

TorreyPines Therapeutics, Inc.
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May 10, 2007

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Registration No. 333-141741

PROSPECTUS

9,858,863 Shares
TORREYPINES THERAPEUTICS, INC.
Common Stock

This prospectus relates to the resale from time to time of up to 9,858,863 shares of our outstanding common stock in the aggregate, including 1,500,000 shares of our common stock issuable upon the exercise of warrants, which are held by the selling stockholders named in this prospectus and such stockholders' donees, pledgees or successors. Of the shares of common stock offered under this prospectus, 8,358,863 shares were issued in connection with the business combination between the registrant (formerly known as Axonyx Inc.) and TorreyPines Therapeutics, Inc. (now known as TPTX, Inc.). We are not selling any securities under this prospectus and will not receive any of the proceeds from the sale of shares by the selling stockholders, although we may receive proceeds upon the exercise of the warrants.

The selling stockholders may sell the shares of common stock described in this prospectus in a number of different ways and at varying prices. We provide more information about how the selling stockholders may sell their shares of common stock in the section entitled "Plan of Distribution" on page 24. We will not be paying any underwriting discounts or commissions in this offering.

Our common stock is traded on the NASDAQ Global Market under the symbol "TPTX". On March 28, 2007, the reported closing price of the common stock was \$6.72 per share.

An investment in the shares offered hereby involves a high degree of risk. See "Risk Factors" beginning on page 4 of this prospectus.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

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ABOUT THIS PROSPECTUS

You should rely only on the information contained or incorporated by reference in this prospectus. We have not, and the selling stockholders have not, authorized anyone to provide you with information different from that contained in this prospectus. The selling stockholders are offering to sell, and seeking offers to buy, shares of our common stock only in jurisdictions where it is lawful to do so. The information in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or any sale of our common stock.

Whenever we refer to we, our or us in this prospectus, we mean TorreyPines Therapeutics, Inc., on a consolidated basis with its subsidiaries unless the context indicates otherwise.

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere or incorporated by reference into this prospectus. Because it is a summary, it does not contain all of the information that you should consider before investing in our securities. You should read this entire prospectus carefully, including the section entitled Risk Factors and the documents that we incorporate by reference into this prospectus, before making an investment decision.

TORREYPINES THERAPEUTICS, INC.

Prior to October 3, 2006, we were known as Axonyx Inc. On October 3, 2006, we completed a business combination, referred to as the Merger, with TorreyPines Therapeutics, Inc. (now known as TPTX, Inc.). For accounting purposes, we were deemed to be the acquired entity in the Merger. In connection with the Merger, we changed our name to TorreyPines Therapeutics, Inc. and effected an 8-for-1 reverse stock split of our Common Stock.

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

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

We currently have one product candidate in clinical trials for cognitive disorders. NGX267 is our lead product candidate for the treatment of cognitive impairment associated with schizophrenia, or CIAS. We have completed two Phase I clinical trials of NGX267. We initiated an additional Phase I clinical trial of NGX267 in March 2007. Assuming favorable results, we intend to initiate a Phase II clinical trial in the second half of 2007. The Phase II clinical trial would evaluate NGX267 for the treatment of CIAS. We expect that NGX267 would be used primarily as adjunctive therapy to current antipsychotic therapy to treat schizophrenia. Our second product candidate for the treatment of CIAS, NGX292, is currently in preclinical development. In addition, although not the primary targeted indication, we may also evaluate NGX267 and NGX292 for the potential treatment of Alzheimer's disease.

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

We were incorporated in Nevada on July 29, 1997 as Axonyx Inc. and reincorporated in Delaware on October 3, 2006 as TorreyPines Therapeutics, Inc. Our principal executive offices are located at 11085 North Torrey Pines Road, Suite 300, La Jolla, California 92037, and our main telephone number is (858) 623-5665. Our web site is located on the world wide web at <http://www.torreypinestherapeutics.com>. We do not incorporate by reference into this prospectus the information on, or accessible through, our Web site, and you should not consider it a part of this prospectus.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risk factors described below, and all other information contained in or incorporated by reference in this prospectus, before deciding to invest in our common stock. If any of the following risks actually occur, the market price of our common stock could decline, and you could lose all or part of your investment. Additional risks not presently known to us or that we currently believe are immaterial may also significantly impair our business operations and could result in a complete loss of your investment.

Risks Related to Our Business

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

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

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

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

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

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

Success in preclinical testing and early clinical trials does not mean that later clinical trials will be successful. Companies frequently suffer significant setbacks in advanced clinical trials, even after earlier clinical trials have

shown promising results. In future clinical trials with larger or somewhat different populations, results from early clinical trials may not be reproduced and analysis of new or additional data may not demonstrate sufficient safety and efficacy to support regulatory approval of a product candidate.

