seek protection under the provisions of the U.S. Bankruptcy Code or liquidate and dissolve the Company.

Our two ionotropic glutamate receptor antagonists, tezampanel and NGX426, are clinical stage product candidates. Tezampanel and NGX426 competitively block the binding of glutamate at the glutamate receptors, specifically the AMPA and kainate receptor subtypes. While normal glutamate levels are essential, excess glutamate has been implicated in a number of diseases and disorders. Tezampanel and NGX426 are the first glutamate receptor antagonists with this combined binding activity to be tested in humans. In October 2007 we released the results of a Phase IIb clinical trial of tezampanel, our most advanced product candidate. In this clinical trial, a single dose of tezampanel given by injection was statistically significant compared to placebo in treating acute migraine headache. This was the sixth Phase II trial in which tezampanel has been shown to have analgesic activity. We held a successful end of Phase II meeting with the U.S. Food and Drug Administration (FDA) on September 29, 2008. Based on a review of the Phase II data, the FDA agreed that we may initiate a Phase III program for tezampanel in acute migraine. The FDA also confirmed that the required thorough QT/QTc study for tezampanel can be conducted in parallel with the first Phase III pivotal trial. In order to pursue further clinical development of tezampanel, including the initiation of a Phase III trial, we will need to secure project financing, equity financing, or a development partner.

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NGX426 is an oral prodrug of tezampanel. In clinical trials, NGX426 has been shown to rapidly convert to tezampanel. During 2008 we completed a Phase I clinical trial that was designed to identify the maximum tolerated single dose of NGX426 when given to healthy adults. Subjects were dosed up to 210 mg, the maximum dose allowable under the protocol. All doses were safe and well tolerated therefore the maximum tolerated dose was not reached. In December 2008 we announced that oral administration of a single dose of NGX426 to healthy male adults demonstrated a statistically significant reduction in spontaneous pain, hyperalgesia (abnormally increased pain state) and allodynia (pain resulting from normally non-painful stimuli to the skin) compared to placebo following injection under the skin of capsaicin in an experimental model of induced pain, hyperalgesia and allodynia. In February 2009 we announced that oral administration of NGX426 was safe and well-tolerated in healthy male and female subjects when dosed once daily for five consecutive days. In order to pursue further clinical development of NGX426 we will need to secure project financing, equity financing, or a development partner.

NGX267 is a muscarinic receptor agonist. We have completed three Phase I clinical trials evaluating single and multiple doses of NGX267 given to healthy adults. In December 2008, we announced positive results from a 26 patient Phase II trial evaluating three doses of NGX267 as a potential treatment for xerostomia, or dry mouth, in patients with Sjögren s syndrome. NGX267 met the primary endpoint of a statistically significant increase in salivary flow production compared to placebo at all three doses: 10 mg, 15 mg, and 20 mg. These doses were safe and well tolerated. In order to pursue further clinical development of NGX267 we will need to secure project financing, equity financing, or a development partner.

We also have one drug discovery program, a gamma-secretase modulator program. We are currently attempting to sell this program.

In addition to our efforts to sell our GSM program, in 2009 we will continue to explore project financing, equity financing, partnership opportunities, asset out-licensing, or an asset sale for tezampanel, NGX426 and NGX267 to enable us to pursue the commercial opportunities we have identified for these product candidates. In addition we will continue to explore opportunities to sell the Company as a whole. However, if we are unable to complete a financing or strategic transaction during the first half of 2009, we will be unable to continue as a going concern and may be forced to cease operations, seek protection under the provisions of the U.S. Bankruptcy Code or liquidate and dissolve the Company.

Our Clinical Development Opportunities

In 2009, the goal of our clinical development plan is to evaluate the analgesic effect of NGX426 in well-accepted models of pain as well as to further evaluate NGX267 as a potential treatment for xerostomia. We do not have plans in 2009 to commence any clinical trials of tezampanel. Our ability to advance either NGX426 or NGX267 in clinical development is contingent upon our ability to continue as a going concern which will require that we secure additional funding through financing or strategic alternatives, including a possible project financing, equity financing, partnership, asset out-licensing, or an asset sale. We currently have worldwide commercial rights to all of our clinical stage product candidates.

Tezampanel and NGX426 Ionotropic Glutamate Receptor Antagonists, AMPA and Kainate Subtype

We in-licensed tezampanel and NGX426 from Eli Lilly & Company, or Eli Lilly, in 2003. Based on their mechanism of action as well as preclinical and clinical data, we believe these first-in-class product candidates have the potential to be effective across numerous indications in a wide range of therapeutic areas.

Mechanism of Action

Tezampanel and NGX426 are ionotropic glutamate receptor antagonists. These product candidates act as competitive antagonists of the AMPA and kainate subtype of ionotropic glutamate receptors. Glutamate receptors mediate the functioning of glutamate, an important excitatory neurotransmitter. While normal glutamate levels

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are essential, excess glutamate levels, either through injury or disease, can have a range of pathological effects. By acting at both the AMPA and kainate receptor site to competitively block the binding of glutamate, both tezampanel and NGX426 have the potential to treat a number of diseases and disorders. These include the acute pain associated with migraine, chronic pain, such as neuropathic pain, and a condition known as central sensitization, a persistent state of hypersensitivity to pain that is a core component of many pain conditions.

Migraine

Migraine is a chronic, intermittent pain condition characterized by acute pain episodes often accompanied by central sensitization. The 2005 American Migraine Prevalence and Prevention 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. This study also confirmed that a large number of migraine sufferers are not getting adequate treatment or the relief they need, despite the number of products available to treat migraines. It has been more than a decade since the FDA has approved a migraine treatment with a new mechanism of action.

The medications most commonly used to treat acute migraine are triptans and ergotamines. These drugs constrict or narrow the blood vessels in the brain, heart and periphery. When the blood vessels in the brain are constricted, the blood flow is decreased thus relieving the throbbing pain associated with migraine.

An emerging theory is that the brain itself, not just the blood vessels, may cause or contribute to the migraine. Published data show that during a migraine, increased levels of glutamate activate AMPA and kainate receptors, resulting in the transmission of pain and, in many patients, the development of central sensitization. Tezampanel has been shown in preclinical studies to block the binding of glutamate to these receptors. In doing so, tezampanel relieves the migraine pain and may prevent or lessen the development of central sensitization without directly constricting the blood vessels. As a result, tezampanel may offer a significant safety advantage over drugs such as the triptans and ergotamines for patients with cardiovascular risk factors.

Migraine is often accompanied by central sensitization, which is characterized by allodynia and hyperalgesia. Allodynia is a painful response to a normally non-painful stimulus such as touch, sound, temperature, or light. Hyperalgesia is an exaggerated sensitivity to a normally painful stimulus. In contrast, preclinical data show that tezampanel s analgesic activity is especially pronounced in the presence of central sensitization. Because of its positive effects in treating central sensitization, tezampanel may have an important role to play not only in treating the acute migraine pain, but also in preventing migraines by addressing the underlying cause.

Neuropathic Pain

Neuropathic pain is a complex, chronic pain condition in which the peripheral or central nervous system itself is damaged, dysfunctional or injured. The malfunctioning nerves become the cause of the pain, sending incorrect signals to pain centers. Because it is often difficult to recognize and determine the cause of the neuropathic pain, it is often under-treated. Some common causes of neuropathic pain include spinal or back injury or surgery, diabetes, HIV infection and herpes. A hallmark of neuropathic pain is central sensitization. The signs and symptoms of central sensitization in patients with neuropathic pain are similar to those in patients with migraine, namely allodynia and hyperalgesia. In a Phase II trial, tezampanel, given intravenously, was shown to relieve neuropathic pain and reduce the signs and symptoms of central sensitization.

Clinical Development Overview Tezampanel

Using intravenous administration of tezampanel, proof of concept clinical testing has been successfully completed in migraine, low back pain, neuropathic pain via a capsaicin model, post-operative dental pain and pain from spinal cord trauma. In order to evaluate tezampanel given by injection, we completed a Phase I clinical trial and determined that a single dose of tezampanel given by injection was well tolerated at all doses up to and

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including 100 mg. To date tezampanel has been shown to be safe and well-tolerated in three Phase I and six Phase II clinical trials involving more than 450 patients and healthy adults.

In October 2007 we released results of a Phase IIb clinical trial of tezampanel, given by injection, in patients who suffered a single acute migraine attack. This clinical trial demonstrated that the 40 mg dose of tezampanel was statistically significant compared to placebo in improvement of headache pain response, the primary endpoint, at two hours post-dose. There were no serious or medically important adverse events reported.

In February 2008 we released results of a multiple dose clinical trial of tezampanel, given by injection. The Phase I double-blind, placebo-controlled trial enrolled 30 normal healthy male and female adults. The data from this trial show that tezampanel given by injection once-daily for four consecutive days at doses of 40 mg, 70 mg and 100 mg was safe and well-tolerated. There were no discontinuations from the study and reported adverse events were generally mild and transient. These Phase I results support our continued development of tezampanel across a variety of chronic conditions.

In September 2008 we held a successful end of Phase II meeting with the FDA regarding the scope of a Phase III program for tezampanel in acute migraine. While the FDA agreed with our planned Phase III program for tezampanel in acute migraine, given financial constraints we will need to secure additional funding in order to pursue the Phase III clinical development of tezampanel for the potential treatment of acute migraine.

Clinical Development Overview NGX426

The results of our first Phase I single dose clinical trial of NGX426, given orally, demonstrated that NGX426 was well-tolerated and rapidly converted to tezampanel at 10 mg, 20 mg, and 30 mg. During 2008 we completed a Phase I clinical trial that was designed to identify the maximum tolerated single dose of NGX426 when given to healthy adults. Subjects were dosed up to 210 mg, the maximum dose allowable under the protocol. All doses were safe and well tolerated therefore the maximum tolerated dose was not reached. In December 2008 we announced that oral administration of a single dose of NGX426 to healthy male adults demonstrated a statistically significant reduction in spontaneous pain, hyperalgesia (abnormally increased pain state) and allodynia (pain resulting from normally non-painful stimuli to the skin) compared to placebo following injections under the skin of capsaicin in a human experimental model of induced pain, hyperalgesia and allodynia. Using a three-period cross-over design, subjects received two intradermal injections of capsaicin at 30 minutes and 120 minutes after administration of a single, oral dose of 90 mg or 150 mg of NGX426, or placebo. In February 2009 we announced that oral administration of NGX426 was safe and well-tolerated in healthy male and female subjects when dosed once daily for five consecutive days. We will need to secure additional funding in order to pursue the Phase II clinical development of NGX426.

NGX267 and NGX292 Muscarinic Receptor Agonists

We in-licensed NGX267 and NGX292 from Life Science Research Israel, or LSRI, in 2004. NGX267 is a clinical stage product candidate for the treatment of xerostomia secondary to Sjogren s syndrome. NGX292 is a structurally similar backup compound to NGX267.

Mechanism of Action

NGX267 is a partial muscarinic receptor agonist with functionally specific M1 and M3 receptor activity, with greater activity on the M1 receptors than the M3 receptors. When muscarinic agonists stimulate the M1 and M3 receptors, they produce cholinergically-mediated side effects such as salivation, sweating, and tearing. The cholinergic system mediates both salivary flow and the sweating response, but there are some differences in the muscarinic subtypes involved. Salivary flow involves both M1 and M3 receptors, but the sweating response is primarily mediated by the M3 receptors.

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Xerostomia

Xerostomia, or dry mouth, may be caused by an underlying disease such as Sjogren s syndrome or may also result from medical treatments such as radiation therapy to the head or neck. In two Phase I trials and a Phase II trial, NGX267 has been shown to stimulate the M1 and M3 receptors and, depending on dose, produce salivation, sweating and tearing. We believe that we have identified a therapeutic dose range for NGX267 that will alleviate complaints of dry mouth without producing unpleasant or intolerable side effects such as excessive sweating. There are currently only two prescription medications for the treatment of xerostomia. Both of these medications have side effects and may not be suitable for all sufferers of dry mouth.

Clinical Development Status

We have completed three Phase I clinical trials and one Phase II trial of NGX267. In the first Phase I trial, we identified the maximum tolerated single dose of NGX267 as 35 mg in healthy young adult males. All doses up to and including 35 mg were well tolerated by the subjects and there were no reports of clinically significant adverse events. In the second Phase I trial, we confirmed the safety and tolerability of a single dose of NGX267 up to 15 mg in a healthy elderly population. In addition, at 15 mg, statistically significant increases in salivary flow were demonstrated for NGX267 in comparison to placebo in the study.

We have also completed a multiple dose Phase I clinical trial of NGX267 in healthy adult males. Subjects received either a 10 mg, 20 mg, 30 mg or 35 mg dose of NGX267 once-daily for each of four consecutive days. NGX267 was safe and well tolerated in the trial with no clinically significant adverse events. In the study, statistically significant increases in peak and total salivary flow were demonstrated for NGX267 in comparison to placebo and these effects were maintained over four days of dosing.

In December 2008 we announced positive results from a 26 patient Phase II trial evaluating three doses of NGX267 as a treatment for xerostomia, or dry mouth, in patients with Sjögren s syndrome. NGX267 met the primary endpoint of a statistically significant increase in salivary flow production compared to placebo at all three doses: 10 mg, 15 mg, and 20 mg. These doses were safe and well tolerated with few reports of excessive sweating and gastrointestinal complaints. The clinical trial was a randomized, double-blind, placebo-controlled design and enrolled 26 patients. Using a cross-over design, each patient received a once-daily oral dose of placebo, 10 mg, 15 mg or 20 mg of NGX267 in four distinct treatment periods. We will need to secure additional funding in order to pursue the Phase II clinical development of NGX267 for the potential treatment of xerostomia.

Our Gamma-secretase Modulator Drug Discovery Program

We have identified two distinct series of compounds that modulate the gamma-secretase enzyme and may have potential as a treatment for Alzheimer s disease. These gamma-secretase modulator, or GSM, compounds reduce the brain levels of $A\beta_{42}$, a toxic peptide, or protein, found in the brain of Alzheimer s disease patients, while maintaining the 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 $A\beta_{42}$ peptide. Because GSM compounds allow the gamma-secretase enzyme to perform its normal functions on other substrates, it is believed they will likely not have some of the side effects associated with the first generation compounds that fully inhibited enzyme function. We are currently attempting to sell this program.

Strategic Alliance, License and Other Commercial Agreements

Drug development is long and costly and we recognize that we will 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. Overall, our strategy is to reach key milestones with our product candidates before entering into strategic alliances. We

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believe that, in this way, we can retain significant commercial value in the product candidates while obtaining strategic and financial assistance to advance our programs. We speak to prospective partners on a regular basis, understanding that beneficial strategic alliances are the result of developing on-going relationships. In 2009 we will need to secure additional funding or a development partner to enable us to pursue the commercial opportunities we have identified for tezampanel, NGX426 and NGX267. This will be in addition to our on-going asset sale activities involving our GSM program.

Since inception, substantially all of our revenue has been derived from our agreements with Eisai Co., Ltd. These agreements expired by their terms in 2008.

Eli Lilly

In 2003, we entered into a development and licensing agreement with Eli Lilly to obtain an exclusive license to Eli Lilly s ionotropic glutamate receptor antagonist asset 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 are 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 2004, we entered into an agreement with LSRI to obtain an exclusive license to their muscarinic receptor agonist assets 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, 2008 we paid LSRI total milestone payments of approximately $2.2 million. If additional specified development, regulatory and commercial milestones are achieved, we are 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.

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.

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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 us 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.

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 acute and chronic pain, such as migraine and neuropathic pain, and xerostomia already approved by the FDA or they are pursuing the same or similar approaches to those which constitute our development programs and operate larger development programs in these fields than ours. We believe that competition for the products that we 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 pharmaceutical industry s leading companies.

For example, 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®. 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.

In the neuropathic pain market, we would compete with companies such as Pfizer, marketing Neurontin and Lyrica®, and Eli Lilly, marketing Cymbalta® in addition to opiods approved for treating neuropathic pain, off-label uses of products to treat neuropathic pain and generic products. Given the size of the neuropathic pain market, approximately $3.5 billion in 2006 and expected to double by 2016, it is likely that most of the large pharmaceutical companies as well as many biotechnology companies will look to develop compounds to treat neuropathic pain.

In the xerostomia market, Salagen®, marketed by MGI Pharma, and Evoxac®, marketed by Daiichi Pharmaceutical Corporation, are the only two prescription medications available to treat xerostomia. Each of these compounds are muscarinic receptor agonists. In addition, there are many over the counter medications that are used to treat dry mouth.

Many of our 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.

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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.

If we are able to overcome our current financial issues and continue as a going concern, our success will depend significantly on our ability to:

- obtain and maintain patent and other proprietary protection for the technology, inventions and improvements we consider 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, 2008, we controlled approximately 135 patents and patent applications worldwide. Of these, 64 pertain to tezampanel and/or NGX426 (including 14 issued U.S. patents), 53 pertain to NGX267 and/or NGX292 (including 4 issued U.S. patents), and 18 pertain to our GSM program (including 1 issued U.S. patent). Issued patents, and patents that may issue from these pending applications, would expire between 2010 and 2028. 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 to us any inventions developed as a result of their relationship with us. 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.

Because 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 product candidates. 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 we must 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.

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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 current good manufacturing practices, or cGMPs. 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. If and when tezampanel, NGX426 or NGX267 obtain 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.

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 development according to good laboratory practices, or GLPs;

submission to the FDA of an investigational new drug application, or 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 a new drug application, or NDA;

satisfactory completion of an FDA Advisory Committee review, if applicable;

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satisfactory completion of an FDA inspection of the manufacturing facility or facilities at which the product is produced to assess compliance with 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 development 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.

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 on-going 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 additional 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 an NDA 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 involve 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 safety and efficacy 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.

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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

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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.

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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.

FDA also imposes a number of complex requirements and restrictions on entities that advertise and promote prescription drugs, which include, among others, standards for and regulations of print and in-person promotion, product sampling, direct-to-consumer advertising, off-label promotion, industry sponsored scientific and educational activities, and promotional activities involving the Internet. The FDA has very broad enforcement authority under the Federal Food, Drug and Cosmetic Act, and failure to abide by FDA requirements can result in penalties and other enforcement actions, including the issuance of warning letters or other letters objecting to violations and directing that deviations from FDA standards be corrected, total or partial suspension of production, and state and federal civil and criminal investigations and prosecutions.

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.

Reimbursement and Pricing

In the United States and elsewhere, sales of pharmaceutical products depend in significant part on the availability of reimbursement to the consumer from third-party payors, such as government and private insurance plans. Third-party payors are increasingly challenging the prices charged for medical products and services. It will be time-consuming and expensive for us to go through the process of seeking reimbursement from Medicare and private payors. Our products may not be considered cost effective, and coverage and reimbursement may not be available or sufficient to allow us to sell our products on a competitive and profitable basis.

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In many foreign markets, including the countries in the European Union, pricing of pharmaceutical products is subject to governmental control. In the United States, there have been, and we expect that there will continue to be, a number of federal and state proposals to implement similar governmental pricing control. While we cannot predict whether such legislative or regulatory proposals will be adopted, the adoption of such proposals could have a material adverse effect on our business, financial condition and profitability.

Hazardous Materials

Our development processes involve the controlled use of hazardous materials, chemicals 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, 2008, we had 10 full-time employees, 2 of whom were engaged in clinical development and 8 of whom were engaged in management, business development and accounting. As of March 25, 2009 we had 5 full-time and 5 part-time employees. Of our employees, approximately 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.tptxinc.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 may not be able to continue as a going concern. We will need substantial additional funds to continue operations, which we may not be able to raise on favorable terms, or at all.

We will need substantial additional funds in order to initiate any further preclinical studies or clinical trials, for debt obligations and to fund our operations through 2009. Our independent registered public accounting firm has included an explanatory paragraph in their report on our 2008 financial statements related to the uncertainty and substantial doubt of our ability to continue as a going concern. Our plan to address these matters is described in Note 1 to the Financial Statements. We believe that our cash and cash equivalents, which were approximately

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$10.9 million at December 31, 2008 will only fund our operations into the second quarter, and possibly the third quarter, of 2009. Although we intend to continue to seek additional financing or a strategic partner, we may not be able to complete a financing or corporate transaction, either on favorable terms or at all. If we are unable to complete a financing or strategic transaction, we do not expect to be able to continue as a going concern and will be required to cease operations, seek protection under the provisions of the U.S. Bankruptcy Code or liquidate and dissolve the Company.

Our forecast of the period of time through which our financial resources will be adequate to support our operations is a forward-looking statement and involves risks and uncertainties, and actual results could vary as a result of a number of factors, including the factors discussed elsewhere in these risk factors. We have based this estimate on assumptions that may prove to be wrong, and we could utilize our available capital resources sooner than we currently expect. If we are able to obtain funds through arrangements with collaborative partners or others that require us to relinquish rights to technologies or product candidates that we would otherwise seek to develop or commercialize ourselves this may have a material adverse effect on our business, results of operations, financial condition or cash flow.

We are seeking to maximize the value of our assets, and address our liabilities and raise additional capital for our existing business. We are attempting to pursue asset out-licenses, asset sales, mergers or similar strategic transactions. We may be unable to satisfy our liabilities and can provide no assurances that we can be successful in executing a strategic transaction.

Due to our financial position, we are unable to initiate further preclinical studies or clinical trials. We are actively considering strategic alternatives with the goal of maximizing the value of our assets. In addition, we are considering our restructuring alternatives, including business arrangements such as the out-licensing or sale of product candidates or the Company as a whole. There are substantial challenges and risks which will make it difficult to successfully implement any of these opportunities. Even if we determine to pursue one or more of these alternatives, we may be unable to do so on acceptable terms, if at all. In such event, we will be forced to cease operations, seek protection under the provisions of the U.S. Bankruptcy Code or liquidate and dissolve the Company.

Stockholders should recognize that in our efforts to address our liabilities and fund future operations and development of our product candidates, we may pursue strategic alternatives that result in the stockholders of the Company having little or no continuing interest in the assets of the Company as stockholders or otherwise. We will continue to evaluate our alternatives in light of our cash position, including the possibility that we may need to liquidate the Company.

We may need to liquidate the Company in a voluntary dissolution under Delaware law or to seek protection under the provisions of the U.S. Bankruptcy Code, and in that event, it is unlikely that stockholders would receive any value for their shares.

We have incurred net operating losses every year since our inception. As of December 31, 2008, we had an accumulated deficit of approximately $119.2 million. As of March 25, 2009 we have been unable to raise the necessary capital to continue our existing operations. We are currently evaluating our strategic alternatives with respect to all aspects of our business. We cannot assure our stockholders that any actions that we take would raise or generate sufficient capital to fully address the uncertainties of our financial position. As a result, we may be unable to realize value from our assets and discharge our liabilities in the normal course of business. If we are unable to settle our obligations to our creditors or if we are unable to consummate a strategic transaction we would likely need to liquidate the Company in a voluntary dissolution under Delaware law or to seek protection under the provisions of the U.S. Bankruptcy Code. In that event, we or a trustee appointed by the court may be required to liquidate our assets. In either of these events, we might realize significantly less value from our assets than their carrying values on our financial statements. The funds resulting from the liquidation of our assets would be used first to satisfy obligations to creditors before any funds would be available to our stockholders,

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and any shortfall in the proceeds would directly reduce the amounts available for distribution, if any, to our creditors and to our stockholders. In the event we were required to liquidate under Delaware law or the federal bankruptcy laws, it is highly unlikely that stockholders would receive any value for their shares.

Our credit facility with Comerica Bank includes a restrictive financial covenant, violation of which could restrict a significant amount of our available cash balances.

Our loan and security agreement with Comerica Bank, or Comerica, contains a restrictive financial covenant requiring us to maintain a minimum of $5.4 million in available cash, cash equivalents and short-term investments, or available cash balances. If our available cash balances drop below $5.4 million, Comerica could declare the loan immediately due and payable, and require us to repay the outstanding balance due pursuant to the loan and security agreement. We would be required to use a significant amount of our available cash balance to repay the outstanding loan balance which would reduce the cash available to fund our operations or satisfy other liabilities.

We are currently not in compliance with Nasdaq rules regarding the minimum bid price and are at risk of being delisted from the Nasdaq Global Market, which may subject us to the SEC s penny stock rules and decrease the liquidity of our common stock.

We received a Nasdaq staff deficiency letter dated August 21, 2008 indicating that, for the prior 30 consecutive days, the bid price for the Company s common stock had closed below the minimum bid price of $1.00 per share as required for continued inclusion of the Nasdaq Global Market under Marketplace Rule 4450(a)(5). In accordance with Marketplace Rule 4450(e)(2), the Company has 180 calendar days to regain compliance with the minimum bid price requirement of $1.00 per share. In addition, as of March 25, 2009, the market value of our publicly held shares was less than $5 million, which is the minimum market value of publicly held shares required for continued listing under the Nasdaq Global Market s Marketplace Rules. However, Nasdaq has temporarily suspended, through July 20, 2009, the application of the continued listing requirements related to minimum bid price and minimum market value of publicly held shares for listing on the Nasdaq Global Market. Assuming the suspension is not extended, we will have until November 19, 2009, to regain compliance with the minimum bid price requirement of $1.00 per share. If the Company does not regain compliance by the end of such period, and does not elect or is unable to transfer to the Nasdaq Capital Market, Nasdaq will provide written notification that the Company s common stock will be delisted, after which the Company may appeal the staff determination to the Nasdaq Listing Qualifications Panel if it so chooses. In addition, as of December 31, 2008 our stockholders equity was less than $10 million, which is the minimum required stockholders equity for continued listing on the Nasdaq Global Market. The minimum stockholders equity requirement has not been suspended by Nasdaq and we could, therefore, receive a deficiency notice requiring that we regain compliance within a specified period of time.

If at the conclusion of compliance periods described above, we have not achieved compliance, we expect that we would be delisted from the Nasdaq Global Market. Following any such delisting, our common stock may be traded over-the-counter on the OTC Bulletin Board or in the pink sheets. These alternative markets, however, are generally considered to be less efficient than, and not as broad as, the Nasdaq Global Market. Many OTC stocks trade less frequently and in smaller volumes than securities traded on the Nasdaq markets, which could have a material adverse effect on the liquidity of our common stock. If our common stock is delisted from the Nasdaq Global Market, there may be a limited market for our stock, trading in our stock may become more difficult and our share price could decrease even further. In addition, if our common stock is delisted, our ability to raise additional capital may be impaired.

Specifically, you may not be able to resell your shares of common stock at or above the price you paid for such shares or at all. In addition, class action litigation has often been instituted against companies whose securities have experienced periods of volatility in market price. Any such litigation brought against us could result in substantial costs and a diversion of management s attention and resources, which could hurt our business, operating results and financial condition.

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In addition, our common stock may become subject to penny stock rules. The SEC generally defines penny stock as an equity security that has a market price of less than $5.00 per share, subject to certain exceptions. We are not currently subject to the penny stock rules because our common stock qualifies for an exception to the SEC s penny stock rules for companies that have an equity security that is quoted on the Nasdaq Stock Market. However, if we were delisted, our common stock would become subject to the penny stock rules, which impose additional sales practice requirements on broker-dealers who sell our common stock. If our common stock were considered penny stock, the ability of broker-dealers to sell our common stock and the ability of our stockholders to sell their shares in the secondary market would be limited and, as a result, the market liquidity for our common stock would be adversely affected. We cannot assure you that trading in our securities will not be subject to these or other regulations in the future.

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, 2008, we had an accumulated deficit of approximately $119.2 million. If we are able to overcome our current financial issues and our operations were to continue, over the next several years we would expect a significant increase in our operating losses as we conduct additional 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 licensing agreements. Given the risks associated with 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 on-going 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.

All of our product candidates are at an early stage of development. We cannot be certain that any of our product candidates will be successfully developed, receive regulatory approval, or be commercialized.

Our product candidates are at an early stage of development and we do not have any products that are commercially available. Our twoionotropic glutamate receptor antagonists, tezampanel and NGX426, and muscarinic receptor agonist NGX267are clinical stage product candidates. NGX292 is a structurally similar backup compound to NGX267. 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 later stage 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 testing 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

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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 to the FDA or other regulatory agencies.

There is no certainty that the safety and efficacy results of our Phase IIb clinical trial for tezampanel in acute migraine announced in October 2007, our Phase I trial of NGX426 in a capsaicin induced pain model announced in December 2008 or our Phase II trial of NGX267 for the potential treatment of xerostomia announced in December 2008 are predictive of results in subsequent trials or are meaningful indicators of the safety and efficacy of the respective compounds. We will be required to perform additional clinical testing in order to obtain regulatory approval of our product candidates and the results of such additional clinical testing may not replicate what has been demonstrated to date regarding the safety and efficacy. Additionally, further testing may not result in data sufficient to support regulatory approval.

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 incidence and severity of any adverse events or undesirable 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.

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 discovery 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 discovery and development activities;
- the prioritization and number of clinical development and discovery 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

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through interest income earned on cash balances. We cannot be certain that our immediate funding needs or future additional funding needs will be available on acceptable terms, or at all. If the near term funds that we need to continue operations do not become available, we may be required to cease operations, seek protection under the provisions of the U.S. Bankruptcy Code or liquidate and dissolve the Company.

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 future clinical trials that will cause us or regulatory authorities to delay or suspend our clinical trials, or delay the analysis of data from such clinical trials. Any of the following factors could delay the clinical development of our product candidates:

- on-going 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 adverse events 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 studies 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.

Before we can demonstrate adequate safety and efficacy we will need to reach agreement with the FDA on the endpoints for some of our Phase III clinical trials where endpoints have not been validated and we may work with the FDA to potentially design and validate one or more endpoints. The FDA may not accept any or all of the

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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 the number of 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 and costs will increase. Additionally, any significant delays in the commencement or completion of clinical testing will delay our ability to generate significant revenue.

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 and Company, or 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 ionotropic glutamate receptor antagonist assets tezampanel and NGX426. Pursuant to the license agreement

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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 development and commercialization obligations. If Eli Lilly were to terminate the agreement, we would lose rights to the ionotropic glutamate receptor antagonist product candidates, and our business would be adversely affected.

We have licensed rights to product candidates NGX267 and NGX292 from Life Science Research Israel, or LSRI. 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 receptor 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 development and commercialization obligations. If LSRI were to terminate the agreement, we would lose rights to the muscarinic receptor agonist product candidates, and our business would be adversely affected.

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

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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 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 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 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.

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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.

Tezampanel and NGX426 belong to a new class of compounds. There are no compounds in this class that have received regulatory approval for any indication. Therefore, we do not know whether our product candidates will yield commercially viable products or receive regulatory approval.

Tezampanel and NGX426 are ionotropic glutamate receptor antagonists of the AMPA and kainite subtype. They are part of a new class of compounds that block the binding of glutamate to AMPA and kainite receptors and, in turn, stop the transmission of pain signals. Tezampanel and NGX426 may represent a novel approach to the treatment of numerous pain and non-pain diseases and disorders. There are currently no approved products that are ionotropic glutamate receptor antagonists of the AMPA and kainite subtype. As a result, we cannot be certain that tezampanel and NGX426 will result in commercially viable drugs.

NGX267 is being developed to treat xerostomia, or dry mouth. There are currently two muscarinic receptor agonists approved to treat xerostomia. We do not know if NGX267 will yield a commercially viable product or receive regulatory approval.

NGX267 is a muscarinic receptor agonist with functionally specific M1 receptor activity that we intend to develop for the treatment of xerostomia, or dry mouth. There are currently two muscarinic receptor agonists marketed in the United States for the treatment of xerostomia. We do not know whether or not NGX267 will have any advantages over the currently marketed products or will be safe and efficacious. Failure to demonstrate an advantage over the currently marketed products or a failure to be safe and efficacious will prevent us from commercializing NGX267 or generating significant revenue.

If our product candidates do not achieve market acceptance among physicians, patients, health care payers 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 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 team could

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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 drug development industry 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 product candidates are experienced 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. 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 on-going 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.

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

A class action securities lawsuit was filed against us, as described under Part II, Item 1 Legal Proceedings. We are defending against this action vigorously; however, we do not know what the outcome of the 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 stock 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.

Risks Related to Our Intellectual Property

Our success depends upon our ability to protect our intellectual property and proprietary technologies.

Our commercial success depends on obtaining and maintaining patent protection and trade secret protection of our product candidates, proprietary technologies and their uses, as well as successfully defending our patents against third- party challenges. We will only be able to protect our product candidates, proprietary technologies and their uses from unauthorized use by third parties to the extent that valid and enforceable patents or trade secrets cover them.

The patent positions of pharmaceutical and biotechnology companies can be highly uncertain and involve complex legal and factual questions for which important legal principles remain unresolved. No consistent policy regarding the breadth of claims allowed in biotechnology patents has emerged to date in the U.S. The biotechnology patent situation outside the U.S. is even more uncertain. Changes in either the patent laws or in interpretations of patent laws in the U.S. and other countries may diminish the value of our intellectual property. Accordingly, we cannot predict the breadth of claims that may be allowed or enforced in our patents or in third-party patents.

The degree of future protection for our proprietary rights is uncertain because legal means afford only limited protection and may not adequately protect our rights or permit us to gain or keep our competitive advantage. For example:

- we or our licensors might not have been the first to make the inventions covered by each of its pending patent applications and issued patents;
- we or our licensors might not have been the first to file patent applications for these inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies;
- it is possible that none of our pending patent applications will result in issued patents;

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- our issued patents may not provide a basis for commercially viable products, may not provide us with any competitive advantages, or may be challenged by third parties;
- our issued patents may not be valid or enforceable;
- we may not develop additional proprietary technologies that are patentable; and
- the patents of others may have an adverse effect on our business.

Proprietary trade secrets and unpatented know-how are also very important to our business. Although we have taken steps to protect our trade secrets and unpatented know-how, including entering into confidentiality agreements with third parties and proprietary information and inventions agreements with employees, consultants and advisors, third parties may still obtain this information. Enforcing a claim that a third party illegally obtained and is using our trade secrets or unpatented know-how is expensive and time consuming, and the outcome is unpredictable. In addition, courts outside the U.S. may be less willing to protect this information. Moreover, our competitors may independently develop equivalent knowledge, methods and know-how.

If we are sued for infringing intellectual property rights of third parties, it will be costly and time consuming, and an unfavorable outcome in that litigation would have a material adverse effect on our business.

Our commercial success depends upon our ability and the ability of any of our collaborators to develop, manufacture, market, and sell our product candidates and use our proprietary technologies without infringing the proprietary rights of third parties. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are developing products. Because patent applications can take many years to issue, there may be currently pending applications, unknown to us, which may later result in issued patents that our product candidates or proprietary technologies may infringe. We have not conducted a complete search of existing patents to identify existing patents that our product candidates or proprietary technologies may inadvertently infringe.

We may be exposed to future litigation by the companies holding these patents or other third parties based on claims that our product candidates and/or proprietary technologies infringe their intellectual property rights. If one of these patents was found to cover our product candidates, proprietary technologies or their uses, we or our collaborators could be required to pay damages and could be unable to commercialize our product candidates or use our proprietary technologies unless we obtained a license to the patent. A license to these patents may not be available to us or our collaborators on acceptable terms, if at all.

There is a substantial amount of litigation involving patent and other intellectual property rights in the biotechnology and biopharmaceutical industries generally. If a third party claims that we or our collaborators infringe on its technology, it may face a number of issues, including:

- infringement and other intellectual property claims which, with or without merit, may be expensive and time-consuming to litigate and may divert management s attention from its core business;
- substantial damages for infringement, including treble damages and attorneys fees, as well as damages for products development using allegedly infringing drug discovery tools or methods which we may have to pay if a court decides that the product or proprietary technology at issue infringes on or violates the third party s rights;
- a court prohibiting us from selling or licensing the product or using the proprietary technology unless the third party licenses its technology to us, which it is not required to do;
- if a license is available from the third party, we may have to pay substantial royalties, fees and/or grant cross licenses to its technology; and

redesigning our products or processes so they do not infringe, which may not be possible or may require substantial funds and time.

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We may also be subject to claims that we or our employees, who were previously employed at universities or other biotechnology or pharmaceutical companies, have inadvertently or otherwise used or disclosed trade secrets or other proprietary information of their former employers. Litigation may be necessary to defend against these claims. If we fail in defending such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel. A loss of key research personnel or their work product could hamper or prevent our ability to commercialize certain potential drugs, which could severely harm our business. Even if we are successful in defending against these claims, litigation could result in substantial costs and be a distraction to management.

Risks Related to Our Industry

Our product candidates are subject to extensive regulation, which can be costly and time consuming, cause unanticipated delays or prevent the receipt of the required approvals to commercialize our product candidates.

The clinical development, manufacturing, labeling, storage, record-keeping, future advertising, promotion, export, marketing and distribution of our product candidates are subject to extensive regulation by the FDA and other regulatory agencies in the U.S. and by comparable foreign governmental authorities. The process of obtaining these approvals is expensive, often takes many years, and can vary substantially based upon the type, complexity and novelty of the products involved. Approval policies or regulations may change. In addition, although members of our management have drug development and regulatory experience, as a company we have not previously filed the marketing applications necessary to gain regulatory approvals for any product. This lack of experience may impede our ability to obtain FDA marketing approval in a timely manner, if at all, for the product candidates we are developing and commercializing. We will not be able to commercialize our product candidates in the U.S. until we obtain FDA approval and in other countries until we obtain approval by comparable governmental authorities. Any delay in obtaining, or inability to obtain, these approvals would prevent us from commercializing our product candidates.

Even if any of our product candidates receive regulatory approval, they may still face future development and regulatory difficulties.

If any of our product candidates receive regulatory approval, the FDA and foreign regulatory authorities may still impose significant restrictions on the uses or marketing of the product candidates or impose on-going requirements for post-approval studies. In addition, regulatory agencies subject a product, its manufacturer and the manufacturer s facilities to continuing review and periodic inspections. If previously unknown problems with a product or its manufacturing facility are discovered, a regulatory agency may impose restrictions on that product, us, or our partners, including requiring withdrawal of the product from the market. Our candidates will also be subject to on-going FDA requirements for submission of safety and other post-market information. If our product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

issue warning letters;

impose civil or criminal penalties;

suspend regulatory approval;

suspend any on-going clinical trials;

refuse to approve pending applications or supplements to approved applications filed by us or our collaborators;

impose restrictions on operations, including costly new manufacturing requirements; or

seize or detain products or require a product recall.

In order to market any products outside of the U.S., we and our partners must establish and comply with numerous and varying regulatory requirements of other countries regarding safety and efficacy. Approval

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procedures vary among countries and can involve additional product testing and additional administrative review periods. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks detailed above regarding FDA approval in the U.S. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others. Failure to obtain regulatory approval in other countries or any delay or setback in obtaining such approval could have the same adverse effects described above regarding FDA approval in the U.S., including the risk that our product candidates may not be approved for all indications requested, which could limit the uses of our product candidates and adversely impact potential royalties and product sales, and that such approval may be subject to limitations on the indicated uses for which the product may be marketed or require costly, post-marketing follow-up studies.

If we and our partners fail to comply with applicable foreign regulatory requirements, we and our partners may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution.

If our competitors have products that are approved faster, marketed more effectively or demonstrated to be more effective than our products, then our commercial opportunity will be reduced or eliminated.

The biotechnology and biopharmaceutical industries are characterized by rapidly advancing technologies, intense competition and a strong emphasis on proprietary products. We face competition from many different sources, including commercial pharmaceutical and biotechnology enterprises, academic institutions, government agencies and private and public research institutions. Due to the high demand for treatments in the areas in which we are competing, research is intense and new treatments are being sought out and developed by our competitors.

In addition, many other competitors are developing products for the treatment of the diseases we are targeting and if successful, these products could compete with our products. If we receive approval to market and sell any of our product candidates, we may compete with these companies and their products as well as others in varying stages of development.

Many of our competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, clinical trials, regulatory approvals and marketing approved products than we do. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. Our competitors may succeed in developing technologies and therapies that are more effective, better tolerated or less costly than ours, or that would render our product candidates obsolete and noncompetitive. Our competitors may succeed in obtaining approvals from the FDA and foreign regulatory authorities for their products sooner than we do. We will also face competition from these third parties in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, and in acquiring and in-licensing technologies and products complementary to our programs or advantageous to our business.

We are subject to uncertainty relating to health care reform measures and reimbursement policies which, if not favorable to our product candidates, could hinder or prevent the commercial success of our product candidates.

The continuing efforts of the government, insurance companies, managed care organizations and other payors of health care costs to contain or reduce costs of health care may adversely affect our:

- ability to set a price we believe is fair for our products;
- ability to generate revenues and achieve profitability;
- future revenues and profitability of potential customers, suppliers and collaborators; and
- the availability of capital.

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In certain foreign markets, the pricing of prescription drugs is subject to government control. In the U.S., given recent federal and state government initiatives directed at lowering the total cost of health care, Congress and state legislatures will likely continue to focus on health care reform, the cost of prescription drugs and the reform of the Medicare and Medicaid systems. For example, a new Medicare prescription drug benefit program began in 2006. While we cannot predict the full outcome of the implementation of this legislation or whether any future legislative or regulatory proposals affecting our business will be adopted, the announcement or adoption of these proposals could materially and adversely affect our business, financial condition, and results of operations.

Our ability to commercialize our product candidates successfully will depend in part on the extent to which governmental authorities, private health insurers and other organizations establish appropriate reimbursement levels for the cost of our products and related treatments. Third-party payors are increasingly challenging the prices charged for medical products and services. Also, the trend toward managed health care in the U.S., which could significantly influence the purchase of health care services and products, as well as legislative proposals to reform health care or reduce government insurance programs, may result in lower prices for our product candidates or exclusion of its product candidates from reimbursement programs. The cost containment measures that health care payors and providers are instituting and the effect of any health care reform could materially and adversely affect our results of operations.

Product liability claims may harm our business if our insurance coverage for those claims is inadequate.

We face an inherent risk of product liability exposure related to the testing of our product candidates in human clinical trials, and will face an even greater risk if we sell our product candidates commercially. An individual may bring a liability claim against us if one of our product candidates causes, or merely appears to have caused, an injury. If we are unable to successfully defend ourselves against any such product liability claim, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for our product candidates;
- injury to our reputation;
- withdrawal of clinical trial participants;
- costs of related litigation;
- substantial monetary awards to patients or other claimants;
- loss of revenues; and
- the inability to commercialize our product candidates.

We have product liability insurance that covers our clinical trials, up to an annual aggregate limit of $5.0 million. We intend to expand our insurance coverage to include the sale of commercial products if marketing approval is obtained for any of our product candidates. However, insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost and we may not be able to obtain insurance coverage that will be adequate to satisfy any liability that may arise.

We use hazardous chemicals and biological materials in our business. Any claims relating to improper handling, storage or disposal of these materials could be time-consuming and costly.

Our development processes involve the controlled use of hazardous materials, including chemicals and biological materials. Our operations produce hazardous waste products. We cannot eliminate the risk of accidental contamination or discharge and any resultant injury from those materials. Federal, state and local laws and regulations govern the use, manufacture, storage, handling and disposal of hazardous materials. We

may be sued for any injury or contamination that results from our use or the use by third parties of these materials. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may impair our research, development and production efforts.

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Risks Related to our Common Stock

Our stock price has been, and is expected to continue to be, volatile.

The market price of our common stock could be subject to significant fluctuations. Market prices for securities of early-stage pharmaceutical, biotechnology and other life sciences companies have historically been particularly volatile. Some of the factors that may cause the market price of our common stock to fluctuate include:

- the results of our current and any future clinical trials of our product candidates;
- the results of on-going preclinical studies and planned clinical trials of our preclinical product candidates;
- the entry into, or termination of, key agreements, including key strategic alliance agreements;
- the results and timing of regulatory reviews relating to the approval of our product candidates;
- the initiation of, material developments in, or conclusion of litigation to enforce or defend any of our intellectual property rights;
- general and industry-specific economic conditions that may affect our research and development expenditures;
- the results of clinical trials conducted by others on drugs that would compete with our product candidates;
- issues in manufacturing our product candidates or any approved products;
- the loss of key employees;
- the introduction of technological innovations or new commercial products by our competitors;
- failure of any of our product candidates, if approved, to achieve commercial success;
- changes in estimates or recommendations by securities analysts, if any, who cover our common stock;
- future sales of our common stock;
- changes in the structure of health care payment systems; and

period-to-period fluctuations in our financial results.

Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of our common stock.

In the past, following periods of volatility in the market price of a company s securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm our profitability and reputation.

Anti-takeover provisions in our stockholder rights plan and in our certificate of incorporation and bylaws may prevent or frustrate attempts by stockholders to change the board of directors or current management and could make a third-party acquisition difficult.

We are a party to a stockholder rights plan, also referred to as a poison pill, which is intended to deter a hostile takeover of us by making such proposed acquisition more expensive and less desirable to the potential acquirer. The stockholder rights plan and our certificate of incorporation and bylaws, as amended, contain provisions that may discourage, delay or prevent a merger, acquisition or other change in control that

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stockholders may consider favorable, including transactions in which stockholders might otherwise receive a premium for their shares. These provisions could limit the price that investors might be willing to pay in the future for shares of our common stock.

Our largest stockholders may take actions that are contrary to your interests, including selling their stock.

A small number of our stockholders hold a significant amount of our outstanding stock. These stockholders may support competing transactions and have interests that are different from yours. In addition, the average number of shares of our stock that trade each day is generally low. As a result, sales of a large number of shares of our stock by these large stockholders or other stockholders within a short period of time could adversely affect our stock price.

Our management has broad discretion over the use of our cash and we may not use our cash effectively, which could adversely affect our results of operations.

Our management has significant flexibility in applying our cash resources and could use these resources for corporate purposes that do not increase our market value, or in ways with which our stockholders may not agree. We may use our cash resources for corporate purposes that do not yield a significant return or any return at all for our stockholders, which may cause our stock price to decline.

Raising additional funds by issuing securities or through collaboration and licensing arrangements may cause dilution to existing stockholders, restrict operations or require us to relinquish proprietary rights.

We may raise additional funds through public or private equity offerings, debt financings or corporate collaboration and licensing arrangements. To the extent that we raise additional capital by issuing equity securities, our existing stockholders ownership will be diluted. Any debt financing we enter into may involve covenants that restrict our operations. These restrictive covenants may include limitations on additional borrowing, specific restrictions on the use of our assets as well as prohibitions on our ability to create liens, pay dividends, redeem stock or make investments. In addition, if we raise additional funds through collaboration and licensing arrangements, it may be necessary to relinquish potentially valuable rights to our potential products or proprietary technologies, or grant licenses on terms that are not favorable to us.

There is only a limited trading market for our common stock and it is possible that investors may not be able to sell their shares easily.

There is currently only a limited trading market for our common stock. Our common stock trades on the Nasdaq Global Market under the symbol TPTX with very limited trading volume. We cannot assure investors that a substantial trading market will be sustained for our common stock.

Item 1B. Unresolved Staff Comments.

None.

Item 2. Properties.

We lease approximately 20,000 square feet of laboratory and office space in La Jolla, California, under a lease that expires on June 30, 2009. We believe that our current facilities are adequate for our needs through June 2009.

Item 3. Legal Proceedings.

Several lawsuits were filed against us in February 2005 in the U.S. District Court for the Southern District of New York asserting claims under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act and Rule 10b-5 thereunder on behalf of a class of purchasers of our common

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stock during the period from June 26, 2003, through and including February 4, 2005, referred to as the class period. Dr. Marvin S. Hausman, M.D., a former director and our former Chief Executive Officer, and Dr. Gosse B. Bruinsma, M.D., also a former director and former Chief Executive Officer, were also named as defendants in the lawsuits. These actions were consolidated into a single class action lawsuit in January 2006. On April 10, 2006, the class action plaintiffs filed an amended consolidated complaint. We filed our answer to that complaint on May 26, 2006. Our motion to dismiss the consolidated amended complaint was filed on May 26, 2006 and was submitted to the court for a decision in September 2006. The motion to dismiss is pending.

The class action plaintiffs allege generally that our Phase III phenserine development program was subject to alleged errors of design and execution which resulted in the failure of the first Phase III phenserine trial to show efficacy. Plaintiffs allege the defendants failure to disclose the alleged defects resulted in the artificial inflation of the price of our shares during the class period.

This complaint seeks unspecified damages. We believe the complaint is without merit and we intend to defend this lawsuit vigorously. However, we cannot make assurances that we will prevail in this action, and, if the outcome is unfavorable to us, our reputation, operations and stock price could be adversely affected.

On February 7, 2009 a pending shareholder derivative suit in New York Supreme Court, New York County, against a current director and former directors and officers was discontinued.

Item 4. Submission of Matters to a Vote of Security Holders

There were no matters submitted to a vote of security holders during the quarter ended December 31, 2008.

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PART II

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

Market Information

Our common stock is currently traded on the Nasdaq Global Market, under the symbol TPTX. On August 21, 2008, we received a deficiency notice from the Listing Qualifications Department of the Nasdaq Stock Market indicating that, for the 30 consecutive business days prior to August 21,2008, the bid price for our common stock closed below the minimum $1.00 per share requirement for continued inclusion on the Nasdaq Global Market under Marketplace Rules 4450(a)(5) (hereafter referred to as the bid price rule). As of August 21, 2008, in accordance with Marketplace Rule 4450(e)(2), we had 180 calendar days, or until February 17, 2009, to regain compliance with the minimum $1.00 price per share requirement. In October 2008 Nasdaq granted a temporary suspension of the bid price rule and extended the deadline for compliance. In both December 2008 and again in March 2009 Nasdaq further extended the temporary suspension of the bid price rule further delaying the deadline for compliance. If we do not regain compliance by November 19, 2009, Nasdaq will provide written notification that our common stock will be delisted, after which we may appeal the staff determination to the Nasdaq Listing Qualifications Panel if we so choose. In addition, the market value of our publicly held shares is currently below the minimum market value of publicly held shares required by the Nasdaq Global Market and our stockholders equity is below the minimum stockholders equity required by the Nasdaq Global Market. However, the minimum market value of publicly held shares requirement was suspended along with the bid price rule in October 2008 and extended in December 2008 and March 2009. We have not yet received a deficiency notice from Nasdaq with respect to the minimum stockholders equity requirement, but could receive such a notice at any time. If we receive such a notice, we will be subject to the delisting process described above.

The following table sets forth the range of high and low sales prices of our common stock for the quarterly periods indicated, as reported by Nasdaq. Such quotations represent inter-dealer prices without retail mark up, mark down or commission and may not necessarily represent actual transactions.

	High	Low
Year Ended December 31, 2008:		
First Quarter	$ 2.59	$ 1.26
Second Quarter	1.71	1.07
Third Quarter	1.28	0.44
Fourth Quarter	0.55	0.16
Year Ended December 31, 2007:		
First Quarter	$ 8.75	$ 6.59
Second Quarter	7.52	6.10
Third Quarter	7.32	5.76
Fourth Quarter	6.15	2.26

Holders

As of March 17, 2009, there were 332 holders of record of our common stock.

Dividends

We have never paid cash dividends on our common stock, and we do not expect to pay any cash dividends in the foreseeable future. Our future dividend policy will depend on our earnings, cash requirements, expansion plans, financial condition and other relevant factors.