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

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

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

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

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

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

- ongoing discussions with the FDA or comparable foreign authorities regarding the scope or design of one or more clinical trials;
- delays in receiving, or the inability to obtain, required approvals from institutional review boards or other reviewing entities at clinical trial sites selected for participation in a clinical trial;
- delays or slower than anticipated enrollment of participants into clinical trials;
- lower than anticipated retention rate of participants in clinical trials;
- need to repeat clinical trials as a result of inconclusive or negative results or unforeseen complications in testing;
- inadequate supply or deficient quality of product candidate materials or other materials necessary to conduct our clinical trials;
- unfavorable FDA inspection and review of a clinical trial site or records of any clinical or preclinical investigation;

- serious, unexpected or undesirable side effects experienced by participants in the clinical trials that delay or

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preclude regulatory approval or limit the commercial use or market acceptance if approved;

- findings that the clinical trial participants are being exposed to unacceptable health risks;
- placement by the FDA of a clinical hold on a clinical trial;
- restrictions on or post-approval commitments with regard to any regulatory approval we ultimately obtain that renders a product candidate not commercially viable; and
- unanticipated cost overruns in preclinical and clinical trials.

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

- failure to conduct the clinical trial in accordance with regulatory requirements;
- inspection of the clinical trial operations or clinical trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold;
- negative clinical trial results;
- adverse events or negative side-effects experienced by the clinical trial participants; or
- lack of adequate funding to continue the clinical trial.

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

Clinical trials require sufficient participant enrollment, which is a function of many factors, including the size of the target population, the nature of the clinical trial protocol, the proximity of participants to clinical trial sites, the availability of effective treatments for the relevant disorder or disease, the eligibility criteria for our clinical trials and competing clinical trials. Delays in enrollment can result in increased costs and longer development times. Failure to enroll participants in our clinical trials could delay the completion of the clinical trials beyond current expectations. In addition, the FDA could require us to conduct clinical trials with a larger number of participants than we may project for any of our product candidates. As a result of these factors, we may not be able to enroll a sufficient number of participants in a timely or cost-effective manner.

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

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

If we experience any such problems, we may not have the financial resources to continue development of the product candidate that is affected or the development of any of our other product candidates. If we experience

significant delays in the commencement or completion of clinical testing, financial results and the commercial prospects for the product candidates will be harmed, costs will increase and our ability to generate revenue will be delayed.

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

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

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

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

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

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

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

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

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

In February 2005, we entered into an agreement with Eisai to discover small molecule gamma-secretase

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

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

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

We have an agreement with Johnson & Johnson Development Corporation, or JJDC, regarding our research and development work into the effects of using M1 agonists, such as NGX267 and NGX292, in the treatment of central nervous system, or CNS, diseases and disorders. Upon completion of a specified level of development of our lead M1 agonist, we are obligated to provide results for the compound to JJDC.

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

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

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

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

We may enter into collaborations with other strategic partners with respect to our product candidates. If we enter into any such collaborations, we may have limited or no control over the amount and timing of resources that our partners dedicate to the development of our product candidates. Our ability to commercialize products we develop with our partners and generate royalties from product sales will depend on the partner's ability to assist us in establishing the safety and efficacy of our product candidates, obtaining regulatory approvals and achieving market acceptance of products. Our partners may elect to delay or terminate development of a product candidate,

independently develop products that could compete with our products, or not commit sufficient resources to the marketing and distribution of products under the collaboration. If our partners fail to perform as expected under the collaborative agreements, our potential for revenue from the related product candidates will be dramatically reduced. In addition, revenue from our future collaborations may consist of contingent payments, such as payments for achieving development and commercialization milestones and royalties payable on sales of any successfully developed drugs. The milestone, royalty or other revenue that we may receive under these collaborations will depend upon both our ability and our partner's ability to successfully develop, introduce, market and sell new products. In some cases, we will not be involved in these processes and, accordingly, will depend entirely on our partners.

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

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

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

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

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

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

We have supplies of tezampanel, NGX426 and NGX267 that we expect to need for current clinical trials. We will need to identify and reach agreement with third parties for the supply of our product candidates for future

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

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

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

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

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

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

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

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

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

achieving those endpoints will prevent us from commercializing our product candidates.

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

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

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

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

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

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

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

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

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

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

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

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

Licensing our product candidates from other companies, universities or individuals does not always prevent them from developing non-identical but competitive products for their own commercial purposes, nor from pursuing patent protection in areas that are competitive with us. Our partners who created these technologies are sophisticated scientists and business people who may continue to do research and development and seek patent protection in the same areas that led to the discovery of the product candidates that they licensed to us. The development and commercialization of successful new drug products from our research program is likely to attract additional research by our licensors in addition to other investigators who have experience in developing products for the CNS market. By virtue of the previous research that led to the discovery of the drugs or product candidates that they licensed to us, these companies, universities, or individuals may be able to develop and market competitive products in less time than might be required to develop a product with which they have no prior experience.