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Stock Price Performance Graph

The information included under the heading Stock Performance Graph included in Item 5 of this Annual Report on Form 10-K shall not be deemed to be soliciting material or subject to Regulation 14A or 14C, shall not be deemed filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act, or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act.

The following graph shows a comparison of the total cumulative returns of an investment of $100 in cash for the period of December 31, 2003 through December 31, 2008, in (i) our common stock, (ii) the Nasdaq Composite Index and (iii) the Nasdaq Biotechnology Index. The comparisons in the graph are required by the SEC and are not intended to forecast or be indicative of the possible future performance of our common stock. The graph assumes that all dividends have been reinvested (to date, we have not declared any dividends).

COMPARISON OF 5 YEAR CUMULATIVE TOTAL RETURN*

Among TorreyPines Therapeutics, Inc, (known as Axonyx Inc. prior to 10/3/06)

The NASDAQ Composite Index And The NASDAQ Biotechnology Index

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Item 6. Selected Financial Data.

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, and the Merger was accounted for as a reverse acquisition. 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. Our financial statements reflect the historical results of TPTX, Inc. prior to the Merger and that of the combined company following the Merger, and do not include the historical results of Axonyx Inc. prior to the completion of the Merger. All share and per share disclosures have been retroactively adjusted to reflect the exchange of shares in the Merger, and the 8-for-1 reverse split of our common stock on October 3, 2006. 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.

The following consolidated selected financial data should be read in conjunction with Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations and Item 8. Financial Statements and Supplementary Data included elsewhere in this Annual Report on Form 10-K. Certain reclassifications have been made to prior period amounts to conform to the current presentation.

	Years Ended December 31,				
	2008	2007	2006	2005	2004
	(In thousands, except share and per share data)				
Statement of Operations Data:					
Revenue	$ 6,071	$ 9,850	$ 9,850	$ 7,967	$ 3,551
Operating expenses:					
Research and development	18,949	27,977	22,353	17,317	11,379
General and administrative	5,801	5,643	3,971	2,588	2,399
Loss on impairment of purchased patents	3,074				
Purchased in-process research and development			8,328		
Total operating expenses	27,824	33,620	34,652	19,905	13,778
Loss from operations	(21,753)	(23,770)	(24,802)	(11,938)	(10,227)
Other income (expense), net	(1,032)	401	(575)	396	(129)
Net loss	(22,785)	(23,369)	(25,377)	(11,542)	(10,356)
Dividends and accretion to redemption value of redeemable convertible preferred stock				(4,434)	(2,593)
Net loss attributable to common stockholders	(22,785)	(23,369)	(25,377)	(15,976)	(12,949)
Basic and diluted net loss per share attributable to common stockholders	$ (1.45)	$ (1.49)	$ (8.18)	$ (30.69)	$ (25.99)
Shares used to compute basic and diluted net loss per share attributable to common stockholders	15,748,967	15,717,984	3,100,852	520,588	498,127

	As of December 31,				
	2008	2007	2006	2005	2004
	(In thousands)				
Selected Balance Sheet Data:					
Cash and cash equivalents	$ 10,864	$ 32,500	$ 55,383	$ 28,757	$ 27,629
Working capital	5,746	24,299	43,694	24,806	24,357
Total assets	11,130	38,652	63,435	31,104	29,888
Long-term debt, net of current portion	2,112	954	4,397	3,826	591
Redeemable convertible preferred stock				72,018	67,584
Accumulated deficit	(119,186)	(96,401)	(73,032)	(58,850)	(42,874)
Total stockholders equity (deficit)	3,713	26,460	44,569	(58,341)	(42,381)

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

The following discussion of our financial condition contains certain statements that are not strictly historical and are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 and involve a high degree of risk and uncertainty. Our actual results may differ materially from those projected in the forward-looking statements due to risks and uncertainties that exist in our operations, development efforts and business environment, including those set forth under the Section entitled Risk Factors in Item 1A, and other documents we file with the Securities and Exchange Commission. All forward-looking statements included in this report are based on information available to us as of the date hereof, and, unless required by law, we assume no obligation to update any such forward-looking statement.

Overview

We are a biopharmaceutical company committed to providing patients with better alternatives to existing therapies through the development and commercialization of small molecule compounds. Our goal is to develop versatile product candidates each capable of treating a number of acute and chronic diseases and disorders such as migraine, acute and chronic pain, and xerostomia. Due to the Company s current financial condition as described further in this report, we have been and are continuing to explore financing and strategic alternatives, including a possible project financing, equity financing, or a partnership in order to continue the development of our three product candidates, two ionotropic glutamate receptor antagonists and one muscarinic receptor agonists. Additionally, we have been and are continuing to explore other strategic alternatives, including a possible asset out-licensing, asset sale or sale of the Company. If we are unable to complete a financing or strategic transaction during the first half of 2009, we will be unable to continue as a going concern and may be forced to cease operations, seek protection under the provisions of the U.S. Bankruptcy Code or liquidate and dissolve the Company.

Our two ionotropic glutamate receptor antagonists, tezampanel and NGX426, are clinical stage product candidates. Tezampanel and NGX426 competitively block the binding of glutamate at the glutamate receptors, specifically the AMPA and kainate receptor subtypes. While normal glutamate levels are essential, excess glutamate has been implicated in a number of diseases and disorders. Tezampanel and NGX426 are the first glutamate receptor antagonists with this combined binding activity to be tested in humans. In October 2007 we released the results of a Phase IIb clinical trial of tezampanel, our most advanced product candidate. In this clinical trial, a single dose of tezampanel given by injection was statistically significant compared to placebo in treating acute migraine headache. This was the sixth Phase II trial in which tezampanel has been shown to have analgesic activity. We held a successful end of Phase II meeting with the U.S. Food and Drug Administration (FDA) on September 29, 2008. Based on a review of the Phase II data, the FDA agreed that we may initiate a Phase III program for tezampanel in acute migraine. The FDA also confirmed that the required thorough QT/QTc study for tezampanel can be conducted in parallel with the first Phase III pivotal trial. In order to pursue further clinical development of tezampanel, including the initiation of a Phase III trial, we will need to secure project financing, equity financing, or a development partner.

NGX426 is an oral prodrug of tezampanel. In clinical trials, NGX426 has been shown to rapidly convert to tezampanel. During 2008 we completed a Phase I clinical trial that was designed to identify the maximum tolerated single dose of NGX426 when given to healthy adults. Subjects were dosed up to 210 mg, the maximum dose allowable under the protocol. All doses were safe and well tolerated therefore the maximum tolerated dose was not reached. In December 2008 we announced that oral administration of a single dose of NGX426 to healthy male adults demonstrated a statistically significant reduction in spontaneous pain, hyperalgesia (abnormally increased pain state) and allodynia (pain resulting from normally non-painful stimuli to the skin) compared to placebo following injection under the skin of capsaicin in an experimental model of induced pain, hyperalgesia and allodynia. In February 2009 we announced that oral administration of NGX426 was safe and well-tolerated in healthy male and female subjects when dosed once daily for five consecutive days. In order to pursue further clinical development of NGX426 we will need to secure project financing, equity financing, or a development partner.

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NGX267 is a muscarinic agonist. We have completed three Phase I clinical trials evaluating single and multiple doses of NGX267 given to healthy adults. In December 2008, we announced positive results from a 26 patient Phase II trial evaluating three doses of NGX267 as a potential treatment for xerostomia, or dry mouth, in patients with Sjögren s syndrome. NGX267 met the primary endpoint of a statistically significant increase in salivary flow production compared to placebo at all three doses: 10 mg, 15 mg, and 20 mg. These doses were safe and well tolerated. In order to pursue further clinical development of NGX267 we will need to secure project financing, equity financing, or a development partner.

We also have one drug discovery program, a gamma-secretase modulator program. We are currently attempting to sell this program.

In addition to our efforts to sell our GSM program in 2009 we continue to explore project financing, equity financing, partnership opportunities, asset out-licensing, or an asset sale for tezampanel, NGX426 and NGX267 to enable us to pursue the commercial opportunities we have identified for these product candidates. In addition we continue to explore opportunities to sell the Company as a whole. However, if we are unable to complete a financing or strategic transaction during the first half of 2009, will be unable to continue as a going concern and may be forced to cease operations, seek protection under the provisions of the U.S. Bankruptcy Code or liquidate and dissolve the Company.

Going Concern and Management s Plan

Our independent registered public accounting firm has included an explanatory paragraph in their report on our 2008 financial statements related to the uncertainty and substantial doubt of our ability to continue as a going concern.

We have incurred net losses of $22.8 million, $23.4 million and $25.4 million for the years ended December 31, 2008, 2007 and 2006, respectively. Since inception, and through December 31, 2008, we have an accumulated deficit of $119.2 million. Based on our operating plan, our existing cash and cash equivalents will only fund our operations into the second quarter, and possibly into the third quarter, of 2009. These conditions raise substantial doubt about our ability to continue as a going concern. The accompanying financial statements have been prepared assuming that we will continue as a going concern. This basis of accounting contemplates the recovery of our assets and the satisfaction of liabilities in the normal course of business.

Our management plans to address the expected shortfall of working capital by securing additional funding through project financing, equity financing, a development partner or the sale of assets. If we are unsuccessful in securing funding from any of these sources, we will defer, reduce or eliminate certain planned expenditures. There can be no assurance that we will be able to obtain any sources of funding.

If we cannot obtain sufficient funding in the short-term, we may be forced to significantly curtail our operations, file for bankruptcy, cease operations or liquidate and dissolve the Company. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts and classification of liabilities that might be necessary should we be forced to take any such actions.

Financial Operations Overview

Revenue

All of our revenue to date has been derived from license and option fees, research funding from our strategic alliance agreements or the sale of a research program. We will continue to seek partners or acquirers for all of our product candidates and our remaining drug discovery program.

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Research and Development

Since inception, we have focused on discovery and development of novel small molecule compounds to treat a number of acute and chronic diseases and disorders.

Research and development expense has represented approximately 68%, 83% and 65% of our total operating expenses for the years ended December 31, 2008, 2007 and 2006, respectively. We expense research and development costs as incurred. Research and development expense consists of expenses incurred in identifying, researching, developing and testing product candidates. These expenses primarily consist of the following:

- compensation of personnel and consultants associated with research and development activities;
- fees paid to contract research organizations and professional service providers for independent monitoring analysis and regulatory services for our clinical trials;
- laboratory supplies and materials;
- manufacturing of product candidates for use in our preclinical testing and clinical trials;
- preclinical studies;
- depreciation of equipment; and
- allocated costs of facilities and infrastructure.

Because of the risks inherent in research and development, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts necessary to complete the development of our programs, the anticipated completion dates of these programs, or the period in which material net cash inflows are expected to commence, if at all, from the programs described above and any potential future product candidates. If either we or any of our partners fail to complete any stage of the development of any potential products in a timely manner, it could have a material adverse effect on our operations, financial position and liquidity.

General and Administrative

General and administrative expense consists primarily of salaries and other related costs for personnel in executive, finance, accounting, business development, information technology and human resource functions. Other costs include facility costs not otherwise included in research and development expense and professional fees for legal and accounting services.

Purchased In-Process Research and Development

Purchased in-process research and development expense represents the fair value of certain of the intangible assets we acquired in the Merger for which technological feasibility had not been established and no alternative future uses exist for the technologies. We cannot predict if we will incur similar expenses in the future.

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Results of Operations

Comparison of the Year Ended December 31, 2008 and 2007

The following table summarizes our results of operations with respect to the items set forth in such table for the years ended December 31, 2008 and 2007, in thousands, together with the change in such items in dollars and as a percentage.

	Years Ended December 31			
	2008	2007	$ Change	% Change
Revenue	$ 6,071	$ 9,850	$ (3,779)	(38)%
Research and development expenses	18,949	27,977	(9,028)	(32)%
General and administrative expenses	5,801	5,643	158	3%
Loss on impairment of purchased patents	3,074		3,074	100%
Interest income	453	2,069	(1,616)	(78)%
Interest expense	376	817	(441)	(54)%
Other income (expense), net	(1,109)	(851)	(258)	(30)%

Revenue. Revenue decreased to $6.1 million for the year ended December 31, 2008 from $9.8 million for the same period in 2007. The decrease of $3.7 million was due to the conclusion of our GSM collaboration agreement with Eisai in February 2008 and the conclusion of our Alzheimer s disease genetics collaboration agreement with Eisai in September 2008, partially offset by the sale of our Alzheimer s disease genetics program for $1.5 million. During 2008 in connection with the GSM collaboration agreement we recognized revenue for two of the twelve months ended December 31, 2008; during 2007 we recognized revenue from this collaboration agreement for each of the twelve months ended December 31, 2007. During 2008 in connection with the Alzheimer s disease genetics collaboration agreement we recognized revenue for nine of the twelve months ended December 31, 2008; during 2007 we recognized revenue from this collaboration agreement for each of the twelve months ended December 31, 2007.

Research and development expense. Research and development expense decreased to $18.9 million in 2008 from $27.9 million in 2007. The $9.0 million decrease was attributable to a $6.0 million decrease in expense for our development programs and a $3.0 million decrease in expense for our discovery programs. The decrease in spending for our development programs was due to decreased clinical development activities for tezampanel in 2008 compared to 2007. The decrease in spending for our discovery programs was primarily due to the conclusion of our GSM collaboration agreement with Eisai in February 2008. Specifically, salaries and benefits expense and lab supplies expense were lower in 2008 compared to 2007.

General and administrative expense. General and administrative expense increased to $5.8 million in 2008 from $5.6 million in 2007. The $0.2 million increase was primarily attributable to increased professional services costs offset by decreased personnel costs and related expenses and decreased stock based compensation expense in 2008 compared to 2007.

Loss on impairment of purchased patents. Loss on impairment of purchased patents increased to $3.1 million in 2008 from $0 in 2007. As of December 31, 2008 we estimate that the purchased patents have a fair value of $0, therefore we recorded an impairment for the total carrying value of the patents. We did not record a loss on impairment of purchased patents during 2007.

Interest income. Interest income in 2008 decreased to $0.5 million in 2008 from $2.1 million in 2007. The decrease of $1.6 million is due to a lower average cash and cash equivalents balance in 2008 compared to 2007.

Interest expense. Interest expense decreased to $0.4 million in 2008 from $0.8 million in 2007. The $0.4 million decrease is attributable to a lower average debt balance in 2008 compared to 2007 and a lower average interest rate in 2008 compared to 2007.

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Other income (expense), net. Other income (expense), net for the twelve months ended December 31, 2008 is comprised of a decline in the fair value of our investment in OXIS International, Inc. (OXIS) of $559,000, a loss on the sale of our investment in OXIS of $377,000, a loss on the extinguishment of debt of $165,000, a loss on impairment of property and equipment of $153,000, and a gain on foreign currency translations of $145,000. Other income (expense), net for the twelve months ended December 31, 2007 is comprised of an impairment of the investment in OXIS of $1,881,000 and other expense of $3,000, offset by income from a warrant valuation adjustment of $892,000 and equity in income of OXIS of $141,000.

Comparison of the Year Ended December 31, 2007 and 2006

The following table summarizes our results of operations with respect to the items set forth in such table for the years ended December 31, 2007 and 2006, in thousands, together with the change in such items in dollars and as a percentage.

	Years Ended December 31			
	2007	2006	$ Change	% Change
Revenue	$ 9,850	$ 9,850	$	%
Research and development expenses	27,977	22,353	5,624	25%
General and administrative expenses	5,643	3,971	1,672	42%
Purchased in-process research and development		8,328	(8,328)	(100)%
Interest income	2,069	1,559	510	33%
Interest expense	817	994	(177)	(18)%
Other income (expense), net	(851)	(1,140)	289	25%

Revenue. Revenue for the year ended December 31, 2007 was unchanged from the same period in 2006. During 2007 there were no changes in our strategic licensing agreements that affected our revenue from license and option fees or research funding.

Research and development expense. Research and development expense increased to $27.9 million in 2007 from $22.3 million in 2006. The $5.6 million increase was attributable to a $7.5 million increase in expense for our development programs, offset by a $1.9 million decrease in expense for our discovery programs. The increase in spending for our development programs was due to increased clinical development activities for tezampanel, NGX426 and NGX267 in 2007 compared to 2006. The decrease in spending for our discovery programs was due to lower costs incurred for our GSM program and our Alzheimer s disease genetics program in 2007 compared to 2006.

General and administrative expense. General and administrative expense increased to $5.6 million in 2007 from $4.0 million in 2006. The $1.6 million increase was primarily attributable to increased personnel costs and related expenses and increased stock based compensation expense in 2007 compared to 2006. The increase in personnel costs and related expenses is due to the addition of key general and administrative personnel during the first quarter of 2007. The increase in stock based compensation expense in 2007 compared to 2006 is due to the recognition of a full year of expense associated with restricted stock units granted to executives in late 2006. We also recognized stock based compensation expense in 2007 in connection with stock options granted to members of our board of directors. There were no similar stock option grants in 2006.

Purchased in-process research and development expense. There was no Purchased in-process research and development expense during the year ended December 31, 2007. Purchased in-process research and development for the year ended December 31, 2006 of $8.3 million resulted from the Merger and represents the estimated fair value of certain intangible assets acquired in that transaction. We determined these assets had not reached technological feasibility and had no alternative future use, therefore the assets were fully expensed in 2006.

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Interest income. Interest income in 2007 increased to $2.1 million in 2007 from $1.6 million in 2006. The increase of $0.5 million is due to higher average cash and cash equivalents balances in 2007 compared to 2006.

Interest expense. Interest expense decreased to $0.8 million in 2007 from $1.0 million in 2006. The $0.2 million decrease is attributable to a lower average debt balance in 2007 compared to 2006.

Other income (expense), net. Other income (expense), net for the twelve months ended December 31, 2007 is comprised of an impairment of the investment in OXIS of $1,881,000 and other expense of $3,000, offset by income from a warrant valuation adjustment of $892,000 and equity in income of OXIS of $141,000. Other income (expense), net for the twelve months ended December 31, 2006 is comprised of equity in loss of OXIS of $916,000, a loss from a warrant valuation adjustment of $240,000 and other income of $16,000.

Liquidity and Capital Resources

Since our inception and until the Merger in October 2006, we have financed our business primarily through private placements of preferred stock, payments from research agreements, debt financing and interest income. We have incurred significant losses since inception.

Through December 31, 2008, we had received net proceeds of approximately $68.0 million from the issuance of equity securities, primarily from the issuance of redeemable convertible preferred stock. In 2006, we sold a total of 689,036 shares of Series C-2 redeemable convertible preferred stock for net proceeds of $6.3 million. Pursuant to the Merger, all outstanding shares of redeemable convertible preferred stock were exchanged for common stock. Additionally, after considering merger related expenses, we acquired $43.7 million of cash in the Merger.

Through December 31, 2008, we had received an aggregate of $47.4 million in option fee and research funding payments in connection with collaboration agreements with Eisai. The last of these agreements expired by their terms in February 2008 and September 2008, respectively.

Through December 31, 2008, we had incurred $22.4 million in debt to finance equipment purchases and our on-going operations. During 2005, we entered into a $10.0 million debt facility agreement (the 2005 Debt), from which we drew down $5.0 million in 2005 and an additional $5.0 million in 2006. During 2008 we repaid the outstanding balance of the 2005 Debt. The total payoff of the 2005 Debt was $3.0 million. Also during 2008 we entered into a new note agreement with a different institution to borrow $3.6 million (the 2008 Debt).

Pursuant to the terms of the 2008 Debt agreement, we are required to maintain a cash balance with the lender s bank of at least $5.4 million. Additionally, we are subject to other financial and non-financial covenants as described in Note 6 to the financial statements included elsewhere in this Annual Report on Form 10-K. As of December 31, 2008 we are in compliance with all covenants. We are projecting that our cash balance will decrease below the $5.4 million requirement in 2009 should we not be successful in securing additional cash sources in the near-term. At the time our cash balance drops below $5.4 million, we expect to have sufficient cash on hand to repay the amount outstanding under the agreement should the bank declare the 2008 Debt immediately due and payable.

At December 31, 2008, we had cash and cash equivalents of $10.9 million as compared to $32.5 million at December 31, 2007. The cash balance at December 31, 2008 is $21.6 million lower than the balance at December 31, 2007 due largely to operating losses, repayments of debt, capital equipment purchases and working capital movements from December 31, 2007 to December 31, 2008, offset by proceeds from the sale of property and equipment and the sale of our investment in OXIS. At December 31, 2007, we had cash and cash equivalents of $32.5 million as compared to $55.4 million at December 31, 2006. The cash balance at December 31, 2007 is $22.9 million lower than the balance at December 31, 2006 due largely to operating losses, capital equipment purchases, repayments of debt and working capital movements from December 31, 2006 to December 31, 2007.

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Based on our operating plan, our cash and cash equivalents will only fund our operations into the second quarter, and possibly into the third quarter, of 2009. Although we will seek additional financing or a strategic partner, we may not be able to complete a financing or corporate transaction, either on favorable terms or at all. If we are unable to complete a financing or strategic transaction, we do not expect to be able to continue as a going concern. See the section titled Going Concern and Management s Plan for further discussion. As of December 31, 2008, we had the following contractual obligations (in thousands):

	Payments Due by Period				
	Total	2009	2010-2011	2012-2013	2014 and beyond
Debt	$ 3,600	$ 1,440	$ 2,160	$	$
Interest on debt(1)	205	131	74		
Operating lease obligations	210	210			
Total contractual cash obligations	$ 4,015	$ 1,781	$ 2,234	$	$

(1) Interest accrues at a rate of prime plus 1%. The prime rate as of December 31, 2008 was 3.25%. For purposes of this disclosure, interest is estimated based upon an assumed prime rate of 3.25%.

We may be obligated to pay up to $72.8 million in payments due upon the occurrence of certain milestones related to regulatory or commercial events described in our license agreements. We may also be required to pay royalties on any net sales of the licensed products. These milestone payments and royalty payments under our license agreements are not included in the table above because we cannot, at this time, determine when or if the related milestones will be achieved or the events triggering the commencement of payment obligations will occur.

We also enter into agreements with contract research organizations and clinical sites for the conduct of our clinical trials. We will make payments to these organizations and sites based upon the number of patients enrolled and the length of their participation in the clinical trials. At this time, due to the variability associated with these agreements, we are unable to estimate with certainty the future costs we will incur.

We have entered into employment agreements with key executives that provide for the continuation of salary if terminated for reasons other than cause, as defined in those agreements. These agreements generally expire upon termination for cause or when the Company has met its obligations under these agreements. As of December 31, 2008, no events have occurred resulting in the obligation of any such payments.

Our future capital uses and requirements depend upon a number of factors, which may include but are not limited to the following:

the rate of progress and cost of our development activities,

the scope, prioritization and number of development programs we pursue,

the costs and timing of regulatory approvals,

the costs of establishing or contracting for manufacturing, sales and marketing capabilities,

the terms and timing of any strategic collaboration or license agreements that we may establish,

the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights,

the effect of competing technological and market developments, and

the extent to which we acquire or in-license new products, technologies or businesses.

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Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements.

Critical Accounting Policies and Significant Judgments and Estimates

Our discussion and analysis of our financial condition and results of operations are based on our financial statements, which have been prepared in accordance with accounting principles generally accepted in the United States, or GAAP. The preparation of these financial statements requires us to make estimates and judgments that affect the reported amounts of assets and liabilities and the disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenue and expenses during the reporting periods. Note 1 of the notes to our financial statements included in this Form 10-K includes a summary of our significant accounting policies and methods used in the preparation of our financial statements. On an on-going basis, our management evaluates its estimates and judgments, including those related to revenue, accrued expenses, in-process research and development and stock-based compensation. Our management bases its estimates on historical experience, known trends and events, and various other factors that it believes to be reasonable under the circumstances, the results of which form its basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions.

Our management believes the following accounting policies and estimates are most critical to aid you in understanding and evaluating our reported financial results.

Revenue Recognition

We recognize revenue in accordance with the SEC s Staff Accounting Bulletin, or SAB, No. 104, *Revenue Recognition*, and Emerging Issues Task Force, or EITF, No. 00-21, *Revenue Arrangements with Multiple Deliverables*. To date we have recorded license and option fee revenue and research funding revenue from four research agreements with Eisai. The terms of the agreements typically include up-front payments to us of non-refundable license and/or option fees and, in some cases, payments for research efforts. Future agreements could also include milestone payments and royalty payments.

We recognize revenue from up-front non-refundable license and option fees on a straight-line basis over the contracted or estimated period of performance, which is typically the research term. Amounts received for research funding for a specific number of full-time researchers are recognized as revenue as the services are provided, as long as the amounts received are not refundable regardless of the results of the research project. Milestone payments, if any, will be recognized on achievement of the milestone, unless the amounts received are creditable against royalties or we have on-going performance obligations. Royalty payments, if any, will be recognized on sale of the related product, provided the royalty amounts are fixed and determinable, and collection of the related receivable is probable.

Accrued Expenses

As part of the process of preparing financial statements, we are required to estimate accrued expenses. This process involves identifying services which have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for such service as of each balance sheet date in our financial statements. Examples of services for which we must estimate accrued expenses include contract service fees paid to contract manufacturers in conjunction with the production of clinical drug supplies and to contract research organizations in connection with our preclinical studies and clinical trials. In connection with such service fees, our estimates are most affected by our understanding of the status and timing of services provided. The majority of our service providers invoice us in arrears for services performed. In the event that we do not identify certain costs which have been incurred, or we under- or over-estimate the level of services performed or the costs of such services in a given period, our reported expenses for such period would be too low or too high. The date on

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which certain services commence, the level of services performed on or before a given date, and the cost of such services are often determined based on subjective judgments. We make these judgments based upon the facts and circumstances known to us. To date, we have been able to reasonably estimate these costs; however, as we increase the level of services performed on our behalf, it will become increasingly more difficult for us to estimate these costs, which could result in our reported expenses for future periods being too high or too low.

Stock-Based Compensation

We estimate the fair value of stock options granted using the Black-Scholes option valuation model and the fair value of restricted stock units granted using a Monte-Carlo simulation option-pricing model. The fair values of stock option and restricted stock unit awards are amortized over the requisite service periods of the awards. Both the Black-Scholes option valuation model and the Monte-Carlo simulation option-pricing model require the input of highly subjective assumptions, including the option or restricted stock unit s expected life, price volatility of the underlying stock, risk free interest rate and expected dividend rate. As stock-based compensation expense related to stock options is based on awards ultimately expected to vest, the stock-based compensation expense has been reduced for estimated forfeitures of stock options. Statement of Financial Accounting Standards, or SFAS, No. 123R, *Share-Based Payment*, requires forfeitures to be estimated at the time of grant and revised, if necessary, in subsequent periods if actual forfeitures differ from those estimates. Stock option forfeitures were estimated based on historical experience. We may elect to use different assumptions under both the Black-Scholes option valuation model or the Monte-Carlo simulation option- pricing model in the future, which could materially affect our net income or loss and net income or loss per share.

Recent Accounting Pronouncements

See Note 1 in the accompanying notes to our consolidated financial statements beginning on page F-1 in this Annual Report on Form 10-K.

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

We are exposed to market risk related to changes in interest rates. Our current investment policy is to maintain an investment portfolio consisting mainly of U.S. money market and high-grade corporate securities, directly or through managed funds, with maturities of one and a half years or less. We do not enter into investments for trading or speculative purposes. Our cash is deposited in and invested through highly rated financial institutions in North America. If market interest rates were to increase immediately and uniformly by 10% from levels at December 31, 2008 and 2007, our cash and cash equivalents balances would not be significantly affected.

We had foreign currency accounts that were exposed to currency exchange risk. The operations of the Belgium subsidiary were closed in December 2008. The functional currency of our European subsidiary, which was based in Belgium, was the local currency. Accordingly, the accounts of this subsidiary were translated from the local currency to the U.S. dollar using the exchange rate at the balance sheet date for the balance sheet accounts, and using the average exchange rate during the period for revenue and expense accounts. The effects of translation are recorded in accumulated other comprehensive loss as a separate component of stockholders deficit through the closure date for the subsidiary and in other income (expense) in the results of operations thereafter. For the years ended December 31, 2008 and 2007, we recorded exchange gains of $145,000 and $0, respectively. For the year ended December 31, 2008 a total of $486,000 of foreign currency translation gains that were recorded in stockholders equity (deficit) were reclassified to other income (expense) upon the closure of the Belgium subsidiary.

Item 8. Financial Statements and Supplementary Data.

Our financial statements appear in a separate section of this Annual Report on Form 10-K beginning on page F-1.

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

Not applicable.

Item 9A(T). Controls and Procedures.

Conclusion Regarding the Effectiveness of Disclosure Controls and Procedures

We maintain disclosure controls and procedures that are designed to ensure that information required to be disclosed in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the SEC s rules and forms, and that such information is accumulated and communicated to our management, including our principal executive officer and principal financial officer, as appropriate, to allow timely decisions regarding required disclosure.

Under the supervision and with the participation of our management, including our principal executive officer and principal financial officer, we conducted an evaluation of our disclosure controls and procedures, as such term is defined under Rule 13a-15(e) under the Exchange Act, as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our principal executive officer and our principal financial officer concluded that our disclosure controls and procedures were designed and operating effectively as of the end of the period covered by this Annual Report on Form 10-K.

Management s Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting, as such term is defined in Rule 13a-15(f) under the Exchange Act. Our internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of our financial reporting and the preparation of published financial statements in accordance with generally accepted accounting principles.

Our management, including our principal executive officer and our principal financial officer, does not expect that our disclosure controls and procedures or our internal controls over financial reporting will prevent all errors and all fraud. A control system, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. Further, the design of a control system must reflect the fact that there are resource constraints, and the benefits of controls must be considered relative to their costs. Because of the inherent limitations in all control systems, no evaluation of controls can provide absolute assurance that all control issues and instances of fraud, if any, within the Company have been detected.

Management conducted its evaluation of the effectiveness of our internal control over financial reporting as of December 31, 2008 based on the framework in *Internal Control-Integrated Framework* Issued by the Committee of Sponsoring Organizations of the Treadway Commission. Based on our evaluation under the framework in *Internal Control-Integrated Framework*, our management concluded that our internal control over financial reporting was effective as of December 31, 2008.

This annual report does not include an attestation report of our independent registered public accounting firm regarding internal control over financial reporting. Management s report was not subject to attestation by our independent registered public accounting firm pursuant to temporary rules of the Securities and Exchange Commission that permit us to provide only management s report in this annual report.

Changes in Internal Control Over Financial Reporting

There has been no change in our internal control over financial reporting during the fourth quarter ended December 31, 2008 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

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PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Directors of the Registrant

Our directors as of March 15, 2009 are as follows:

Name	Age	Position
Peter Davis, Ph.D.	64	Chairman of the Board and Director
Jean Deleage, Ph.D.	68	Director
Steven H. Ferris, Ph.D.	65	Director
Jason Fisherman, M.D.	52	Director
Evelyn A. Graham	60	Chief Executive Officer and Director
Steven B. Ratoff	66	Director
Patrick Van Beneden	46	Director

Peter Davis, Ph.D., has served as a director of our Company since October 2006 and the Chairman of our Board since May 2007. He previously served as a director of TPTX, Inc., our subsidiary, from August 2005 to February 2007. Since 2002, Dr. Davis has worked as an independent consultant to a number of companies. Dr. Davis served as president of DNA Plant Technologies Corp., an agriculture biotechnology company, from 2001 to 2002. Dr. Davis was a member of the Executive Committee of Pulsar International, S.A., a management consultant company and an affiliate of A.G. Biotech Capital, from 1993 to 2001. From 1975 to 1993, Dr. Davis was a faculty and staff member of the Wharton School of the University of Pennsylvania. His primary appointments included Director of the Applied Research Center and Director of Executive Education. He is a member of the Board of Directors of several private companies. Dr. Davis received a B.A. in physics from Cambridge University, a Masters Degree in operations research from the London School of Economics and a Ph.D. in operations research from the Wharton School of the University of Pennsylvania.

Jean Deleage, Ph.D. has served as a director since October 2006 and previously served as a director of TPTX, Inc., our subsidiary, from May 2000 to February 2007. Dr. Deleage was the chairman of our Board from October 2006 to May 2007. Dr. Deleage is a founder and managing director of Alta Partners, a venture capital firm investing in information technologies and life science companies, since founding the firm in February 1996. From 1979 to 1996, Dr. Deleage was a founder and a managing partner of Burr, Egan, Deleage & Co., a venture capital firm. In 1971, Dr. Deleage was the founder of Sofinnova, a venture capital organization in France, and in 1976 formed Sofinnova, Inc., Sofinnova s U.S. subsidiary. Dr. Deleage currently serves as a director of Innate Pharma SA, LifeCycle Pharma A/S, Rigel Pharmaceuticals, Inc. and several privately held companies. Dr. Deleage received a Baccalaureate in France, a M.A. in electrical engineering from Ecole Superieure d Electricite, and a Ph.D. in economics from the Sorbonne.

Steven H. Ferris, Ph.D. has served as a director of our Company since January 2003. Dr. Ferris is a neuropsychologist, psychopharmacologist, and gerontologist who has been studying brain aging and Alzheimer s disease for over 30 years. Dr. Ferris is the Friedman Professor and Director of the Alzheimer s Disease Center in the Department of Psychiatry at New York University (NYU) School of Medicine, and Executive Director of the Aging and Clinical Dementia Research Center of the NYU Center of Excellence for Brain Aging and Dementia. Dr. Ferris has been at the NYU School of Medicine since 1973, where he has conducted a major research program focusing on cognitive assessment, early diagnosis and treatment of brain aging and Alzheimer s disease. He has served as the Associate Editor in Chief of *Alzheimer Disease and Associated Disorders*, is a former member of the Medical and Scientific Affairs Council of the national *Alzheimer s Association*, has served on several National Institutes of Health peer review panels, and has been a member of the U.S. Food and Drug Administration Advisory Committee which reviews new drugs for Alzheimer s disease. He has conducted more than 75 clinical trials in aging and dementia and has been a consultant to numerous pharmaceutical companies who are developing new treatments for Alzheimer s disease.

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Jason Fisherman, M.D. has served as a director of our Company since October 2006 and previously served as a director of TPTX, Inc., our subsidiary, from May 2000 to February 2007. Dr. Fisherman is a Managing Director of Advent Healthcare Ventures, a life science venture capital firm he co-founded in 2007. From 1994 to 2007, Dr. Fisherman was at Advent International Corporation, a global private equity firm, where he was a Managing Director since 2002. Prior to Advent, Dr. Fisherman served for four years as Senior Director of Medical Research for Enzon, Inc, a biopharmaceutical company, and previously managed the clinical development of a number of oncology drugs at the National Cancer Institute. Dr. Fisherman currently serves as a director of several private biopharmaceutical companies. Dr. Fisherman received his B.A from Yale University, his M.D. from the University of Pennsylvania and his M.B.A. form the Wharton School of the University of Pennsylvania.

Evelyn A. Graham has served as our Chief Executive Officer and a director of our Company since November 2008. Ms. Graham served as our Acting Chief Executive Officer from September 2008 to November 2008 and as our Chief Operating Officer from October 2006 to August 2008. Ms. Graham joined TPTX, Inc., our subsidiary, in 2004 as Vice President, Development; she became TPTX Inc. s Vice President, Corporate Development in 2005 and Chief Operating Officer in 2006. Ms. Graham was Executive Director, Development Operations at Purdue Pharma, a privately-held pharmaceutical company, from 2000 to 2003. From 1998 to 2000, Ms. Graham was Senior Vice President of Business Development of Ingenix Pharmaceutical Services, a health information technology company and a division of UHG, and served as Vice President of Clinical Operations at Worldwide Clinical Trials, a contract research organization, prior to its acquisition by UHG. Previously, Ms. Graham held positions in operations management, healthcare utilization, and organizational planning at Bayer Corporation and Wyeth Pharmaceuticals (formerly Ayerst Laboratories). Ms. Graham holds a B.A. in biology from the University of Delaware and an M.B.A. from the University of Connecticut.

Steven B. Ratoff has served as a director of our Company since May 2005. From September 2005 to October 2006, Mr. Ratoff served as the Chairman of our Board. Mr. Ratoff is currently a private investor and has been a Venture Partner with Proquest Investments, a biopharmaceutical venture firm, since 2004. In addition, he is currently serving as the Chairman and Interim Chief Executive Officer of Novadel Pharma, Inc., a publicly traded specialty pharmaceutical company. He served as Chairman and Interim Chief Executive Officer of Cima Labs, Inc., a publicly traded specialty pharmaceutical company, from May 2003 through its sale to Cephalon, Inc. in August 2004. He was the President and Chief Executive Officer of MacroMed, Inc., a privately owned drug delivery company, from February 2001 to December 2001, and also as director of that company from 1998 to 2001. Mr. Ratoff s experience includes serving as Executive Vice President and Chief Financial Officer of Brown-Forman Corporation, a publicly traded diversified manufacturer of consumer products, as well as 15 years in a variety of senior financial positions with Bristol-Myers Squibb. Mr. Ratoff received a B.S. in Business Administration from Boston University and an M.B.A. with Distinction from the University of Michigan. Mr. Ratoff is also a retired Certified Public Accountant.

Patrick Van Beneden has served as a director of our Company since October 2006 and previously served as a director of TPTX, Inc., our subsidiary, from 2003 to February 2007. Since 2001, Mr. Van Beneden has been Executive Vice President Life Sciences of GIMV N.V., a Belgian investment company, and he has held various positions with GIMV since 1985. Mr. Van Beneden serves as a director of a number of private healthcare companies. Mr. Van Beneden holds a Masters Degree in applied economics from VLEKHO-Brussels.

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Executive Officers of the Registrant

Our executive officers as of March 15, 2009 are as follows:

Name	Age	Position
Evelyn A. Graham	60	Chief Executive Officer and Director
Craig A. Johnson	47	Chief Financial Officer and Vice President, Finance
Susan J. Mellberg	57	Vice President, Project Management
Paul R. Schneider	38	Vice President and General Counsel

Craig A. Johnson has been our Chief Financial Officer and Vice President, Finance since October 2006. Mr. Johnson has served as Chief Financial Officer and Vice President, Finance of TPTX, Inc., our subsidiary since January 2004 and as director since February 2007. From 1994 to 2004, Mr. Johnson served in a number of financial positions with MitoKor, Inc., a biotechnology company, and last held the position of Chief Financial Officer and Senior Vice President of Operations. Prior to joining MitoKor, Mr. Johnson served as a senior financial executive for several early-stage technology companies, and from 1984 to 1988 Mr. Johnson worked for the accounting firm Price Waterhouse. Mr. Johnson received his B.B.A. in accounting from the University of Michigan and is a certified public accountant. He has been actively involved in the Association of Bioscience Financial Officers since 1998. Mr. Johnson serves as a director and the Chairman of the Audit Committee for Ardea Biosciences, Inc., a publicly traded biotechnology company.

Susan J. Mellberg has been our Vice President of Project Management since 2004. Ms. Mellberg brings over 23 years of clinical operation experience. Prior to 2004, she was Vice President of Clinical Operations at Ingenix Pharmaceutical Services, a division of UnitedHealth Group (UHG), and Senior Director of Clinical Operations at Worldwide Clinical Trials, prior to its acquisition by UHG. Ms. Mellberg has also held positions of increasing responsibility in clinical operations at Hoechst Marion Roussel Pharmaceuticals (formerly Marion Merrell Dow). She received her B.A. in healthcare administration from Ottawa University, her M.B.A. from Baker University, and she is also a Registered Nurse.

Paul R. Schneider has been our Vice President and General Counsel since 2007. From 2002 to 2007, Mr. Schneider was an associate with the law firm of Cooley Godward Kronish, LLP. From 1993 to 1999, Mr. Schneider worked as an analytical chemist for Eli Lilly & Company. Mr. Schneider is a member of the State Bar of California and holds B.S. degrees in Chemistry and Economics from the University of Wisconsin, Madison and a J.D. from Duke Law School.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Securities Exchange Act of 1934 requires our directors and executive officers, and persons who own more than 10% of a registered class of our equity securities, to file with the SEC initial reports of ownership and reports of changes in ownership of common stock and other equity securities of the Company. Officers, directors and greater than 10% stockholders are required by SEC regulation to furnish the Company with copies of all Section 16(a) forms they file.

To our knowledge, based solely on a review of the copies of such reports furnished to the Company and written representations that no other reports were required, during the fiscal year ended December 31, 2008, all Section 16(a) filing requirements applicable to its officers, directors and greater than 10% beneficial owners were complied with.

Code of Business Conduct and Ethics

We have adopted a code of ethics for directors, officers (including our principal executive officer, principal financial officer and principal accounting officer) and employees, known as the Code of Business Conduct and

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Ethics. The Code of Business Conduct and Ethics is available on our website at *http://www.tptxinc.com* under the Corporate Governance section of our Investor Center page. We will promptly disclose on our website (i) the nature of any amendment to the policy that applies to our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions and (ii) the nature of any waiver, including an implicit waiver, from a provision of the policy that is granted to one of these specified individuals, the name of such person who is granted the waiver and the date of the waiver. Stockholders may request a free copy of the Code of Business Conduct and Ethics from our corporate compliance officer, Paul Schneider c/o TorreyPines Therapeutics, Inc., 11085 North Torrey Pines Road, Suite 300, San Diego, CA 92037.

Identification of Audit Committee; Audit Committee Financial Expert

The Company s board of directors has established an audit committee. Dr. Peter Davis, Dr. Steven Ferris and Steven Ratoff each serve on the audit committee, with Dr. Davis serving as chairman. The Company s board of directors has determined that Dr. Davis and Mr. Ratoff are audit committee financial experts and are independent.

Item 11. Executive Compensation.

Compensation Committee Report

The material in this report is not soliciting material, is not deemed filed with the SEC, and is not to be incorporated by reference into any filing of the Company under the Securities Act of 1933, or the Securities Act, or the Exchange Act.

The Compensation Committee has reviewed and discussed with management the Compensation Discussion and Analysis, or CD&A, contained in this Annual Report. Based on this review and discussion, the Compensation Committee has recommended to the Board that the CD&A be included in this Annual Report on Form 10-K for the fiscal year ended December 31, 2008.

Mr. Steven Ratoff

Dr. Jason Fisherman

Mr. Patrick Van Beneden

Compensation Discussion and Analysis

Objectives and Philosophy of Executive Compensation

The Compensation Committee of our Board is responsible for establishing, implementing and monitoring the policies governing compensation for our executives. The objective of the Compensation Committee is to provide a competitive compensation package that will attract, motivate and retain talented and dedicated executives who will enable us to achieve our key strategic goals. The Compensation Committee believes it is important to align incentives for executives with value creation for stockholders. In order to accomplish this purpose, the Compensation Committee believes it is appropriate for a significant amount of the total compensation of each executive to be based on performance, which compensation may or may not be earned. The Compensation Committee intends to make compensation decisions that:

- support our overall business objectives;
- reward outstanding performance in discovery, preclinical development and clinical development;
- recognize disciplined management of financial resources;

motivate employees in a high performance environment; and

demand the highest standards of corporate governance and personal integrity.

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The Compensation Committee believes that:

- the overall compensation package for each of our executives should be based on performance, should motivate our executives to achieve our key strategic goals, and should be aligned with the compensation package of our other executive officers and employees;

- for the purpose of recruitment and retention, executive base salaries should be competitive with salaries paid to executives at peer group companies in the life sciences industry that are comparable to us in size and stage of development, and should be targeted near the median salary range for executives with similar responsibilities at public companies in our peer group and base salaries should represent a portion of the overall compensation package that provides sufficient incentives to strive for achievement of goals;

- actual bonus amounts should be conditioned upon the achievement of corporate and individual goals that reflect key strategic objectives that are expected to create overall stockholder value if achieved, target bonus amounts for executives should be competitive with bonus amounts paid to executives at companies in our peer group, and target bonus amounts should represent a portion of the overall compensation package that provides sufficient incentives to strive for achievement of goals; and

- long-term equity incentive awards offer an important element of our overall compensation package that reward our executives for meeting our long-term goals while preserving available cash and align executive interests with those of our stockholders.

In addition the Compensation Committee believes that it is necessary to provide severance payments to certain executives in order to remain competitive with our peer group. However, the Compensation Committee believes that any severance payments paid in the event of a change of control of the Company should be triggered only in the event that the executive no longer remains an executive of the combined company following the change of control. In addition, any severance paid to executives, either in connection with a change of control or otherwise, should be in the lower range of severance paid to executives by companies in our peer group.

The Compensation Committee believes that providing executives with a mix of stock options and restricted stock units is the appropriate means of retaining executives, focusing our executives on delivering long-term value to stockholders and providing long-term value to our executives. Stock options vest over time and only have value to the extent our stock price on the date the option is exercised exceeds the exercise price of the option. The restricted stock units will vest on the achievement of certain objectively defined results and have value to the executives at that time without the requirement of further payment by the executive. The Compensation Committee believes that the combination of stock option grants and restricted stock unit grants will achieve the proper balance between upside potential and volatility while providing good long-term incentives to our executives.

Material tax and accounting implications of executive compensation policies

We account for the equity compensation expense for our employees under the rules of SFAS 123R, which requires us to estimate and record an expense for each award of equity compensation over the service period of the award. Accounting rules also require us to record cash compensation as an expense at the time the obligation is accrued. Unless and until we achieve sustained profitability, the availability to us of a tax deduction for compensation expense is not material to our financial position. We structure discretionary cash bonus compensation so that it is taxable to our employees at the time it becomes available to them. Federal income tax law prohibits publicly held companies from deducting certain compensation paid to a named executive officer that exceeds $1 million during the tax year. To the extent that compensation is based upon the attainment of performance goals set by the Compensation Committee pursuant to plans approved by our stockholders, the compensation is not included in the computation of this limit. Although the Compensation Committee intends, to the extent feasible and where it believes it is in the best interests of the Company and our stockholders, to attempt to qualify executive compensation as tax deductible, it does not intend to permit this tax provision to dictate the Compensation Committee s development and execution of effective compensation plans.

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Evaluation of Executive Compensation Package

During the months of November and December 2008 and January 2009, the Compensation Committee, along with the Board, had numerous informal discussions regarding the appropriate compensation packages for our executives. The Compensation Committee, in conjunction with the Board, determined that given the financial constraints of the Company there would be no salary adjustment for 2009 and no bonuses paid for 2008.

Elements of Executive Compensation

Executive compensation consists of the following elements:

Base Salary. Base salaries for our executives are established based on the particular scope of each executive s responsibilities as well as their qualifications, experience and performance, taking into account competitive market compensation paid by other companies in our peer group for individuals with similar responsibilities. Base salaries are reviewed annually, and additionally may be adjusted from time to time to realign salaries with market levels after taking into account individual responsibilities, performance and experience. The Compensation Committee intends to conduct an annual review of base salaries, and the overall compensation package, each year toward the end of the year.

Discretionary Annual Cash Bonus. Discretionary annual cash bonuses are a means of rewarding individuals based on achievement of annual corporate and individual goals. The Compensation Committee has the authority to award discretionary annual cash bonuses to our executives. Each of our executives has an annual cash bonus target ranging from 20% to 40% of base salary for 2008 depending on such executive s responsibilities. At the beginning of 2008 the Compensation Committee met with our management team to specify a limited number of key corporate goals for the year. These goals were then weighted to reflect their importance in determining overall corporate performance. At the end of 2008 the Compensation Committee reviewed corporate performance and determined whether the particular goal was achieved. The sum of the goals achieved is the basis for any bonus payout amount for each executive.

2008 Bonus Amounts. In 2008, the Compensation Committee and the Board determined that given the current financial condition of the Company no bonuses would be paid to any of the Company s executives.

Long-Term Equity Incentive Awards. Long-term equity incentive awards are a means of encouraging executive ownership of our stock, promoting executive retention, and providing a focus on long-term corporate goals as well as increased stockholder value. The Compensation Committee approves equity incentive award grants at year end following an increase in responsibilities by an executive.

In December 2006, the Compensation Committee developed a three year equity award plan that would result in fair and equitable level of ownership in the Company by the senior executives should we be successful in achieving our long-term goals. The Compensation Committee s plan involves the use of both stock option grants, which vest over time, and restricted stock units that vest based on corporate and individual performance. In order to provide a significant incentive to our executives at a reasonable cost, the Compensation Committee determined that a substantial portion of the equity awards to be issued in the three year plan would be granted in 2006, with vesting periods that extend over four years.

Stock Options. Stock options granted by us have an exercise price equal to the fair market value of our common stock on the day of grant, typically vest over a four-year period with 25% vesting 12 months after the vesting commencement date and the remainder vesting ratably each month thereafter based upon continued employment, and generally expire ten years after the date of grant. Incentive stock options also include certain other terms necessary to assure compliance with the Code.

Restricted Stock and Restricted Stock Units. Our stock plans authorize us to grant restricted stock and restricted stock units. Restricted stock units vest on the attainment of a specified milestone or time period. Once the restricted stock unit has vested, the executive has the ability to obtain shares of our common stock.

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In determining the number of stock options and restricted stock units to be granted to executives, the Compensation Committee takes into account the individual s position, scope of responsibility, qualifications and experience, ability to affect stockholder value, historic and recent performance, existing vested and unvested awards, and the value of stock options in relation to the other elements of the individual executive s total compensation package. In order to control overall stockholder dilution, the Compensation Committee also evaluates the aggregate outstanding stock options to all our employees in relation to those granted to our executives when determining the number of options and restricted stock units that should be granted.

2008 Equity Awards. In 2008, our executives were awarded stock options in the amounts indicated in the section entitled Grants of Plan-Based Awards. These awards are based on the executives performance during 2008 and as part of the three year equity plan developed by the Compensation Committee in 2006.

2009 Equity Awards. In 2009, our executives were awarded stock options in the amounts indicated in the section entitled Grants of Plan-Based Awards. These awards were granted as a means of promoting executive retention and focus on near-term corporate goals.

Broad-Based Benefit Plans. Broad-based benefit plans are an integral component of competitive executive compensation packages. Our benefits include a 401(k) savings plan, health benefits such as medical, dental, and vision plans, and disability and life insurance benefits. We have no structured perquisite benefits, and we do not provide any deferred compensation programs or supplemental pensions to any executives. In its discretion, the Compensation Committee may revise, amend or add to the executive s benefits if it deems it advisable.

Change in Control and Severance Benefits. Change in control arrangements are designed to retain executives and provide continuity of management in the event of a change in control. We have entered into employment agreements with our Chief Executive Officer, our Chief Financial Officer and our Vice President and General Counsel. These agreements are described in more detail elsewhere in this annual report, including the section titled Potential Payments Upon Termination or Change-in-Control Arrangements . These agreements provide for severance compensation to be paid if the executives are terminated under certain conditions, such as a termination following a change in control or a termination without cause by us, each as set forth in the applicable agreement.

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The following table provides information regarding the annual and long-term compensation earned for services rendered in all capacities to TorreyPines Therapeutics, Inc. for the years ended December 31, 2008, 2007 and 2006 of those persons who (i) served at any time during the last fiscal year as our Principal Executive Officer, (ii) served at any time during the last fiscal year as our Principal Financial Officer, (iii) were serving at fiscal year-end as our two most highly compensated executive officers, other than the Principal Executive Officer and the Principal Financial Officer, whose total compensation exceeded $100,000 (collectively, the Named Executive Officers) and (iv) any additional persons who would have been a Named Executive Officer but for not serving as of December 31, 2008.

SUMMARY COMPENSATION TABLE FOR 2008

Name and Principal Position	Year	Salary ($)	Bonus ($)	Stock Awards (1)($)	Option Awards (1)($)	Non-Equity Incentive Plan Compensation (2)($)	All Other Compensation ($)	Total ($)
Evelyn A. Graham	2008	$ 304,667		$ 34,270	$ 45,206	$	$	$ 384,143
Chief Executive Officer	2007	271,200		34,175	40,418	69,200		414,993
	2006	228,757		1,609	15,107	88,400		333,873
Craig A. Johnson	2008	282,000		34,270	44,214			360,484
Vice President, Chief Financial Officer	2007	271,200		34,175	40,431	69,200		415,006
	2006	223,221		1,609	15,120	61,951		301,901
Susan J. Mellberg	2008	197,400		20,562	23,155			241,117
Vice President, Project Management								
Paul R. Schneider	2008	217,700		1,007	75,208			293,915
Vice President and General Counsel								
Neil M. Kurtz, M.D.	2008	320,015		(93,040)	51,515			278,490
Former President & Chief Executive	2007	417,200		88,856	78,436	141,800		726,292
Officer(3)	2006	354,272		4,184	18,639	135,364		512,459
Steven Wagner, Ph.D.	2008	249,068		(14,314)	8,987		12,249(5)	255,990
Former Chief Scientific Officer(4)	2007	237,800		13,670	13,809	50,500		315,779
	2006	228,000		644	2,039	59,850		290,533

(1) The amounts shown reflect the dollar amount recognized for financial statement reporting purposes for the fiscal years ended December 31, 2008, 2007 and 2006, in accordance with FAS 123R of restricted stock units granted pursuant to our 2006 Equity Incentive Plan (the 2006 Plan) or stock option grants pursuant to both the 2000 Stock Option Plan (the 2000 Plan) and the 2006 Plan and thus may include amounts from restricted stock units or stock options granted in and prior to 2008, 2007 and 2006, respectively. Assumptions used in the calculation of these amounts are included in the footnotes of the consolidated Financial Statements included in Part IV, Item 15, of this Annual Report on Form 10-K.

(2) Amounts listed in this column for 2007 were awarded for corporate and individual performance in 2007 but were paid in January 2008. Amounts listed in this column for 2006 were awarded for corporate and individual performance in 2006 but were paid in February 2007.

(3) Dr. Kurtz resigned from the Company effective August 31, 2008.

(4) Dr. Wagner s last date of employment was September 30, 2008 and his total salary for 2008 includes severance pay totaling $61,225.

(5) Amount consists of a reimbursement for the cost of health benefits under COBRA.

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Grants of Plan-Based Awards

The following table presents information concerning grants of plan-based awards to each of the Named Executive Officers for the fiscal year ended December 31, 2008.

GRANTS OF PLAN-BASED AWARDS IN 2008

Name	Grant Date	Estimated Possible Payouts Under Non-Equity Incentive Plan Awards(1) Threshold ($)	Target ($)	Maximum ($)	All Other Option Awards: Number of Securities Underlying Options (2)(#)	Exercise or Base Price of Option Awards ($/Sh)	Grant Date Fair Value of Stock and Option Awards (3)($)
Evelyn A. Graham	10/15/08				300,000	0.27	53,580
	n/a	110,250	157,500	236,250			
Craig A. Johnson	10/15/08				250,000	0.27	44,650
	n/a	59,220	84,600	126,900			
Paul R. Schneider	10/15/08				120,000	0.27	21,432
		38,098	54,425	81,638			
Susan J Mellberg	10/15/08				120,000	0.27	21,432
		29,036	41,480	62,220			
Neil M. Kurtz, M.D.(4)	n/a	131,418	187,740	281,610			
Steven L. Wagner, Ph.D.(5)	n/a	42,858	61,225	91,838			

(1) The amounts shown in these columns represent the threshold, target and maximum payout levels for discretionary annual cash bonuses for 2008 performance. The actual amount of incentive bonus earned by each Named Executive Officer in 2008 was $0 and is reported under the Non-Equity Incentive Plan Compensation column in the Summary Compensation Table. The potential payouts for Named Executive Officers are performance driven and therefore are completely at risk.

(2) This column reflects the number of stock options granted under our 2006 Plan during 2008. The terms of these awards are summarized in the Outstanding Equity Awards at Fiscal Year-End Table below.

(3) Amount represents the grant date fair value for stock options granted under our 2006 Plan during 2008 and is computed in accordance with FAS 123R. Assumptions used in the calculation of these amounts are included in the footnotes of the consolidated Financial Statements included in Part IV, Item 15, of this Annual Report on Form 10-K.

(4) Dr. Kurtz was our former President and Chief Executive Officer; he resigned from the Company effective August 31, 2008.

(5) Dr. Wagner was our former Chief Scientific Officer; his last date of employment was September 30, 2008.

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Outstanding Equity Awards at Fiscal Year-End

The following table presents the outstanding equity awards held by each of the Named Executive Officers as of the fiscal year ended December 31, 2008 including the value of outstanding stock awards.

OUTSTANDING EQUITY AWARDS AT DECEMBER 31, 2008

	Option Awards				Stock Awards	
Name	Number of Securities Underlying Unexercised Options (#) Exercisable	Number of Securities Underlying Unexercised Options (#) Unexercisable	Option Exercise Price ($)	Option Expiration Date	Equity Incentive Plan Awards: Number of Unearned Shares, Units or Other Rights That Have Not Vested (#)	Equity Incentive Plan Awards: Market or Payout Value of Unearned Shares, Units or Other Rights That Have Not Vested ($)(3)
Evelyn A. Graham(9)	8,120		1.24	2/04/2014		
	28,420	4,060(4)	1.24	6/12/2015		
	12,500	12,500(5)	6.37	12/13/2016		
	2,125	6,375(6)	2.90	12/05/2017		
	25,000	275,000(8)	0.27	10/14/2018		
					25,000(1)	6,750
Craig A. Johnson(10)	8,120		1.24	2/04/2014		
	28,420	4,060(4)	1.24	6/12/2015		
	12,500	12,500(5)	6.37	12/13/2016		
	2,125	6,375(6)	2.90	12/05/2017		
	20,833	229,167(8)	0.27	10/14/2018		
					25,000(1)	6,750
Susan J. Mellberg	8,628		1.24	2/04/2014		
	7,578	1,083(4)	1.24	6/12/2015		
	7,500	7,500(5)	6.37	12/13/2016		
	1,219	3,656(6)	2.90	12/05/2017		
	10,000	110,000(8)	0.27	10/14/2018		
					15,000(1)	4,050
Paul R. Schneider(11)	25,208	29,792(7)	7.77	1/31/2017		
	1,219	3,656(6)	2.90	12/05/2017		
	10,000	110,000(8)	0.27	10/14/2018		
					15,000(2)	4,050

(1) Amount reflects restricted stock units awarded during 2006. These restricted stock units will vest on March 31, 2009, provided our average closing stock price for the six-month period ending March 31, 2009 is at or above a specified amount. The restricted stock units are subject to forfeiture if the individual officers do not meet the service requirements and have an expiration date of December 31, 2016.

(2) Amount reflects restricted stock units awarded during 2006. These restricted stock units will vest on March 31, 2009, provided our average closing stock price for the six-month period ending March 31, 2009 is at or above a specified amount. The restricted stock units are subject to forfeiture if the individual officer does not meet the service requirements and have an expiration date of December 31, 2017.

(3) The amounts reflected as Market or Payout Value are based on the closing price of our common stock ($0.27) on December 31, 2008, the last business day of 2008, as reported by Nasdaq.

(4) These options vest in equal monthly installments on the 25th of each month and will be fully vested on April 25, 2009.

(5) These options vest in equal monthly installments on the 14th of each month and will be fully vested on December 14, 2010.

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(6) Twenty-five percent (25%) of the shares underlying the options vested on December 6, 2008 and thereafter the options vest in equal monthly installments on the 6th of each month. These options vest will be fully vested on December 6, 2011.
(7) These options vest in equal monthly installments on the 1st of each month and will be fully vested on February 1, 2011.
(8) These options vest in equal monthly installments on the 15th of each month and will be fully vested on October 15th, 2011.
(9) On February 23, 2009 the Board of Directors granted 300,000 stock options to Ms. Graham. These options have an exercise price of $0.23 per share, were one hundred percent (100%) vested as of the grant date and will expire on February 22, 2019.
(10) On February 23, 2009 the Board of Directors granted 250,000 stock options to Mr. Johnson. These options have an exercise price of $0.23 per share, were one hundred percent (100%) vested as of the grant date and will expire on February 22, 2019.
(11) On February 23, 2009 the Board of Directors granted 250,000 stock options to Mr. Schneider. These options have an exercise price of $0.23 per share, were one hundred percent (100%) vested as of the grant date and will expire on February 22, 2019.

Option Exercises and Stock Vested at Fiscal Year End

There were no option exercises by the Named Executive Officers and no stock awards vested during the fiscal year ended December 31, 2008.

Pension Benefits

None of our Named Executive Officers participates in or has account balances in qualified or non-qualified defined benefit plans sponsored by us.

Nonqualified Deferred Compensation

None of our Named Executive Officers participate in or have account balances in non-qualified defined contribution plans or other deferred compensation plans maintained by us.

Potential Payments Upon Termination or Change-in-Control Arrangements

Employment Agreement with Ms. Graham

We entered into an employment agreement with Ms. Graham on December 14, 2006. We entered into an amended and restated employment agreement with Ms. Graham on September 1, 2008 in connection with Ms. Graham being appointed acting Chief Executive Officer. On February 3, 2009 we entered into an amendment to such amended and restated employment agreement extending the time of severance payments to twelve (12) months following a change in control. Ms. Graham s employment agreement provides for an initial annual base salary of not less than $350,000 and provides that she will be eligible to earn an annual bonus for 2008 in an amount up to 150% of her target bonus of 45% of her annual base salary, as determined by our Board.

Pursuant to the terms of Ms. Graham s employment agreement, in the event that Ms. Graham s employment is terminated without cause or is terminated (either by us without cause or by such executive for good reason) three (3) months prior to or twelve (12) months after a change in control, Ms. Graham will be entitled to continue to receive for twelve months following the date of her termination or resignation (a) her base salary and (b) an amount equal to one-twelfth of the greater of (i) the average of the three annual bonuses paid to Ms. Graham by us prior to the date of termination or resignation, (ii) the last annual bonus paid to Ms. Graham by us prior to the date of termination or resignation, or (iii) if the termination occurs within the first 12 months following October 3, 2008, 45% of her base salary, which payments will be without reduction by any amount of Ms. Graham s earnings from any other employment during the 12-month severance period. Additionally, under

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those circumstances, the vesting of each of Ms. Graham s equity awards will be treated as if Ms. Graham had completed an additional 12 months of service immediately before the date on which her employment is terminated or she resigns. Ms. Graham s execution of a release in favor of the Company is a condition to the receipt of these severance benefits, and she has agreed to a non-solicitation obligation and to confidentiality and assignment of inventions obligations in connection with her employment agreement.

Under the agreement, a change in control is deemed to have occurred under any of the following circumstances, subject to certain exceptions and limitations: (i) a person becomes the owner of 50% or more of our voting power; (ii) the composition of our Board changes over a period of 24 consecutive months or less in a way that results in a majority of our Board (rounded up to the next whole number) ceasing, by reason of one or more proxy contests for the election of Board members, to be comprised of individuals who either (A) have been Board members continuously since the beginning of the period or (B) have been elected or nominated for election as Board members during the period by at least two-thirds of the Board members described in clause (A) who were still in office at the time the election or nomination was approved by the Board; (iii) (A) a merger or consolidation occurs in which we are not the surviving entity, or (B) any reverse merger occurs in which we are not the surviving entity, or (C) any merger involving one of our subsidiaries occurs in which we are a surviving entity, but in each case in which holders of our outstanding voting securities immediately prior to such transaction, as such, do not hold, immediately following such transaction, securities possessing 50% or more of the total combined voting power of the surviving entity s outstanding securities (in the case of clause (A)) or our outstanding voting securities (in the case of clauses (B) and (C)); or (iv) all or substantially all of our assets are sold of transferred other than in connection with an internal reorganization or our complete liquidation (other than a liquidation of us into a wholly-owned subsidiary).

Employment Agreement with Mr. Johnson

We entered into an employment agreement with Mr. Johnson on December 14, 2006. We entered into an amended and restated employment agreement with Mr. Johnson on November 12, 2008 to comply with Section 409A of the Internal Revenue Code of 1986, as amended and the final regulations issued thereunder. On February 3, 2009 we entered into an amendment to such amended and restated employment agreement extending the time of severance payments to twelve (12) months following a change in control. Mr. Johnson s employment agreement provides for an initial annual base salary of not less than $282,000 and provides that he will be eligible to earn an annual bonus for 2008 in an amount up to 150% of his target bonus of 35% of his annual base salary, as determined by our Board.

Pursuant to the terms of Mr. Johnson s employment agreement, in the event that Mr. Johnson s employment is terminated without cause or is terminated (either by us without cause or by such executive for good reason) three (3) months prior to or twelve (12) months after a change in control, Mr. Johnson will be entitled to continue to receive for twelve months following the date of his termination or resignation (a) his base salary and (b) an amount equal to one-twelfth of the greater of (i) the average of the three annual bonuses paid to Mr. Johnson by us prior to the date of termination or resignation, (ii) the last annual bonus paid to Mr. Johnson by us prior to the date of termination or resignation, or (iii) if the termination occurs within the first 12 months following November 12, 2008, 35% of his base salary, which payments will be without reduction by any amount of Mr. Johnson s earnings from any other employment during the 12-month severance period. Additionally, under those circumstances, the vesting of each of Mr. Johnson s equity awards will be treated as if Mr. Johnson had completed an additional 12 months of service immediately before the date on which his employment is terminated or he resigns. Mr. Johnson s execution of a release in favor of the Company is a condition to the receipt of these severance benefits, and he has agreed to a non-solicitation obligation and to confidentiality and assignment of inventions obligations in connection with his employment agreement. The definition of change in control in Mr. Johnson s employment agreement is the same as in Ms. Graham s employment agreement.

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Employment Agreement with Mr. Schneider

We entered into an employment agreement with Mr. Schneider on February 1, 2007. We entered into an amended and restated employment agreement with Mr. Schneider on November 12, 2008 to comply with Section 409A of the Internal Revenue Code of 1986, as amended and the final regulations issued thereunder. On February 3, 2009 we entered into an amendment to such amended and restated employment agreement extending the time of severance payments to twelve (12) months following a change in control. Mr. Schneider s employment agreement provides for an initial annual base salary of not less than $217,700 and provides that he will be eligible to earn an annual bonus for 2008 in an amount up to 150% of his target bonus of 25% of his annual base salary, as determined by our Board.

Pursuant to the terms of Mr. Schneider s employment agreement, in the event that Mr. Schneider s employment is terminated without cause or is terminated (either by us without cause or by such executive with good reason) three months prior to or twelve (12) months after a change in control, Mr. Schneider resigns for good reason, Mr. Schneider will be entitled to continue to receive for twelve months following the date of his termination or resignation (a) his base salary and (b) an amount equal to one-twelfth of the greater of (i) the average of the three annual bonuses paid to Mr. Schneider by us prior to the date of termination or resignation, (ii) the last annual bonus paid to Mr. Schneider by us prior to the date of termination or resignation, or (iii) if the termination occurs within the first 12 months following November 12, 2008, 25% of his base salary, which payments will be without reduction by any amount of Mr. Schneider s earnings from any other employment during the 12-month severance period. Additionally, under those circumstances, the vesting of each of Mr. Schneider s equity awards will be treated as if Mr. Schneider had completed an additional 12 months of service immediately before the date on which his employment is terminated or he resigns. Mr. Schneider s execution of a release in favor of the Company is a condition to the receipt of these severance benefits, and he has agreed to a non-solicitation obligation and to confidentiality and assignment of inventions obligations in connection with his employment agreement. The definition of change in control in Mr. Schneider s employment agreement is the same as in Ms. Graham s employment agreement.

The table below estimates amounts payable upon a separation as if the individuals were separated on December 31, 2008 using the closing share price of our common stock as of that day.

		Severance Payments					
Name	**Salary During Severance Period**	**Severance Bonus**	**Cobra Payments During Severance Period**	**Total Value of Severance Payment**	**Accrued But Unused PTO**	**Value of Options Vesting Upon Termination(1)**	**Total Value of Benefits Due Upon Termination**
Evelyn A. Graham	$ 350,000	$ 157,500	$ 20,926	$ 528,426	$ 33,652	$	$ 562,078
Craig A. Johnson	282,000	69,200	21,210	372,410	27,114		399,524
Paul R. Schneider	217,700	54,425	18,630	290,755	12,769		303,524

(1) The Value of Options Vesting Upon Termination is calculated by multiplying the total options vesting upon termination (as outlined in the respective Employment Agreements) by the difference between the exercise price of the option and the closing price of our common stock ($0.27) on December 31, 2008 as reported by Nasdaq.

Director Compensation

Non-employee directors receive as compensation:

an annual retainer of $20,000 payable on the date of the annual meeting of the Company s stockholders;

an additional annual retainer of $20,000 for the Chairman of our Board payable on the date of the annual meeting of the Company s stockholders;

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an annual $10,000 retainer for service as the Audit Committee chair payable on the date of the annual meeting of the Company s stockholders;

an annual $10,000 retainer for service as the Compensation Committee chair payable on the date of the annual meeting of the Company s stockholders;

an annual $3,000 retainer for service as the Corporate Governance and Nominating Committee chair payable on the date of the annual meeting of the Company s stockholders;

$1,500 per board meeting attended in person or telephonically; and

$1,000 per meeting of the Audit Committee, Compensation Committee or Corporate Governance and Nominating Committee attended in person or telephonically.

In addition to the cash compensation set forth above, on the date of each Annual meeting of stockholders each continuing non-employee director will receive an annual stock option grant for 10,000 shares of our common stock which will fully vest on the one year anniversary of the grant date. Each non-employee director who first becomes a director of the Company will receive an initial stock option grant for 20,000 shares which would vest over four years in equal monthly installments. Stock options granted to non-employee directors have an exercise price equal to the closing price of the Company s common stock on the date of grant as reported by Nasdaq. Each non-employee director was also reimbursed for reasonable out-of-pocket expenses incurred in attending meetings of the Board or any committee of the Board.

The following table sets forth summary information concerning compensation paid or accrued for services rendered to us in all capacities to the non-employee members of our Board for the fiscal year ended December 31, 2008.

DIRECTOR COMPENSATION FOR 2008

Name(1)	Fees Earned or Paid in Cash ($)	Option Awards ($)(2)	All Other Compensation ($)	Total ($)
Peter Davis, Ph.D.	69,000	22,285(3)		91,285
Jean Deleage, Ph.D.	38,000(4)	22,285(5)		60,285
Steven H. Ferris, Ph.D.	41,500	22,285(6)		63,785
Jason S. Fisherman, M.D.	39,500	22,285(7)		61,785
Steven B. Ratoff	52,500	22,285(8)		74,785
Patrick Van Beneden	38,500			38,500

(1) Neil M. Kurtz, M.D., our former President and Chief Executive Officer, is not included in this table as he is an employee of the Company and thus received no compensation for his service as a director. Evelyn Graham, our Chief Executive Officer, is not included in this table as she is an employee of the Company and thus received no compensation for her service as a director.

(2) The amounts shown reflect the dollar amount recognized for financial statement reporting purposes for the year ended December 31, 2008, in accordance with FAS 123R, of stock options granted pursuant to the Company s stock option plans and thus may include amounts from stock options granted in and prior to 2008.

(3) Dr. Davis has outstanding options to purchase an aggregate of 21,624 shares of common stock as of December 31, 2008. The amount shown in the table reflects compensation expense we recorded for the year ended December 31, 2008 for the following stock option grants:

Grant Date	Total Shares of	Exercise Price	Grant Date Fair Value

	Common Stock		
May 23, 2007	10,000	7.12	47,155
June 19, 2008	10,000	1.35	7,856

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(4) Fees earned by Dr. Deleage for his Board service were paid to Alta Partners.

(5) Dr. Deleage has outstanding options to purchase an aggregate of 20,000 shares of common stock as of December 31, 2008. The amount shown in the table reflects compensation expense we recorded for the year ended December 31, 2008 for the following stock option grants:

Grant Date	Total Shares of Common Stock	Exercise Price	Grant Date Fair Value
May 23, 2007	10,000	7.12	47,155
June 19, 2008	10,000	1.35	7,856

(6) Dr. Ferris has outstanding options to purchase an aggregate of 45,687 shares of common stock as of December 31, 2008. The amount shown in the table reflects compensation expense we recorded for the year ended December 31, 2008 for the following stock option grants:

Grant Date	Total Shares of Common Stock	Exercise Price	Grant Date Fair Value
May 23, 2007	10,000	7.12	47,155
June 19, 2008	10,000	1.35	7,856

(7) Dr. Fisherman has outstanding options to purchase an aggregate of 20,000 shares of common stock as of December 31, 2008. The amount shown in the table reflects compensation expense we recorded for the year ended December 31, 2008 for the following stock option grants:

Grant Date	Total Shares of Common Stock	Exercise Price	Grant Date Fair Value
May 23, 2007	10,000	7.12	47,155
June 19, 2008	10,000	1.35	7,856

(8) Mr. Ratoff has outstanding options to purchase an aggregate of 56,662 shares of common stock as of December 31, 2007. The amount shown in the table reflects compensation expense we recorded for the year ended December 31, 2008 for the following stock option grants:

Grant Date	Total Shares of Common Stock	Exercise Price	Grant Date Fair Value
May 23, 2007	10,000	7.12	47,155
June 19, 2008	10,000	1.35	7,856

Compensation Committee Interlocks and Insider Participation

No member of our Compensation Committee has served as one of our officers or employees at any time. None of our executive officers serves, or has served during the last fiscal year, as a member of the compensation committee or a member of the Board of any other company that has an executive officer serving as a member of our Compensation Committee or Board.

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Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

Security Ownership of Certain Beneficial Owners and Management

The following table sets forth certain information regarding the ownership of our common stock as of February 28, 2009 by: (i) all those known by us to be beneficial owners of more than five percent of our common stock; (ii) each director; (iii) each of the executive officers named in the Summary Compensation Table; and (iv) all of our current executive officers and directors as a group.

We have determined beneficial ownership in accordance with the rules of the SEC. These rules generally attribute beneficial ownership of securities to persons who possess sole or shared voting power or investment power with respect to those securities. In addition, the rules include shares of common stock issuable pursuant to the exercise of stock options or warrants that are either immediately exercisable or exercisable on or before February 28, 2009, which is 60 days after February 28, 2009. These shares are deemed to be outstanding and beneficially owned by the person holding those options or warrants for the purpose of computing the percentage ownership of that person, but they are not treated as outstanding for the purpose of computing the percentage ownership of any other person. Unless otherwise indicated, the persons or entities identified in this table have sole voting and investment power with respect to all shares shown as beneficially owned by them, subject to applicable community property laws.

	Beneficial Ownership(1)	
Beneficial Owner	**Number of Shares**	**Percent of Total**
Entities affiliated with Alta Partners(2)	2,652,583	16.2%
Entities affiliated with GIMV N.V.(3)	2,628,603	16.0%
Entities affiliated with Advent International(4)	1,570,559	9.7%
Wellington Capital Management Co. LLP	1,137,937	7.1%
Peter Davis, Ph.D.(5)	16,496	*
Jean Deleage, Ph.D.(5)	2,652,583	16.2%
Steven H. Ferris, Ph.D.(5)	35,687	*
Jason S. Fisherman, M.D.(5)	1,570,559	9.7%
Steven B. Ratoff(5)	127,870	*
Patrick Van Beneden(5)	2,628,603	16.2%
Evelyn A. Graham(5)	465,496	2.8%
Craig A. Johnson(5)	402,996	2.5%
Paul R. Schneider(5)	311,416	1.9%
Susan J. Mellberg(5)	77,727	*
Neil M. Kurtz, M.D.(6)	2,000	*
Steven L. Wagner, Ph.D.(7)	67,666	*
All executive officers and directors as a group (10 persons)(8)	5,937,009	45.2%

* Less than one percent.

(1) This table is based upon information supplied by officers, directors and principal Stockholders and Schedules 13D and 13G filed with the SEC. Unless otherwise indicated in the footnotes to this table and subject to community property laws where applicable, the Company believes that each of the stockholders named in this table has sole voting and investment power with respect to the shares indicated as beneficially owned. Applicable percentages are based on 15,974,058 shares outstanding on February 28, 2009 adjusted as required by rules promulgated by the SEC.

(2) Includes 1,258,044 shares held of record and a warrant to purchase 229,823 shares held by Alta California Partners II, L.P., 358,414 shares held of record and a warrant to purchase 67,557 shares held by Alta California Partners II, L.P. New Pool, 15,893 shares held of record and a warrant to purchase 2,903 shares held by Alta Embarcadero Partners II, LLC, 547,128 shares held of record and a warrant to purchase 103,127 shares held by Alta BioPharma Partners III, L.P., 36,744 shares held of record and a warrant to purchase 6,926 shares held by

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Alta BioPharma Partners III GmbH & Co. Beteiligungs KG, 13,483 shares held of record and a warrant to purchase 2,541 shares held by Alta Embarcadero BioPharma Partners III, LLC and an option to purchase 10,000 shares held by Jean Deleage, Ph.D. Alta Partners LP, as the parent of each of Alta BioPharma Partners III GmbH & Co. Beteiligungs, Alta BioPharma Partners III, L.P., Alta California Partners II, L.P., Alta California Partners II, L.P. New Pool, Alta Embarcadero BioPharma Partners III, LLC and Alta Embarcadero Partners II, LLC, may be deemed to beneficially own such shares. Dr. Deleage is a managing director of Alta Partners. Dr. Deleage, a member of our Board and a former member of the board of directors of TPTX, Inc. disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein. The address of Alta Partners LP is One Embarcadero Center, Suite 3700, San Francisco, CA 94111.

(3) Includes 1,544,403 shares held of record and a warrant to purchase 286,897 shares held by GIMV N.V., 477,704 shares held of record and a warrant to purchase 90,041 shares held by Biotech Fonds Vlaanderen, N.V., and 193,776 shares held of record and a warrant to purchase 35,782 shares held by Adviesbeheer GIMV Life Sciences N.V. GIMV N.V., as the parent of each of Biotech Fonds Vlaanderen, N.V. and Adviesbeheer GIMV Life Sciences N.V., may be deemed to beneficially own such shares. Patrick Van Beneden is the Executive Vice President Life Sciences of GIMV, N.V. Mr. Van Beneden, a member of our Board and a former member of the board of directors of TPTX Inc., disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein. The address of GIMV, N.V. is Karel Oomsstraat 37, B-2018, Antwerp, Belgium.

(4) Includes 1,197,723 shares held of record and a warrant to purchase 217,930 shares held by Advent Health Care and Life Sciences II Limited Partnership; 93,350 shares held of record and a warrant to purchase 16,984 shares held by Advent Health Care and Life Sciences II Beteiligung GmbH & Co. KG; 26,567 shares held of record and a warrant to purchase 4,835 shares held by Advent HLS II Limited Partnership; 2,677 shares held of record and a warrant to purchase 493 shares held by Advent Partners Limited Partnership and an option to purchase 10,000 shares held by Jason S. Fisherman, M.D. Advent International has engaged Advent Healthcare Ventures to advise it with respect to the operation of certain private equity funds, including the above listed funds. Dr. Fisherman is a managing director of Advent Healthcare Ventures. Dr. Fisherman, a member of our Board and a former member of the board of directors of TPTX, Inc. disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein. Each fund disclaims beneficial ownership of the others shares. The address of Advent Healthcare Ventures is 75 State Street, Boston, MA 02109.

(5) Includes shares described in notes (1), (2), (3) and (4), as applicable, including shares issuable upon exercise of the warrants described in the notes above, which the applicable holder has the right to acquire within 60 days after the date of this table. Includes shares which certain executive officers and directors of the Company have the right to acquire within 60 days after the date of this table pursuant to outstanding options, as follows: Peter Davis, 11,624 shares; Steven H. Ferris, 35,687 shares; Steven B. Ratoff, 46,662 shares; Evelyn A. Graham, 433,016 shares; Craig A. Johnson, 370,516 shares; Paul R. Schneider, 311,416 shares, Susan J. Mellberg, 57,664 shares; and all executive officers and directors as of February 28, 2009 as a group, 1,286,585 shares.

(6) Dr. Kurtz resigned from TorreyPines Therapeutics, Inc. effective August, 31, 2008.

(7) Dr. Wagner s last date of employment was September 30, 2008.

(8) Total includes executive officers and directors as of February 28, 2009

Information regarding our equity compensation plans will be set forth in our Proxy Statement and is incorporated in this report by reference.

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Equity Compensation Plan Information

The following table provides certain information with respect to all of our equity compensation plans in effect as of December 31, 2008:

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights (a)	Weighted average exercise price of outstanding options, warrants and rights (b)	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column) (a)(c)(1)
Equity compensation plans approved by security holders	4,326,123	$ 14.86	1,526,270
Equity compensation plans not approved by security holders			
Total	4,326,123	$ 14.86	1,526,270

(1) The number of securities available for future issuance under the 2006 Plan automatically increases on the first day of each calendar year from 2008 to 2016. The number of shares added each year will be equal to the lesser of: (i) two percent of the shares of Common Stock outstanding on such date, (ii) 625,000 shares, or (iii) a lesser number of shares of Common Stock that may be determined by the Board prior to the first day of any fiscal year. On January 1, 2009 there were 319,481 shares added to our 2006 Plan pursuant to the automatic increase.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Related-Person Transactions Policy and Procedures

In 2007 we adopted a written Related-Person Transactions Policy that sets forth our policies and procedures regarding the identification, review, consideration and approval or ratification of related-persons transactions. There have been no revisions to the Related-Persons Transactions Policy following its adoption in 2007. For purposes of our policy only, a related-person transaction is a transaction, arrangement or relationship (or any series of similar transactions, arrangements or relationships) in which the Company and any related person are participants involving an amount that exceeds $120,000. Transactions involving compensation for services provided to the Company as an employee, director, consultant or similar capacity by a related person are not covered by this policy. A related person is any executive officer, director, or more than 5% stockholder of the Company, including any of their immediate family members, and any entity owned or controlled by such persons.

Under the policy, where a transaction has been identified as a related-person transaction, management must present information regarding the proposed related-person transaction to the Audit Committee (or, where Audit Committee approval would be inappropriate, to another independent body of the Board) for consideration and approval or ratification. The presentation must include a description of, among other things, the material facts, the interests, direct and indirect, of the related persons, the benefits to the Company of the transaction and whether any alternative transactions were available. To identify related-person transactions in advance, the Company relies on information supplied by its executive officers and directors. In considering related-person transactions, the Audit Committee takes into account the relevant available facts and circumstances including, but not limited to (a) the risks, costs and benefits to the Company, (b) the impact on a director s independence in the event the related person is a director, immediate family member of a director or an entity with which a director is affiliated, (c) the terms of the transaction, (d) the availability of other sources for comparable services or products and (e) the terms available to or from, as the case may be, unrelated third parties or to or from employees generally. In the event a director has an interest in the proposed transaction, the director must recuse himself or herself from the deliberations and approval. The policy requires that, in determining whether to

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approve, ratify or reject a related-person transaction, the Audit Committee look at, in light of known circumstances, whether the transaction is in, or is not inconsistent with, the best interests of the Company and its stockholders, as the Audit Committee determines in the good faith exercise of its discretion.

Certain Related-Person Transactions

The Company has entered into indemnity agreements with certain officers and directors which provide, among other things, that the Company will indemnify such officer or director, under the circumstances and to the extent provided for therein, for expenses, damages, judgments, fines and settlements he or she may be required to pay in actions or proceedings which he or she is or may be made a party by reason of his or her position as a director, officer or other agent of the Company, and otherwise to the fullest extent permitted under Delaware law and our Bylaws.

Independence of the Board

As required under the Nasdaq Stock Market (Nasdaq) listing standards, a majority of the members of a listed company s board of directors must qualify as independent, as affirmatively determined by the board of directors. The Board consults with our counsel to ensure that the Board s determinations are consistent with relevant securities and other laws and regulations regarding the definition of independent, including those set forth in pertinent listing standards of the Nasdaq, as in effect from time to time.

Consistent with these considerations, after review of all relevant transactions or relationships between each director, or any of his family members, and us, our senior management and our independent registered public accounting firm, the Board has affirmatively determined that the following six directors are independent directors within the meaning of the applicable Nasdaq listing standards: Dr. Davis, Dr. Deleage, Dr. Ferris, Dr. Fisherman, Mr. Ratoff and Mr. Van Beneden. In making this determination, the Board found that none of these directors or nominees for director had a material or other disqualifying relationship with us. Ms. Graham, our Chief Executive Officer is not an independent director by virtue of her employment with us.

Item 14. Principal Accountant Fees and Services.

The Audit Committee has appointed Ernst & Young LLP as the Company s independent auditors to perform audit and other services for the Company and its subsidiaries for the fiscal year 2008. In connection with the audit of the 2008 financial statements, the Company entered into an engagement agreement with Ernst & Young LLP, which sets forth the terms by which Ernst & Young LLP will perform audit services for the Company. That agreement is subject to alternative dispute resolution procedures.

The following table represents aggregate fees billed to us for the fiscal years ended December 31, 2008 and December 31, 2007 by Ernst & Young LLP.

	2008	2007
Audit Fees	$ 223,000	$ 217,000
Audit-related Fees		
Tax Fees		
All Other Fees		
Total Fees	$ 223,000	$ 217,000

All fees described above were approved by the Audit Committee.

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Pre-Approval Policies and Procedures

The Audit Committee has adopted a policy and procedures for the pre-approval of audit and non-audit services rendered by our independent registered public accounting firm, Ernst & Young LLP. The policy generally pre-approves specified services in the defined categories of audit services, audit-related services, and tax services up to specified amounts. Pre-approval may also be given as part of the Audit Committee s approval of the scope of the engagement of the independent registered public accounting firm or on an individual explicit case-by-case basis before the independent registered public accounting firm is engaged to provide each service. The pre-approval of services may be delegated to one or more of the Audit Committee s members, but the decision must be reported to the full Audit Committee at its next scheduled meeting. All of the audit-related and tax fees incurred in 2008 and 2007 were approved in accordance with our pre-approval policies and procedures.

The Audit Committee has determined that the rendering of the services other than audit services by Ernst & Young LLP is compatible with maintaining the principal accountant s independence.

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PART IV

Item 15. Exhibits and Financial Statement Schedules.

(a) *Documents filed as part of this report:*

(1) *Financial Statements:*

The following financial statements of TorreyPines Therapeutics, Inc. are included in a separate section of this Annual Report on Form 10-K beginning on page F-1 hereto:

(2) *Financial Statement Schedules:*

All schedules have been omitted, since they are not applicable or not required, or the relevant information is included in the consolidated financial statements or the notes thereto.

(3) *Exhibits:*

Exhibit No.	Description
2.1	Agreement and Plan of Merger and Reorganization, dated as of June 7, 2006, by and among Axonyx Inc., Autobahn Acquisition, Inc. and TorreyPines Therapeutics, Inc. (incorporated by reference to Annex A to Registration Statement No. 333-136018 filed with the Securities and Exchange Commission on July 25, 2006).
2.2	Amendment No. 1 to Agreement and Plan of Merger and Reorganization, dated as of August 25, 2006, by and among Axonyx Inc., Autobahn Acquisition, Inc. and TorreyPines Therapeutics, Inc. (incorporated by reference to Annex A to Amendment No. 1 to Registration Statement No. 333-136018 filed with the Securities and Exchange Commission on August 25, 2006).
3.1	Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).
3.2	Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).
3.3	Certificate of Amendment filed with the Secretary of State of the State of Nevada effecting an 8-for-1 reverse stock of the Registrant s common stock and changing the name of the Registrant from Axonyx Inc. to TorreyPines Therapeutics, Inc. (incorporated by reference to Exhibit 3.3 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).
3.4	

	Articles of Conversion filed with the Secretary of State of the State of Nevada changing the state of incorporation of the Registrant (incorporated by reference to Exhibit 3.4 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).
3.5	Certificate of Conversion filed with the Secretary of State of the State of Delaware (incorporated by reference to Exhibit 3.5 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).
3.6	Amendment to Bylaws of the Registrant (incorporated by reference to Exhibit 3.6 to the Registrant s Annual Report on Form 10-K, filed on March 29, 2007).

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Exhibit No.	Description
4.1	Specimen common stock certificate of the Registrant (incorporated by reference to Exhibit 4.1 to the Registrant s Quarterly Report on Form 10-Q, filed on August 14, 2007).
4.2	Form of Warrant to Purchase Common Stock issued to previous holders of TPTX, Inc. redeemable convertible preferred stock in connection with the business combination between TorreyPines Therapeutics, Inc. and Axonyx, Inc. (incorporated by reference to Exhibit 4.2 to the Registrant s Annual Report on Form 10-K, filed on March 29, 2007).
4.3	Form of Registration Rights Agreement 1999 (incorporated by reference to Exhibit 4.4 to the Registrant s Annual Report on Form 10-KSB filed on March 13, 2000, file No. 000-25571)
4.4	Registration Rights Agreement dated as of January 8, 2004 between Axonyx Inc. and certain investors (incorporated by reference to Exhibit 4.2 to the Registrant s current report on Form 8-K, filed on January 12, 2004, file No. 000-25571)
4.5	Registration Rights Agreement dated as of May 3, 2004, between Axonyx Inc. and certain investors (incorporated by reference to Exhibit 4.2 to the Registrant s current report on Form 8-K, filed on May 5, 2004, file No. 000-25571)
4.6	Form of Warrant issued to Comerica Bank on July 1, 2003 (incorporated by reference to Exhibit 4.14 to the Registrant s Annual Report on Form 10-K, filed on March 29, 2007).
4.7	Form of Warrant issued to Silicon Valley Bank on December 8, 2000 (incorporated by reference to Exhibit 4.15 to the Registrant s Annual Report on Form 10-K, filed on March 29, 2007).
4.8	Form of Warrant issued to Oxford Financial and Silicon Valley Bank on September 27, 2005 (incorporated by reference to Exhibit 4.16 to the Registrant s Annual Report on Form 10-K, filed on March 29, 2007).
4.9	Rights Agreement, dated as of May 13, 2005, between the Registrant and American Stock Transfer & Trust Company (replacing The Nevada Agency and Trust Company), as Rights Agent (incorporated by reference to Exhibit 99.2 to the Registrant s Current Report on Form 8-K, filed on May 16, 2005)
4.10	Amendment to Rights Agreement, dated as of June 7, 2006, between the Registrant and Registrant and American Stock Transfer & Trust Company (replacing The Nevada Agency and Trust Company), as Rights Agent (incorporated by reference to Exhibit 4.1 to the Registrant s Current Report on Form 8-K, filed on June 12, 2006).
4.11	Amendment to Rights Agreement, dated as of October 3, 2006, between the Registrant and Registrant and American Stock Transfer & Trust Company (replacing The Nevada Agency and Trust Company), as Rights Agent (incorporated by reference to Exhibit 4.19 to the Registrant s Annual Report on Form 10-K, filed on March 29, 2007).
4.12	Reference is made to Exhibits 3.1 through 3.6.
10.1#	TorreyPines Therapeutics, Inc. 2006 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant s Current Report on Form 8-K, filed on October 4, 2006).
10.2#	Form of Stock Option Agreement under TorreyPines Therapeutics, Inc. 2006 Equity Incentive Plan (incorporated by reference to Exhibit 10.9 to the Registrant s Current Report on Form 8-K, filed on October 14, 2006).
10.3*	Development and License Agreement between TPTX, Inc. (formerly Neurogenetics, Inc.) and Eli Lilly and Company, effective as of April 21, 2003 (incorporated by reference to Exhibit 10.1 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).

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Exhibit No.	Description
10.4*	Research and License Agreement by and between TPTX, Inc. and Life Science Research Israel Ltd. dated as of May 10, 2004 (incorporated by reference to Exhibit 10.2 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).
10.5*	License Agreement by and between TPTX, Inc. and University of Iowa Research Foundation dated as of May 10, 2006 (incorporated by reference to Exhibit 10.5 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).
10.6#	TPTX, Inc. 2000 Equity Incentive Plan (incorporated by reference to Exhibit 10.1 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).
10.7#	Form of Stock Option Agreement under TPTX, Inc. 2000 Equity Incentive Plan (incorporated by reference to Exhibit 10.9 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).
10.8	Lease Agreement by and between TPTX, Inc. and Slough TPSP LLC dated as of July 18, 2005, which became effective February 10, 2006 (incorporated by reference to Exhibit 10.10 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).
10.9	Form of Indemnity Agreement (incorporated by reference to Exhibit 10.13 to the Registrant s Current Report on Form 8-K, filed on October 10, 2006).
10.10#	Employment Agreement by and between Evelyn Graham and TorreyPines Therapeutics, Inc. dated December 14, 2006 (incorporated by reference to Exhibit 10.2 to the Registrant s Current Report on Form 8-K, filed on December 20, 2006).
10.11#	Employment Agreement by and between Craig Johnson and TorreyPines Therapeutics, Inc. dated December 14, 2006 (incorporated by reference to Exhibit 10.3 to the Registrant s Current Report on Form 8-K, filed on December 20, 2006).
10.12#	Form of Restricted Stock Unit Award Agreement under TorreyPines Therapeutics, Inc. 2006 Equity Incentive Plan. (incorporated by reference to Exhibit 10.17 to the Registrant s Annual Report on Form 10-K, filed on March 29, 2007).
10.13	Loan And Security Agreement dated June 11, 2008, by and between Comerica Bank and TPTX, Inc. (incorporated by reference to Exhibit 10.1 to the Registrant s Current Report on Form 8-K, filed on June 17, 2008).
10.14	Third Party Security Agreement dated June 11, 2008 by and between Comerica Bank and TorreyPines Therapeutics, Inc. (incorporated by reference to Exhibit 10.2 to the Registrant s Current Report on Form 8-K, filed on June 17, 2008).
10.15	First Amendment dated January 7, 2009 to Lease by and between TorreyPines Therapeutics, Inc. and HCP TPSP LLC dated July 18, 2005 (attached hereto).
10.16*	Amendment dated November 21, 2008 to Development and License Agreement by and between TPTX, Inc. and Eli Lilly and Company, effective as of April 21, 2003 (attached hereto).
10.17#	Amended and Restated Employment Agreement by and between Evelyn Graham and TorreyPines Therapeutics, Inc. dated September 1, 2008 (attached hereto).
10.18#	Amendment dated February 3, 2009 to Amended Employment Agreement by and between Evelyn Graham and TorreyPines Therapeutics, Inc. dated September 1, 2008 (attached hereto).
10.19#	Amended and Restated Employment Agreement by and between Craig Johnson and TorreyPines Therapeutics, Inc. dated November 12, 2008 (attached hereto).
10.20#	Amendment dated February 3, 2009 to Amended Employment Agreement by and between Craig Johnson and TorreyPines Therapeutics, Inc. dated November 12, 2008 (attached hereto).

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Exhibit No.	Description
10.21#	Amended and Restated Employment Agreement by and between Paul Schneider and TorreyPines Therapeutics, Inc. dated November 12, 2008 (attached hereto).
10.22#	Amendment dated February 3, 2009 to Amended Employment Agreement by and between Paul Schneider and TorreyPines Therapeutics, Inc. dated November 12, 2008 (attached hereto).
16	Letter from Eisner LLP to the Securities and Exchange Commission, dated December 13, 2006 (incorporated by reference to Exhibit 16 to the Registrant s Current Report on Form 8-K, filed on December 13, 2006).
21.1	List of Subsidiaries of the Registrant
23.1	Consent of Independent Registered Public Accounting Firm
24.1	Power of Attorney (See p. 70)
31.1	Certification of Chief Executive Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Chief Financial Officer pursuant to Exchange Act Rules 13a-14(a) and 15d-14(a), adopted pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certification of Chief Executive Officer pursuant to 18 U.S.C Section 1350, adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2	Certification of Chief Financial Officer pursuant to 18 U.S.C Section 1350, adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

# Indicates management contract or compensatory plan or arrangement.

* Portions of this exhibit have been granted confidential treatment pursuant to an order granted by the SEC. The confidential portions of this exhibit are marked by an asterisk and have been omitted and filed separately with the SEC pursuant to our request for confidential treatment.

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SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

TORREYPINES THERAPEUTICS, INC.

By: /s/ EVELYN A. GRAHAM
Evelyn A. Graham,

Chief Executive Officer

Date: March 27, 2009

KNOW ALL PERSONS BY THESE PRESENTS, that each individual whose signature appears below constitutes and appoints Evelyn A. Graham and Craig Johnson, and each of them, his true and lawful attorneys-in-fact and agents with full power of substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments to this Annual Report on Form 10-K, and to file the same, with all exhibits thereto and all documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that said attorneys-in-fact and agents or any of them, or his or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ EVELYN A. GRAHAM **Evelyn A. Graham**	Chief Executive Officer and Director *(Principal Executive Officer)*	March 25, 2009
/s/ CRAIG JOHNSON **Craig Johnson**	Vice President, Finance and Chief Financial Officer *(Principal Financial and Accounting Officer)*	March 25, 2009
/s/ PETER DAVIS, PH.D. **Peter Davis, Ph.D.**	Director	March 25, 2009
/s/ JEAN DELEAGE, PH.D. **Jean Deleage, Ph.D.**	Director	March 25, 2009
/s/ STEVEN H. FERRIS, PH.D. **Steven H. Ferris, Ph.D.**	Director	March 25, 2009
/s/ JASON FISHERMAN, M.D **Jason Fisherman, M.D**	Director	March 25, 2009

/s/ STEVEN B. RATOFF **Steven B. Ratoff**	Director	March 25, 2009
/s/ PATRICK VAN BENEDEN **Patrick Van Beneden**	Director	March 25, 2009

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TorreyPines Therapeutics, Inc.

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Directors and Stockholders

TorreyPines Therapeutics, Inc.

We have audited the accompanying consolidated balance sheets of TorreyPines Therapeutics, Inc. as of December 31, 2008 and 2007, and the related consolidated statements of operations, stockholders equity, and cash flows for each of the three years in the period ended December 31, 2008. These financial statements are the responsibility of the Company s management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audits to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company s internal control over financial reporting. Our audits included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company s internal control over financial reporting. Accordingly, we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of TorreyPines Therapeutics, Inc. at December 31, 2008 and 2007, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2008, in conformity with U.S. generally accepted accounting principles.

The accompanying financial statements have been prepared assuming that TorreyPines Therapeutics, Inc. will continue as a going concern. As more fully described in Note 1, the Company s existing working capital is not sufficient to meet its cash requirements to fund planned operating expenses and working capital requirements through December 31, 2009 without additional sources of cash. This condition raises substantial doubt about the Company s ability to continue as a going concern. Management s plans in regard to these matters also are described in Note 1. The most recent year financial statements do not include any adjustments to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

/s/ Ernst & Young LLP

San Diego, California

March 24, 2009

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TorreyPines Therapeutics, Inc.

Consolidated Balance Sheets

(in thousands, except share and per share data)

	December 31, 2008	December 31, 2007
Assets		
Current assets		
Cash and cash equivalents	$ 10,864	$ 32,500
Prepaid expenses and other current assets	187	835
Total current assets	11,051	33,335
Property and equipment, net	40	774
Purchased patents, net		3,515
Investment in OXIS International, Inc.		979
Other assets	39	49
Total assets	$ 11,130	$ 38,652
Liabilities and stockholders equity		
Current liabilities		
Accounts payable and accrued liabilities	$ 3,865	$ 5,462
Long-term debt, current portion	1,440	3,574
Total current liabilities	5,305	9,036
Long-term debt, net of current portion	2,112	954
Deferred revenue		2,183
Deferred rent		19
Total liabilities	7,417	12,192
Commitments		
Stockholders equity		
Preferred stock, $0.001 par value, 15,000,000 shares authorized, 0 shares outstanding at December 31, 2008 and 2007, respectively		
Common stock, $0.001 par value, 150,000,000 shares authorized, 15,974,058 and 15,738,496 shares issued and outstanding at December 31, 2008 and 2007, respectively	16	16
Additional paid-in capital	122,883	122,359
Accumulated other comprehensive income		486
Accumulated deficit	(119,186)	(96,401)
Total stockholders equity	3,713	26,460
Total liabilities and stockholders equity	$ 11,130	$ 38,652

See accompanying notes.

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TorreyPines Therapeutics, Inc.

Consolidated Statements of Operations

(in thousands, except share and per share data)

	Years Ended December 31,		
	2008	**2007**	**2006**
Revenue			
License and option fees	$ 2,283	$ 6,800	$ 6,800
Research funding	2,288	3,050	3,050
Other revenue	1,500		
Total revenue	6,071	9,850	9,850
Operating expenses			
Research and development	18,949	27,977	22,353
General and administrative	5,801	5,643	3,971
Loss on impairment of purchased patents	3,074		
Purchased in-process research and development			8,328
Total operating expenses	27,824	33,620	34,652
Loss from operations	(21,753)	(23,770)	(24,802)
Other income (expense)			
Interest income	453	2,069	1,559
Interest expense	(376)	(817)	(994)
Other income (expense), net	(1,109)	(851)	(1,140)
Total other income (expense)	(1,032)	401	(575)
Net loss	$ (22,785)	$ (23,369)	$ (25,377)
Basic and diluted net loss per share	$ (1.45)	$ (1.49)	$ (8.18)
Weighted average shares used in the computation of basic and diluted net loss per share	15,748,967	15,717,984	3,100,852

See accompanying notes.

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TorreyPines Therapeutics, Inc.

Consolidated Statements of Stockholders Equity (Deficit)

(in thousands, except share and per share data)

	Common Stock		Additional Paid-In Capital	Accumulated Other Comprehensive Income (Loss)	Accumulated Deficit	Total Stockholders (Deficit) Equity
	Shares	Amount				
Balance at December 31, 2005	535,311	$ 1	$ 719	$ (211)	$ (58,850)	$ (58,341)
Issuance of common stock for exercise of options	329,965		331			331
Issuance of common stock for exercise of warrants	143,845		9			9
Dividends accrued on redeemable convertible preferred stock					(3,371)	(3,371)
Accrete redeemable convertible preferred stock to redemption value					(205)	(205)
Warrant issued in conjunction with debt			213			213
Stock-based compensation under SFAS No. 123R			139			139
Additional accretion to redemption value upon conversion of redeemable convertible preferred stock					(342)	(342)
Reversal of redeemable convertible preferred stock dividends upon conversion to common stock					13,958	13,958
Redeemable convertible preferred stock converted to common stock	7,958,059	8	67,137		1,155	68,300
Effect of Merger	6,709,784	7	53,444			53,451
Issuance of warrants in connection with Merger			(4,575)			(4,575)
Net loss					(25,377)	(25,377)
Foreign currency translation adjustments				379		379
Comprehensive loss						(24,998)
Balance at December 31, 2006	15,676,964	$ 16	$ 117,417	$ 168	$ (73,032)	$ 44,569
Issuance of common stock for exercise of options	61,532		50			50
Stock-based compensation under SFAS No. 123R			970			970
Reclassification of fair value of warrants from current liabilities to Additional paid-in capital upon receipt of warrant clarification letters			3,922			3,922
Net loss					(23,369)	(23,369)
Foreign currency translation adjustments				318		318
Comprehensive loss						(23,051)
Balance at December 31, 2007	15,738,496	$ 16	$ 122,359	$ 486	$ (96,401)	$ 26,460
Issuance of common stock for exercise of options	15,562		19			19
Issuance of common stock under the Employee Stock Purchase Program	20,000		3			3
Stock-based compensation under SFAS No. 123R			404			404
Warrant issued in conjunction with debt			58			58
Common stock issued to Eli Lilly	200,000		40			40
Net loss					(22,785)	(22,785)
Foreign currency translation adjustments				(486)		(486)
Comprehensive loss						(23,271)
Balance at December 31, 2008	15,974,058	$ 16	$ 122,883	$	$ (119,186)	$ 3,713

See accompanying notes.

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TorreyPines Therapeutics, Inc.

Consolidated Statements of Cash Flows

(in thousands)

	Years Ended December 31,		
	2008	2007	2006
Operating activities			
Net loss	$ (22,785)	$ (23,369)	$ (25,377)
Adjustments to reconcile net loss to net cash used in operating activities:			
Purchased in-process research and development			8,328
Depreciation	236	369	639
Amortization of purchased patents	391	391	95
Amortization of debt discount and deferred charges	79	132	114
Stock-based compensation	404	970	139
Common stock issued to Eli Lilly, Inc.	40		
Deferred revenue	(2,183)		(6,800)
Deferred rent and other	(19)	7	15
Loss on impairment of property and equipment	154		
Loss on extinguishment of debt	105		
Decrease in fair value of investment in OXIS International, Inc.	559		
Loss on sale of investment in OXIS International, Inc	377		
Impairment of purchased patents	3,124		
Impairment of equity investment in OXIS International, Inc.		1,881	
Equity in (income) loss of OXIS International, Inc.		(141)	916
Gain on currency translation	(486)		
(Increase) decrease in warrant valuation		(892)	240
Changes in operating assets and liabilities:			
Prepaid expenses and other current assets	648	(247)	208
Other assets	49		330
Accounts payable and accrued liabilities	(1,597)	1,205	(5,694)
Net cash used in operating activities	(20,904)	(19,694)	(26,847)
Investing activities			
Proceeds from sale of investment in OXIS International, Inc.	42		
Proceeds from sale of investments obtained in the Merger			45,300
Cash paid for Merger transaction costs, net of cash received			(1,629)
Proceeds from the sale of property and equipment	364		
Purchases of property and equipment	(19)	(351)	(134)
Net cash provided by (used in) investing activities	387	(351)	43,537
Financing activities			
Issuance of common stock upon exercise of options and warrants	22	50	340
Debt issuance costs	(48)		
Issuance of redeemable convertible preferred stock, net			6,322
Proceeds from long-term debt	3,600		5,000
Payments on long-term debt	(4,693)	(3,201)	(2,106)
Net cash provided by (used in) financing activities	(1,119)	(3,151)	9,556
Effect of exchange rate changes on cash		313	380

Net increase (decrease) in cash and cash equivalents	(21,636)	(22,883)	26,626
Cash and cash equivalents at beginning of year	32,500	55,383	28,757
Cash and cash equivalents at end of year	$ 10,864	$ 32,500	$ 55,383
Supplemental disclosure of cash flow information			
Cash paid for interest	$ 297	$ 686	$ 880
Warrant issued in conjunction with debt	$ 58	$	$ 213
Noncash purchases of property and equipment	$	$	$ 3

See accompanying notes.

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TorreyPines Therapeutics, Inc.

Notes to Consolidated Financial Statements

December 31, 2008

1. Organization and Summary of Significant Accounting Policies

Organization and Business

TorreyPines Therapeutics, Inc. is a biopharmaceutical company committed to providing patients with better alternatives to existing therapies through the development and commercialization of small molecule compounds. Our goal is to develop versatile product candidates each capable of treating a number of acute and chronic diseases and disorders such as migraine, acute and chronic pain, and xerostomia. TorreyPines is a Delaware corporation and operates in one business segment.

Prior to October 3, 2006 the name of the Company was Axonyx Inc. (Axonyx). On October 3, 2006, Axonyx completed a merger with TorreyPines Therapeutics, Inc. pursuant to which a wholly-owned subsidiary of Axonyx merged with and into TorreyPines Therapeutics, Inc. (the Merger). TorreyPines Therapeutics, Inc. was the surviving entity in the Merger, and became a wholly owned subsidiary of Axonyx. TorreyPines Therapeutics, Inc. changed its name to TPTX, Inc., and Axonyx changed its name to TorreyPines Therapeutics, Inc. (TorreyPines). The Merger was accounted for as a reverse acquisition. These financial statements reflect the historical results of TPTX, Inc. prior to the Merger and that of the combined company following the Merger, and do not include the historical results of Axonyx prior to the completion of the Merger. All share and per share disclosures have been retroactively adjusted to reflect the exchange of shares in the Merger, and the 8-for-1 reverse split of our common stock on October 3, 2006. All references to TorreyPines, we, us or our mean TorreyPines Therapeutics, Inc. and its subsidiaries, except where it is made clear that the term means only the parent company.

We have incurred net losses of $22.8 million, $23.4 million and $25.4 million for the years ended December 31, 2008, 2007 and 2006, respectively. Since inception, and through December 31, 2008, we have an accumulated deficit of $119.2 million. Based on our operating plan, our existing working capital is not sufficient to meet our cash requirements to fund our planned operating expenses and working capital requirements through December 31, 2009 without additional sources of cash.

These conditions raise substantial doubt about our ability to continue as a going concern. The accompanying financial statements have been prepared assuming that we will continue as a going concern. This basis of accounting contemplates the recovery of our assets and the satisfaction of liabilities in the normal course of business.

Our management plans to address the expected shortfall of working capital by securing additional funding through project financing, equity financing, a development partner or the sale of assets. If we are unsuccessful in securing funding from any of these sources, we will defer, reduce or eliminate certain planned expenditures. There can be no assurance that we will be able to obtain any sources of funding.

If we cannot obtain sufficient funding in the short-term, we may be forced to significantly curtail our operations, file for bankruptcy, cease operations or liquidate and dissolve the Company. Additionally, if we do not obtain sufficient funding in the short-term, we project that we will violate the minimum cash balance covenant of our debt agreement which would cause a default under the agreement. At the time cash drops below the minimum requirement, we project we will have sufficient cash to repay the outstanding balance of the debt agreement should the lender declare the debt immediately due and payable. The consolidated financial statements do not include any adjustments relating to the recoverability and classification of recorded asset amounts and classification of liabilities that might be necessary should we be forced to take any such actions.

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Basis of Consolidation

The accompanying consolidated financial statements include the accounts of TorreyPines Therapeutics, Inc., TPTX, Inc. and our wholly owned subsidiaries located in Belgium and the Netherlands. The Netherlands subsidiary was acquired in the Merger and the operations of the Netherlands subsidiary were discontinued in November 2006. The operations of the Belgium subsidiary were discontinued in December 2008. All significant intercompany accounts and transactions are eliminated in consolidation.

Use of Estimates

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities and disclosure of contingent assets and liabilities at the date of the financial statements and the reported amounts of revenues and expenses during the reporting period. Actual results could differ from those estimates.

Cash and Cash Equivalents

Cash and cash equivalents consist of cash and highly liquid investments with original maturities of three months or less when purchased.

Property and Equipment

Property and equipment is stated at cost less accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets. The estimated useful life for lab equipment and furniture, fixtures and office equipment is five years and the estimated useful life for computer equipment and software is three years.

Purchased Patents

Purchased patents are comprised of patents acquired in the Merger. The patents are amortized on a straight-line basis using the following lives:

Patent	Life (years)
Phenserine	8
Posiphen	12
Bisnorcymserine	10

Amortization expense for the years ended December 31, 2008, 2007 and 2006 was $391,000, $391,000 and $95,000, respectively. In December 2008 we determined that the carrying value of the purchased patents was impaired; see related discussion within this footnote under Long-Lived Assets . As a result of the impairment, the patents have a weighted average life equal to zero years.

Investment in OXIS International, Inc.

Prior to January 1, 2008, we accounted for our investment in OXIS International, Inc. (OXIS) under the equity method of accounting following Accounting Principles Bulletin No. 18. Effective January 1, 2008 we elected to apply the provisions of Statement of Financial Accounting Standards (SFAS) No. 159, *Fair Value Option for Financial Assets and Liabilities-Including an Amendment of FASB Statement No. 115*, to our investment in OXIS. This investment was sold in September 2008. See Note 4.

Fair Value of Financial Instruments

Our financial instruments, including cash, cash equivalents, accounts payable and accrued liabilities, are carried at cost which approximates fair value due to the relative short-term maturities of these instruments. Based on the borrowing rates currently available to us for debt with similar terms, we believe the fair value of the long-term debt approximates its carrying value.

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Long-Lived Assets

In accordance with SFAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*, we assess the recoverability of the affected long-lived assets, including intangible assets, by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If impairment is indicated, we measure the amount of such impairment by comparing the fair value to the carrying value.

In September 2008 we initiated a strategic restructuring in connection with the September 30, 2008 conclusion of our Alzheimer s disease genetics cooperation agreement with Eisai Co., Ltd. (Eisai). As part of the restructuring, we transitioned from a discovery and development company to a development-only company. We performed a recoverability test of the long-lived assets related to our discovery efforts in accordance with SFAS No. 144. The recoverability test was based on the estimated undiscounted future cash flows expected to result from the disposition of the assets that supported our discovery efforts. Based on the recoverability analysis performed, we determined that the estimated undiscounted future cash flows expected to result from the disposition of the discovery assets would not be sufficient to recover the carrying value of these assets. Accordingly, we recorded a non-cash charge for the impairment of long-lived assets of $154,000 to write-down the carrying value of these assets to their estimated fair value. The fair value was estimated based upon sales prices of similar assets. During the fourth quarter of 2008 we sold the equipment that supported our discovery efforts for total proceeds of $364,000. The impairment of long-lived assets was recorded as other expense in the statement of operations for the twelve months ended December 31, 2008.

In December 2008 we performed a recoverability test of our purchased patents in accordance with SFAS No. 144. The recoverability test was based on the estimated undiscounted future cash flows expected to result from anticipated milestone payments potentially due to us under agreements to out-license the development of the compounds associated with the purchased patents. Based on the recoverability analysis performed, we determined the estimated undiscounted future cash flows associated with the purchased patents would not be sufficient to recover the carrying value of these assets. As of December 31, 2008 we estimate the fair value of the purchased patents to be $0; accordingly, we recorded a non-cash charge for the impairment of the purchased patents of $3,124,000. During 2008 we received $50,000 of license revenues associated with the purchased patents. These license revenues were credited against the impairment loss to arrive at a net impairment loss of $3,074,000. The net impairment loss on the purchased patents is classified as an operating expense in the statement of operations for the twelve months ended December 31, 2008.

Revenue Recognition

We recognize revenue when all four of the following criteria are met: (i) persuasive evidence that an arrangement exists; (ii) delivery of the products and/or services has occurred; (iii) the selling price is fixed or determinable; and (iv) collectibility is reasonably assured. We follow the provisions of the Securities and Exchange Commission s Staff Accounting Bulletin (SAB) 104, *Revenue Recognition*, which sets forth guidelines in the timing of revenue recognition based upon factors such as passage of title, installation, payment and customer acceptance.

Upfront amounts received as option fees and license fees under our alliance and collaboration agreements are classified as deferred revenue and recognized as revenue over the period of service or performance if such arrangements require on-going services or performance. Amounts received for milestones will be recognized upon achievement of the milestone, unless the amounts received are creditable against royalties or we have on-going performance obligations. Royalty revenue will be recognized upon sale of the related products, provided the royalty amounts are fixed and determinable, and collection of the related receivable is probable. Any amounts received prior to satisfying the revenue recognition criteria will be recorded as deferred revenue in the accompanying balance sheets.

Research and Development

Research and development costs are expensed as incurred.

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Comprehensive Income or Loss

SFAS No. 130, *Reporting Comprehensive Income,* requires that all components of comprehensive income, including net income or loss and foreign currency translation adjustments, be reported in the financial statements in the period in which they are recognized. Comprehensive income or loss is defined as the change in equity during a period from transactions and other events and circumstances from non-owner sources.

Stock-Based Compensation

Effective January 1, 2006, we adopted SFAS No. 123 (revised 2004) (SFAS No.123R), *Share Based Payment*, which supersedes our previous accounting under SFAS No. 123, *Accounting for Stock-Based Compensation*. SFAS No.123R requires the recognition of compensation expense, using a fair-value based method, for costs related to all share-based payments to employees, including grants of stock options. SFAS No.123R requires companies to estimate the fair value of share-based payment awards on the date of grant using an option-pricing model. The Black-Scholes model has been used to determine the fair value for our option awards and the Monte-Carlo simulation option-pricing model has been used to determine the fair value of certain of our restricted stock unit awards. The value of the portion of the award that is ultimately expected to vest is recognized as expense over the service period in the statements of operations.

Income Taxes

We account for income taxes and the related assets and liabilities in accordance with SFAS No. 109, *Accounting for Income Taxes.* Deferred tax assets and liabilities are determined based on the difference between the financial statement and tax basis of assets and liabilities using enacted rates expected to be in effect during the year in which the differences reverse. We provide a valuation allowance against net deferred tax assets unless, based upon the available evidence, it is more likely than not that the deferred tax assets will be realized.

Foreign Currency Translation and Transactions

The functional currencies of our subsidiaries in Belgium and the Netherlands are the local currencies. The operations of the Netherlands subsidiary were closed in November 2006 and the operations of the Belgium subsidiary were closed in December 2008. Assets and liabilities of these subsidiaries are translated at the rate of exchange at the balance sheet date. Income and expense items are translated at the average rate of exchange rates in effect during the reporting period. Gains and losses resulting from foreign currency translation are included as a component of stockholders equity (deficit) through the closure date for each subsidiary. Foreign currency transaction gains and losses are included in the results of operations. A total of $486,000 of foreign currency translation gains that were recorded in stockholders equity (deficit) were reclassified to other income (expense) upon the closure of the Belgium subsidiary. Realized foreign exchange transaction gains for the years ended December 31, 2008, 2007 and 2006 were $145,000, $1,000 and $15,000, respectively.

Net Loss per Share

We calculate net loss per share in accordance with SFAS No. 128, *Earnings Per Share*. Net loss per share is computed on the basis of the weighted-average number of common shares outstanding during the periods presented. Loss per share assuming dilution is computed on the basis of the weighted-average number of common shares outstanding and the dilutive effect of all common stock equivalents. Net loss per share attributable to common stockholders assuming dilution for the years ended December 31, 2008, 2007 and 2006 is equal to net loss per share attributable to common stockholders since the effect of common stock equivalents outstanding during the periods, including stock options, restricted stock units and warrants, is antidilutive.

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Shares used in calculating basic and diluted net loss per common share exclude these potential common shares (in thousands):

	Years Ended December 31,		
	2008	2007	2006
Antidilutive options to purchase common stock	2,073	1,606	1,408
Antidilutive warrants to purchase common stock	2,148	2,410	2,464
Antidilutive restricted stock units	105	195	155
	4,326	4,211	4,027

Recently Issued Accounting Standards

In May 2008, the FASB issued SFAS No. 162, *The Hierarchy of Generally Accepted Accounting Principles*. SFAS No. 162 identifies the sources of accounting principles and the framework for selecting the principles to be used in the preparation of financial statements that are presented in conformity with GAAP in the United States (the GAAP hierarchy). SFAS No. 162 is effective 60 days following the SEC s approval of the Public Company s Oversight Board amendments to AU Section 411, *The Meaning of Present Fairly in Conformity With Generally Accepted Accounting Principles*. We do not expect the adoption of SFAS No. 162 to have a material effect on our financial statements.

In May 2008, the FASB issued FASB Staff Position (FSP) No. APB 14-1, *Accounting for Convertible Debt Instruments That May Be Settled in Cash upon Conversion (Including Partial Cash Settlement)* (FSP APB 14-1). FSP APB 14-1 requires the issuer of certain convertible debt instruments that may be settled in cash (or other assets) on conversion to separately account for the liability and equity components of the instrument. The debt would be recognized at the present value of its cash flows discounted using the Company s nonconvertible debt borrowing rate. The equity component would be recognized as the difference between the proceeds from the issuance of the note and the fair value of the liability. The FSP also requires an accretion of the resultant debt discount over the expected life of the debt. The transition guidance requires retrospective application to all periods presented, and does not grandfather existing instruments. The effective date of FSP APB 14-1 is for financial statements issued for fiscal years beginning after December 15, 2008. We do not expect the adoption of FSP APB 14-1 to have a material effect on our financial statements.

In June 2008, the FASB ratified Emerging Issues Task Force (EITF) EITF Issue No. 07-5, *Determining Whether an Instrument (or an Embedded Feature) is Indexed to an Entity s Own Stock* (EITF 07-5). EITF 07-5 provides that we should use a two-step approach to evaluate whether an equity-linked financial instrument (or embedded feature) is indexed to our own stock, including evaluating the instrument s contingent exercise and settlement provisions. EITF 07-5 is effective for financial statements issued for fiscal years beginning after December 15, 2008, and interim periods within those fiscal years. Early application is not permitted. We do not expect the adoption of EITF 07-5 to have a material effect on our financial statements.

Adoption of New Accounting Standards

On January 1, 2008 we adopted the provisions of SFAS No. 157, Fair Value Measurement and the provisions of SFAS No. 159, *The Fair Value Option for Financial Assets and Financial Liabilities Including an Amendment of FASB Statement No. 115.* This standard permits an entity to choose to measure many financial instruments and certain other items at fair value with any gains or losses for the period recorded in the statement of income. We elected to apply the provisions of SFAS No. 159 to our investment in OXIS. See Note 4 for further information.

On January 1, 2008 we adopted the provisions of EITF Issue No. 07-3, *Accounting for Nonrefundable Advance Payments for Goods or Services to be Used in Future Research and Development Activities*. EITF Issue No. 07-3 requires companies to defer and capitalize prepaid, nonrefundable research and development payments

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to third parties over the period that the research and development activities are performed or the services are provided, subject to an assessment of recoverability. The adoption of EITF Issue No. 07-3 did not have a material impact on our financial statements.

On January 1, 2008 we adopted EITF Issue No. 07-1, *Accounting for Collaborative Arrangements Related to the Development and Commercialization of Intellectual Property.* Companies may enter into arrangements with other companies to jointly develop, manufacture, distribute, and market a product. Often the activities associated with these arrangements are conducted by the collaborators without the creation of a separate legal entity (that is, the arrangement is operated as a virtual joint venture). The arrangements generally provide that the collaborators will share, based on contractually defined calculations, the profits or losses from the associated activities. Periodically, the collaborators share financial information related to product revenues generated (if any) and costs incurred that may trigger a sharing payment for the combined profits or losses. The consensus requires collaborators in such an arrangement to present the result of activities for which they act as the principal on a gross basis and report any payments received from (made to) other collaborators based on other applicable GAAP or, in the absence of other applicable GAAP, based on analogy to authoritative accounting literature or a reasonable, rational, and consistently applied accounting policy election. As our collaborative agreements do not incorporate such revenue- and cost-sharing arrangements, the adoption of EITF Issue No. 07-1 did not have an impact on our financial statements.

2. Merger

As described in Note 1, we completed the Merger on October 3, 2006. Pursuant to the Merger, stockholders of TPTX, Inc. exchanged their shares of TPTX, Inc. stock for a total of approximately 9.0 million shares of TorreyPines common stock and a total of 1.5 million warrants to purchase TorreyPines common stock. Immediately following the Merger, approximately 58% of the fully-diluted shares of TorreyPines common stock were owned by former stockholders of TPTX, Inc. According to SFAS No. 141, *Business Combinations*, TPTX, Inc. was the acquiring entity for accounting purposes, and the Merger was accounted for as a reverse acquisition.

The intangible assets acquired in the Merger were purchased in-process research and development and purchased patents. These intangible assets were valued with the assistance of independent valuation experts, using the income approach. The value assigned to purchased in-process research and development is comprised of the following two projects, both related to the potential treatment of Alzheimer s disease: Phenserine valued at $3.0 million and Posiphen valued at $5.3 million. The purchased in-process research and development was expensed upon acquisition because the projects had not reached technological feasibility and the projects did not have a future alternative use. The value assigned to purchased patents was comprised of the following patents: Phenserine valued at $1.3 million, Posiphen valued at $2.5 million and bisnorcymserine valued at $0.2 million. The purchased patents were capitalized upon acquisition because they had future alternative uses for the potential treatment of diseases and disorders other than Alzheimer s disease.

3. Balance Sheet Account Details

Prepaid expenses and other current assets consist of the following (in thousands):

	December 31,	
	2008	**2007**
Prepaid expenses	$ 95	$ 746
Non trade receivables	43	81
Deposits	49	8
	$ 187	$ 835

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Property and equipment consist of the following (in thousands):

	December 31,	
	2008	2007
Lab equipment	$ 27	$ 3,808
Computer equipment and software	283	782
Furniture and fixtures and office equipment	271	363
	581	4,953
Less accumulated depreciation	(541)	(4,179)
	$ 40	$ 774

Purchased patents consist of the following (in thousands):

	December 31,	
	2008	2007
Purchased patents	$	$ 4,000
Less accumulated amortization		(485)
	$	$ 3,515

As discussed in Note 1, we determined the carrying value of the purchased patents was impaired as of December 31, 2008. Accordingly, we recorded a charge for the impairment of the purchased patents of $3,074,000.

Accounts payable and accrued liabilities consist of the following (in thousands):

	December 31,	
	2008	2007
Accounts payable	$ 2,410	$ 2,543
Accrued benefits	166	891
Accrued other	1,289	2,028
	$ 3,865	$ 5,462

4. Investment in OXIS

As indicated in Note 1, effective January 1, 2008, we elected to apply the fair value option under the provisions of SFAS No. 159 to our investment in OXIS. Prior to this election, we accounted for our investment in OXIS under the equity method of accounting following Accounting Principles Bulletin No. 18. We believe fair value provides a more objective measurement of the value of this investment than the equity method of accounting. The investment in OXIS is a Level 1 asset within the fair value hierarchy established by SFAS No. 157 because the investment has a quoted price in an active market, the Over-The-Counter Bulletin Board.

As of December 31, 2007 our investment in OXIS was carried at fair value because we determined that an other-than-temporary impairment of value had occurred. As such, there was no cumulative-effect adjustment to the opening balance of retained earnings as a result of our electing to apply the fair value option for our investment in OXIS.

In September 2008 we sold our entire investment in OXIS common stock. As of the date of the sale, the quoted price of OXIS common stock on the Over-The-Counter Bulletin Board was $0.03. The total fair value of the investment in OXIS at the time of the sale was $419,000. We received proceeds from the sale of the investment in OXIS of $42,000, resulting in a loss on the sale of $377,000. The loss on the sale of the investment

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in OXIS is included in other expense in the statement of operations. For the year ended December 31, 2008, the total decline in the fair value of the investment in OXIS was $559,000 and was recorded in the statement of operations in other expense. The adoption of SFAS No. 159 for our investment in OXIS has no effect on our deferred tax assets and liabilities.

5. Significant Agreements

Eisai Co., Ltd.

In February 2005, we signed a collaboration agreement with Eisai Co., Ltd. (Eisai). Under this agreement, Eisai had an exclusive right of first negotiation and refusal for validated compounds discovered through the research. In exchange for these rights, we have received $15.0 million under the agreement. This collaboration agreement expired in February 2008.

In October 2005, we signed a collaboration agreement with Eisai. Under this agreement, Eisai had exclusive rights of first negotiation and refusal for gene targets discovered and validated through the research. In exchange for these rights, we received $14.6 million under the agreement. This agreement expired in September 2008. In November 2008 we sold the genetics research program to Eisai for $1.5 million and recorded the amount as Other revenue.

The upfront payments for all agreements were recognized as revenue on a straight-line basis over the term of each agreement. Revenue associated with the full-time employees we committed to the project was recognized as research efforts were expended.

We recognized revenue of $6.1 million, $9.9 million and $9.9 million for each year ended December 31, 2008, 2007 and 2006, respectively and have deferred revenues related to option fees and research funding received but not earned of $0 and $2.2 million as of December 31, 2008 and 2007, respectively.

Eli Lilly and Company

In April 2003, we signed a license agreement with Eli Lilly and Company (Lilly). Under the agreement, we paid Lilly a $6.0 million license payment in 2003. We are also subject to certain milestone and royalty payments as specified in the agreement. During the twelve months ended December 31, 2007, we expensed $1.0 million in connection with milestones specified in the agreement. During 2008 we issued 200,000 shares of common stock to Lilly in exchange for a reduction in the royalty rates and the timing of milestone payments under the agreement.

Life Science Research Israel, Ltd.

In May 2004, we entered into a research and license agreement with Life Science Research Israel, Ltd. (LSRI). Under the agreement, we were required to make research funding payments to LSRI totaling $800,000 over a two-year period. Through December 31, 2006, we had made payments totaling $800,000. We did not make any research funding payments in 2007 or 2008. We are also subject to certain milestone and royalty payments as specified in the agreement. Through December 31, 2006 we had made payments totaling $2.2 million. We did not make any milestone payments in 2007 or 2008.

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6. Long-Term Debt

The notes payable and unamortized discount balances as of December 31, 2008 and 2007 are shown below (in thousands):

	December 31, 2008	2007
Notes payable, bearing an interest rate of 11.39%, due March 2009	$	$ 4,692
Notes payable, bearing an interest rate of prime plus 1% with interest-only payments through December 2008, due June 2011	3,600	
Total notes payable	3,600	4,692
Less unamortized discount	(48)	(164)
Total long-term debt	3,552	4,528
Less current portion	(1,440)	(3,574)
Non-current portion	$ 2,112	$ 954

In 2005 we entered into two notes that allowed us to borrow up to $10.0 million (the 2005 Debt). In 2005 we borrowed an initial $5.0 million under these notes and in 2006 we borrowed the remaining $5.0 million. The notes were payable in monthly installments of principal and interest. In June 2008, we repaid the outstanding balance on the 2005 Debt. The total payoff of the 2005 Debt was $3.0 million and included early payoff fees of $60,000. The 2005 Debt had an unamortized debt discount as of the date of payoff of $105,000. The payoff of the 2005 Debt was accounted for as a debt extinguishment, therefore the unamortized debt discount and early payoff fees were recorded as a loss on the early extinguishment of debt on the statement of operations.

In June 2008 we entered into a new note agreement with a different financial institution to borrow $3.6 million with an annual interest rate of prime plus 1% (4.25% at December 31, 2008). The note has a three year term and is payable in 30 equal monthly installments of principal and interest, with interest-only payments payable during the period July through December 2008 and principal and interest payments beginning in January 2009. The note is collateralized by a security interest in substantially all of our assets, including our right to payments that may arise from the sale, license or other disposition of our intellectual property and to the underlying intellectual property only to the extent necessary to enforce the security interest in such payments. In connection with the note agreement, we incurred debt issuance costs of $48,000 which were recorded as a deferred charge and classified as other assets on the balance sheet. The debt issuance costs are being amortized as a component of interest expense over the term of the loan. The aggregate unamortized debt issuance costs as of December 31, 2008 were $39,000.

In connection with this new note agreement, we issued a warrant to the lender to purchase 78,832 shares of our common stock at an exercise price of $1.37 per share. The warrant was valued using the Black-Scholes model assuming a risk-free interest rate of 3.5%, a dividend yield of 0%, expected volatility of 63% and a contractual life of the warrants of five years. The fair value of the warrant was $58,000 and was recorded as a debt discount. The debt discount is being amortized as additional interest expense over the term of the loan. The aggregate unamortized debt discount as of December 31, 2008 was $48,000.

Pursuant to the terms of the agreement, we are required to maintain a cash balance with the lender s bank of at least $5.4 million. Additionally, we are subject to other financial and non-financial covenants, including a Material Adverse Effect clause. The Material Adverse Effect clause permits the holder of the note to call the balance in the event of a circumstance that could have a Material Adverse Effect. A Material Adverse Effect is defined as any circumstance that has a material adverse effect on (i) our business operations or condition (financial or otherwise), (ii) our ability to repay the note or otherwise perform our obligations under the agreement, or (iii) our interest in, or the value, perfection or priority of the lender s security interest in the collateral. As of December 31, 2008 no Material Adverse Effect circumstances have occurred and we are in

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compliance with all covenants. As discussed in Note 1, we are projecting that our cash balance will decrease below the $5.4 million requirement in 2009 should we not be successful in securing additional cash sources in the near-term. At the time cash drops below $5.4 million, management expects to have sufficient cash on hand to repay the amount outstanding under the agreement should the bank call the balance as a result of that covenant violation. In accordance with EITF 86-30, Classification of Obligations When a Violation Is Waived by the Creditor , the principal amount outstanding under the note agreement due beyond December 31, 2009 has been classified as non-current.

Annual debt maturities at December 31, 2008, are as follows (in thousands):

2009	$ 1,440
2010	1,440
2011	720
2012 and thereafter	
	$ 3,600

7. Commitments

We lease our office facilities under a noncancelable operating lease which expires in 2009. The lease requires us to pay for all maintenance, insurance and property taxes. Rent expense for the years ended December 31, 2008, 2007 and 2006, was $614,000, $612,000 and $666,000, respectively. There were no outstanding purchase commitments in existence as of December 31, 2008.

Future minimum payments of all operating leases are as follows at December 31, 2008 (in thousands):

2009	$ 210
2010 and thereafter	
Total minimum lease payments	$ 210

8. Redeemable Convertible Preferred Stock

Beginning in 2000 and continuing until 2006, we issued redeemable convertible preferred stock which was convertible at the option of the holder on a one-for-one basis into shares of common stock. The holder of each share of redeemable convertible preferred stock was entitled to one vote for each share of common stock into which it would have converted.

We increased the carrying amount of the redeemable convertible preferred stock by periodic accretions related to offering costs and the fair value of the warrants and the related beneficial conversion feature, so that the carrying amount would have equaled the minimum redemption value on the earliest redemption date. Increases in the carrying amount of the redeemable convertible preferred stock were recorded as increases in our accumulated deficit.

Holders of the redeemable convertible preferred stock had parity with holders of common stock on an as-if converted basis for all dividends declared by the Board of Directors. Holders of the redeemable convertible preferred stock were entitled to cash dividends, which accrued at the rate of 6% of the applicable original issue price per annum, compounded annually. The dividends were cumulative and payable when and if declared by the Board of Directors.

In the event of liquidation, the holders of the redeemable convertible preferred stock would have received a liquidation preference equal to the original issuance price plus accrued but unpaid dividends. The liquidation preference had priority over all distributions to common stockholders. After payment of the liquidation preference, all remaining assets from liquidation, if any, were to be distributed to the holders of the redeemable convertible preferred stock and the common stock according to the number of shares held.

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On October 3, 2006, pursuant to the Merger, the outstanding shares of redeemable convertible preferred stock were exchanged for a total of 7,958,059 shares of common stock, and warrants to purchase 1,500,000 shares of common stock. On October 3, 2006, the carrying amount of the redeemable convertible preferred stock was increased by $342,000, the amount of unamortized issuance costs as of that date. Upon the exchange of the redeemable convertible preferred stock for common stock we reversed a total of $14.0 million of redeemable convertible preferred stock dividends accrued through October 3, 2006. As of December 31, 2008, there are no issued or outstanding shares of redeemable convertible preferred stock.

The following is a summary of the redeemable convertible preferred stock exchanged for common stock in the Merger:

Description	Share Price	Total Shares
Series A	$ 5.60	1,429,617
Series B	9.24	2,068,455
Series C	9.24	3,770,951
Series C-2	9.24	689,036
Total redeemable convertible preferred stock exchanged for common stock		7,958,059

9. Stockholders Equity (Deficit)

Warrants

In connection with the Merger, certain stockholders of TPTX, Inc. received 1,500,000 warrants to purchase TorreyPines common stock at an exercise price of $8.32. In accordance with EITF 00-19, Accounting for Derivative Financial Instruments Indexed to, and Potentially Settled in, a Company s Own Stock , we classified the warrants as a liability, and valued the warrants using the Black-Scholes model as of the date of issuance. The warrants were valued using the Black-Scholes model assuming a risk free interest rate at 4.7%, an expected dividend yield of 0%, expected volatility of 69% and an expected life of the warrants of 2.75 years. The fair value of the warrant liability is remeasured quarterly and a warrant valuation adjustment is recorded to the income statement. For the year ended December 31, 2006, we recorded $240,000 in other expense as a warrant valuation adjustment.

During 2007, we obtained letters from the holders of these warrants clarifying the warrant agreement to allow for settlement of these warrants with the issuance of unregistered shares and to further clarify that a net cash settlement is prohibited. On each of the effective dates of these clarification letters (for which no additional consideration was given or received), the aggregate fair value of $3,922,000 for these warrants, as calculated using the Black-Scholes model, was reclassified from current liabilities to additional paid-in capital. For the year ended December 31, 2007, we recorded $892,000 in other income as a warrant valuation adjustment.

As discussed in Note 6, during 2008 we issued warrants to a lender in connection with a new note agreement.

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As of December 31, 2008, outstanding warrants to acquire shares of our common stock are as follows:

Number of Shares	Exercise Price	Expiration Date
370,909	$ 58.00	January 8, 2009
119,227	68.00	May 3, 2009
1,500,000	8.32	October 3, 2009
12,992	9.24	July 1, 2010
6,246	5.60	December 7, 2010
78,832	1.37	June 11, 2013
59,544	9.24	September 26, 2015
2,147,750		

The weighted average exercise price of warrants outstanding at December 31, 2008 was $19.98 and the weighted average remaining contractual life of the warrants was 0.9 years.

Stock Options and Restricted Stock Units

Various employees, directors, and consultants have been granted options to purchase common shares under an equity incentive plans adopted in 2000 and 2006 (the 2000 Plan and the 2006 Plan). The 2000 Plan provides for the grant of up to 973,588 stock options and the 2006 Plan provides for the grant of up to 2,188,539 stock options. Options granted under both plans generally expire no later than 10 years from the date of grant (five years for a 10% stockholder). Options generally vest and become fully exercisable over a period of four years. The exercise price of incentive stock options must be equal to at least the fair market value of our common stock on the date of grant, and the exercise price of nonstatutory stock options may be no less than 85% of the fair value of our common stock on the date of grant. The exercise price of any incentive stock option granted to a 10% stockholder may be no less than 110% of the fair value of our common stock on the date of grant.

The following table summarizes our stock option activity and related information through December 31, 2008:

	Shares	Weighted Average Exercise Price Per Share
Outstanding at December 31, 2007	1,605,742	$ 14.62
Granted	1,051,384	0.32
Exercised	(15,562)	1.19
Canceled	(568,191)	4.32
Outstanding at December 31, 2008	2,073,373	10.30
Vested and exercisable at December 31, 2008	990,073	$ 20.56

The weighted-average grant-date fair value of options granted during the years ended December 31, 2008, 2007 and 2006, was $0.21, $4.07 and $3.45, per share, respectively.

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The following table summarizes information concerning outstanding and exercisable stock options as of December 31, 2008:

	Options Outstanding			Options Exercisable	
Range of Exercise Price	Number Outstanding	Weighted-Average Remaining Contractual Life (in years)	Weighted-Average Exercise Price	Number Exercisable	Weighted-Average Exercise Price
$ 0.27 - $ 0.27	1,001,384	9.7	$ 0.27	83,445	$ 0.27
$ 0.62 - $ 1.48	218,776	5.4	1.25	158,392	1.22
$ 2.90 - $ 7.62	239,114	7.9	6.42	163,929	6.72
$ 7.77 - $23.00	240,510	5.3	12.04	210,718	12.64
$23.12 - $42.16	236,717	3.1	32.24	236,717	32.24
$46.00 - $64.00	95,747	4.4	57.60	95,747	57.60
$65.00 - $65.00	9,375	0.8	65.00	9,375	65.00
$76.00 - $76.00	18,750	1.8	76.00	18,750	76.00
$88.00 - $88.00	500	1.2	88.00	500	88.00
$92.00 - $92.00	12,500	1.0	92.00	12,500	92.00
$ 0.27 - $92.00	2,073,373	7.4	$ 10.30	990,073	$ 20.56

The following shares of common stock are reserved for future issuance at December 31, 2008:

Warrants	2,147,750
Stock options and restricted stock units:	
Stock options issued and outstanding	2,073,373
Restricted stock units issued and outstanding	105,000
Available for grant	1,501,270
Total common stock reserved for future issuance	5,827,393

10. Stock-Based Compensation

Stock Options

For purposes of calculating the stock-based compensation under SFAS No. 123R, we estimate the fair value of stock options using the Black-Scholes model. The Black-Scholes model incorporates various and highly sensitive assumptions including expected volatility, expected term and interest rates. In accordance with SFAS No. 123R share-based compensation expense recognized in the consolidated statement of operations for the years ended December 31, 2008, 2007 and 2006 is based on awards ultimately expected to vest and is reduced for estimated forfeitures.

The assumptions used to estimate the fair value of stock options granted to employees and directors are listed below.

	Years Ended December 31,		
	2008	2007	2006
Expected Volatility	63% to 78%	64% to 69%	69%
Risk-Free Interest Rate	2.41% to 3.31%	3.88% to 4.78%	4.55% to 5.00%
Forfeitures	0.00% to 20.98%	0.00% to 10.98%	0.00% to 11.81%
Dividend Yield			
Expected Term (in years)	5.5 to 6.1	6.1	6.1

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The estimated volatility reflects the application of the SEC s SAB No. 107, *Share-Based Payment*, incorporating the historical volatility of comparable companies whose share prices are publicly available. The weighted average expected life of options was calculated using the simplified method as prescribed by SAB No. 107. This decision was based on the lack of relevant historical data due to our limited historical experience. The risk-free interest rate assumption was based on the U.S. Treasury s rates for U.S. Treasury securities with maturities similar to those of the expected term of the award being valued. The assumed dividend yield was based on our expectation of not paying dividends in the foreseeable future.

The intrinsic value of options exercised represents the difference between the market price of the stock on the date of the exercise and the exercise price multiplied by the number of options. The total intrinsic value of options exercised for the years ended December 31, 2008, 2007 and 2006 was $5,000, $392,000, and $223,000, respectively. The aggregate intrinsic value represents the difference between the fair market value of our common stock as of December 31, 2008, which was $0.27 per share, and the weighted exercise price of all in-the-money options multiplied by the number of options outstanding. As of December 31, 2008, the aggregate intrinsic value of options outstanding and exercisable was $0. At December 31, 2008, the weighted average remaining contractual term for options vested and exercisable was 5.2 years. The total fair value of shares vested during the three years ended December 31, 2008 was $559,000, $299,000 and $128,000, respectively.

Employee Stock Purchase Plan

At our 2008 Annual Meeting of Stockholders on June 19, 2008, our stockholders approved the adoption of our 2008 Employee Stock Purchase Plan (the ESPP). The ESPP qualifies under Section 423 of the Internal Revenue Service and permits substantially all employees to purchase shares of our common stock at a discount to market. Under the ESPP, employees can choose to have up to 15% of their annual compensation withheld to purchase shares of common stock, subject to certain limitations. The shares of common stock may be purchased over an offering period with a maximum duration of two years at 85% of the lower of the fair market value of the common stock on the first day of the applicable offering period or on the last day of the six-month purchase period. A total of 1,000,000 shares of common stock may be issued pursuant to the ESPP. During the year ended December 31, 2008, 20,000 shares were purchased under the ESPP at a price of $0.16.

Restricted Stock Units

During the years ended December 31, 2008, 2007 and 2006 we granted 0, 40,000 and 155,000 restricted stock units. As of December 31, 2008 there were 105,000 restricted stock units outstanding. The restricted stock unit activity for 2008 is summarized as follows:

	Shares	Weighted Average Grant Date Fair Value
Restricted stock units outstanding at December 31, 2007	195,000	$ 3.39
Granted		
Vested		
Canceled	(90,000)	3.14
Restricted stock units outstanding at December 31 2008	105,000	$ 3.60

Of the restricted stock units awarded during the year ended December 31, 2007, 25,000 units contained a performance condition which was not met nor was probable during the year ended December 31, 2007, therefore no expense was recorded during the twelve months ended December 31, 2007 for these units. During the year ended December 31, 2008 the performance condition was met and expense of $8,000 was recorded for the units. The remaining 15,000 restricted stock units awarded during the year ended December 31, 2007 and all of the restricted stock units awarded during the year ended December 31, 2006 contained a market price condition and

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were valued using a Monte Carlo simulation option-pricing model. The weighted-average grant-date fair value of restricted stock units granted during the years ended December 31, 2008, 2007 and 2006 was $0, $4.36 and $3.14.

The assumptions used to value restricted stock units for the three years ended December 31, 2008 were as follows:

	Years Ended December 31,		
	2008	2007	2006
Expected Volatility		64%	59% to 75%
Risk-Free Interest Rate		3.1%	4.7% to 5.1%
Dividend Yield			
Expected Term (in years)		1.3	2.3

We recognized $403,000 in total stock-based compensation expense for our share-based awards during the twelve-month period ended December 31, 2008, of which $403,000 is related to employee and director awards valued under SFAS No. 123R. For the three years ended December 31, 2008, stock-based compensation expense was allocated among the following expense categories (amounts in thousands, except per share amounts):

	Years Ended December 31,		
	2008	2007	2006
Research and development	$ 56	$ 422	$ 75
General and administrative	348	548	64
Stock-based compensation expense	$ 404	$ 970	$ 139
Stock-based compensation expense per share, basic and diluted	$ 0.03	$ 0.06	$ 0.04

As of December 31, 2008, the total unrecognized stock-based compensation expense related to non-vested stock options was $723,000. This expense is expected to be recognized on a straight-line basis over a weighted average period of approximately 1.8 years.

Equity instruments issued to non-employees are recorded at their fair values as determined in accordance with SFAS No. 123R and EITF 96-18, *Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling Goods and Services*, and are periodically revalued as the options vest and are recognized as expense over the related service period. During the years ended December 31, 2008, 2007 and 2006, we recognized $0, $240,000 and $20,000 respectively, for stock options issued to non-employees.

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11. Income Taxes

Significant components of our deferred tax assets as of December 31, 2008 and 2007 are shown below (amounts in thousands). A valuation allowance of $51,361,000 has been recognized to offset the net deferred tax assets as of December 31, 2008, as realization of such assets is uncertain.

	December 31,	
	2008	2007
Deferred tax assets:		
Capitalized research and development expenses	$ 16,206	$ 4,823
Net operating loss carryforwards	25,967	30,126
Research and development and manufacturers investment credits	5,414	4,565
Stock based compensation	312	277
Investment in OXIS		2,895
Capital loss carryforwards	3,268	
Depreciation	32	
Other	162	157
Total deferred tax assets	51,361	42,843
Deferred tax liabilities		
Acquired patents		(1,249)
Depreciation		(19)
Total deferred tax liabilities		(1,268)
Net deferred tax assets and liabilities	51,361	41,575
Valuation allowance for deferred tax assets	(51,361)	(41,575)
Net deferred tax assets	$	$

Reconciliation of the statutory federal income tax to our effective tax rate for the three years ended December 31, 2008 is shown below (amounts in thousands):

	December 31,		
	2008	2007	2006
Tax at federal statutory rate	$ (7,747)	$ (7,946)	$ (8,628)
State tax benefit, net of federal effect	(1,491)	(1,623)	(1,473)
Non deductible in-process research and development			2,832
Research and development credit	(462)	(253)	(734)
Change in valuation allowance	9,593	9,874	7,893
Non deductible warrant valuation adjustment		(304)	82
Stock based compensation	104	109	6
Reduction of operating loss carryforward		139	
Other	3	4	22
Provision for taxes	$	$	$

During the year ended December 31, 2008, we recorded an increase to our valuation allowance of $9.8 million. Of this amount, approximately $0.2 million relates primarily to changes in deferred tax liabilities recorded in other comprehensive income.

Pursuant to Internal Revenue Code Sections 382 and 383, use of our net operating loss and tax credit carryforwards may be limited if a cumulative change in ownership of more than 50% occurs within a three-year period. We completed a study as of December 31, 2006. As of December 31, 2006, we had deferred tax assets related to net operating losses of $24.3 million and research and tax credit carryforwards of $4.7 million which are not restricted. We have not updated our study to determine if a change in control has occurred subsequent to

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December 31, 2006. If we have experienced a change in control subsequent to December 31, 2006 utilization of our net operating losses and tax credit carryforwards could be subject to an annual limitation. Any limitation may result in expiration of a portion of the carryforwards before utilization. Once a study is completed and any limitation known, the amounts currently presented as an uncertain tax position under FIN No. 48 may change. Any carryforwards that will expire prior to utilization as a result of such limitations will be removed from deferred tax assets with a corresponding reduction of the valuation allowance.

We have federal net operating loss carryforwards of approximately $103.4 million of which $37.1 million are subject to limitation under IRC Section 382 and will expire unused, the remaining federal net operating losses will begin to expire in 2020 unless previously utilized. We have California net operating loss carryforwards of approximately $52.6 million of $0.6 million are subject to limitation under IRC Section 382 and will expire unused, the remaining California net operating losses will begin to expire in 2012 unless previously utilized. We also have federal research credit carryforwards of approximately $7.3 million, of which $2.1 million are subject to limitation under IRC Section 382, the remaining federal research and development credits will begin expiring in 2020 unless previously utilized. In addition we have state research credit carryforwards of approximately $2.2 million, which carryforward indefinitely. We also have state manufacturers investment credit carryforwards of approximately $103,000, which will begin expiring in 2011.

Effective January 1, 2007, we adopted the provisions of FASB Interpretation No. 48, *Accounting for Uncertainty in Income Taxes an Interpretation of FASB Statement No. 109* (FIN 48). FIN 48 prescribes a recognition threshold and measurement attribute criteria for the financial statement recognition and measurement of tax positions taken or expected to be taken in a tax return. For those benefits to be recognized, a tax position must be more-likely-than-not to be sustained upon examination by taxing authorities. Upon implementation, we had unrecognized tax benefits of approximately $711,000. The implementation of FIN 48 would have resulted in a charge to retained earnings of $603,000, except that the charge was fully offset by the application of a valuation allowance.

Our policy is to recognize interest and penalties related to income tax matters in income tax expense. As of December 31, 2008, no interest or penalties associated with any unrecognized tax benefits were accrued, nor was any interest expense recognized during the year.

A rollforward of changes in our unrecognized tax benefits is shown below (in thousands):

	December 31,	
	2008	2007
Balance at beginning of year	$ 920	$ 711
Additions based on tax positions related to the current year	154	210
Additions for tax positions of prior years	13	
Reductions for tax positions of prior years		(1)
Settlements		
Balance at end of year	$ 1,087	$ 920

The December 31, 2008 balance of unrecognized tax benefits of $1.1 million, if recognized, would result in adjustments to the related deferred tax assets and valuation allowance and not affect our effective tax rate.

We are subject to taxation in the United States and various state and foreign jurisdictions. Our tax years for 2000 and forward are subject to examination by the United States and various state taxing authorities due to the carryforward of unutilized net operating losses and credits. Tax years 2004 and forward remain open to examination by foreign taxing jurisdictions. We currently are not under examination by any taxing authorities.

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12. Employee Benefit Plan

Effective January 1, 2001, we adopted a defined contribution 401(k) Plan covering substantially all employees that meet certain age requirements. Employees may contribute up to 60% of their compensation per year, subject to a maximum limit by federal law. We are not required to, and have not, matched any portion of the employee contributions through December 31, 2008.

13. Related-Party Transactions

During the year ended December 31, 2008 there were no related party transactions. During the two years ended December 31, 2007, two directors provided consulting services to us. Combined total payments for these services were $30,000 and $40,000 for 2007 and 2006, respectively.

14. Selected Quarterly Data (Unaudited)

The following tables set forth certain unaudited quarterly information for each of the eight fiscal quarters in the two-year period ended December 31, 2008. This quarterly financial data has been prepared on a consistent basis with the audited financial statements and, in the opinion of management, includes all adjustments, consisting of normal recurring adjustments, necessary for a fair presentation of the information for the periods presented. Our quarterly operating results may fluctuate significantly as a result of a variety of factors and operating results for any quarter are not necessarily indicative of results for a full fiscal year or future quarters.

2008 Quarter Ended

	March 31	June 30	September 30	December 31
Total revenue	$ 2,046	$ 1,212	$ 1,223	$ 1,590
Operating expenses	6,708	7,242	6,105	7,769
Net loss	$ (3,893)	$ (7,450)	$ (5,394)	$ (6,048)
Basic and diluted net loss per share	$ (0.25)	$ (0.47)	$ (0.34)	$ (0.38)

2007 Quarter Ended

	March 31	June 30	September 30	December 31
Total revenue	$ 2,463	$ 2,463	$ 2,463	$ 2,461
Operating expenses	6,572	8,515	9,512	9,021
Net loss attributable to common stockholders	$ (3,281)	$ (5,158)	$ (6,774)	$ (8,156)
Basic and diluted net loss per share attributable to common stockholders	$ (0.21)	$ (0.33)	$ (0.43)	$ (0.52)

15. Contingencies

Several lawsuits were filed against us in February 2005 in the U.S. District Court for the Southern District of New York asserting claims under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934, as amended, or the Exchange Act and Rule 10b-5 thereunder on behalf of a class of purchasers of Axonyx common stock during the period from June 26, 2003, through and including February 4, 2005, referred to as the class period. Dr. Marvin S. Hausman, M.D., a former director and our former Chief Executive Officer, and Dr. Gosse B. Bruinsma, M.D., also a former director and a former Chief Executive Officer, were also named as defendants in the lawsuits. These actions were consolidated into a single class action lawsuit in January 2006. On April 10, 2006, the class action plaintiffs filed an amended consolidated complaint. We filed our answer to that complaint on May 26, 2006. Our motion to dismiss the consolidated amended complaint was filed on May 26, 2006 and was submitted to the court for a decision in September 2006. The motion to dismiss is pending.

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The class action plaintiffs allege generally that our Phase III phenserine development program was subject to alleged errors of design and execution which resulted in the failure of the first Phase III phenserine trial to show efficacy. Plaintiffs allege the defendants failure to disclose the alleged defects resulted in the artificial inflation of the price of our shares during the class period.

The complaint seeks unspecified damages. Management believes the claim is without merit and plans to defend the claim vigorously. We have determined that a loss in connection with this matter is possible, but not probable. Accordingly, we have not recorded any liability relating to these matters.

On February 7, 2009 a pending shareholder derivative suit in New York Supreme Court, New York County, against a current director and former directors and officers was discontinued.

16. Subsequent Event

On February 3, 2009, the Board of Directors granted a total of 800,000 stock options to purchase shares of our common stock to three members of executive management. The options were granted under the 2006 Plan, contain an exercise price of $0.23 per share and were 100% vested on the date of grant. The options have a contractual life of ten years.