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

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

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

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

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

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

A class action securities lawsuit and a stockholder derivative lawsuit was filed against us prior to the Merger. We are defending against these actions vigorously; however, we do not know what the outcome of these

proceedings will be and, if we do not prevail, we may be required to pay substantial damages or settlement amounts. Furthermore, regardless of the outcome, we may incur significant defense costs, and the time and attention of our management may be diverted from normal business operations. If we are ultimately required to pay significant defense costs, damages or settlement amounts, such payments could materially and adversely affect our operations and results. We have purchased liability insurance, however, if any costs or expenses associated with the litigation exceed the insurance coverage, we may be forced to bear some or all of these costs and expenses directly, which could be substantial and may have an adverse effect on our business, financial condition, results of operations and cash flows. In any event, publicity surrounding the lawsuits and/or any outcome unfavorable to us could adversely affect our reputation and share price. The uncertainty associated with substantial unresolved lawsuits could harm our business, financial condition and reputation.

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

Fluctuations in currency exchange rates may negatively impact our business.

We currently have operations in Belgium and conduct clinical trials in Europe. Costs resulting from our operations in Europe are denominated primarily in local currencies, including the Euro, and are subject to fluctuations in currency exchange rates. Further, we incur other operating expenses, including expenses related to clinical trials, which are denominated in Euros and other local currencies. Significant fluctuations in the currency exchange rates and general economic conditions in the countries in which we do business, could harm our operating results.

The carrying value of our investment in OXIS International may face future impairment.

We account for our investment in OXIS under the equity method of accounting following accounting principles bulletin (APB) No. 18. Any impairment charge would be required if we determined that any reduction in the OXIS market value over the carry value was permanent.

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;
- 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.

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, 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 ongoing 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 ongoing 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 ongoing 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 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 for CNS diseases and disorders, 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.

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 cannot successfully defend ourself against the 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.

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We use hazardous chemicals and radioactive 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 research and development processes involve the controlled use of hazardous materials, including chemicals, radioactive 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.

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 ongoing 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 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.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

Any statements in this prospectus about our expectations, beliefs, plans, objectives, assumptions or future events or performance that are not historical facts are forward-looking statements. Such forward-looking statements include statements regarding the efficacy, safety and intended utilization of our product candidates, the conduct and results of future clinical trials, and plans regarding regulatory filings, future research and clinical trials and plans regarding partnering activities. You can identify these forward-looking statements by the use of words or phrases such as believe, may, could, will, estimate, continue, anticipate, intend, seek, plan, expect, should, or would. Among the factors that could cause results to differ materially from those indicated in the forward-looking statements are risks and uncertainties inherent in our business including, without limitation, statements about the progress and timing of our clinical trials; difficulties or delays in development, testing, obtaining regulatory approval, producing and marketing our product candidates; unexpected adverse side effects or inadequate therapeutic efficacy of our product candidates that could delay or prevent product development or commercialization, or that could result in recalls or product liability claims; the scope and validity of patent protection for our product candidates; competition from other pharmaceutical or biotechnology companies; our ability to obtain additional financing to support our operations; and other risks detailed in our Annual Report on Form 10-K filed with the Securities and Exchange Commission, or SEC, on March 29, 2007 and the discussions set forth above under the caption Risk Factors.

Although we believe that the expectations reflected in our forward-looking statements are reasonable, we cannot guarantee future results, events, levels of activity, performance or achievement. We undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events or otherwise, unless required by law.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale of shares by the selling stockholders pursuant to this prospectus.

A portion of the shares covered by this prospectus are issuable upon exercise of warrants to purchase our common stock. Upon any exercise of the warrants for cash, the selling stockholders would pay us the exercise price of the warrants. The cash exercise price of the warrants is \$8.32 per share of our common stock.

SELLING STOCKHOLDERS

In the Merger, former TPTX stockholders received shares of our common stock and certain former TPTX stockholders received warrants to purchase our common stock. Of our shares of common stock and warrants to purchase shares of our common stock issued to former TPTX stockholders, 9,858,863 shares and warrants to purchase 1,500,000 shares at a cash exercise price of \$8.32 per share were issued to persons and entities that held shares of TPTX preferred stock prior to the Merger. Pursuant to the terms of the warrants, if certain changes occur to our capitalization, such as a stock split or stock dividend of the common stock, then the exercise price and number of shares issuable upon exercise of the warrants will be adjusted appropriately. Under the Merger Agreement, we agreed to file a registration statement, of which this prospectus is a part, with the SEC to register the disposition of the shares of our common stock that were issued to the former affiliates of TPTX, including the shares of our common stock issuable upon exercise of the warrants issued in the Merger, and to keep the registration effective until the earlier of (a) the date upon which all of the shares first become eligible for resale pursuant to Rule 145 under the Securities Act of 1933, as amended, or the Securities Act, without restriction or (y) the first date upon which all of the shares covered by such registration statement have been sold pursuant to such registration statement.

The following table sets forth:

- the name of each of the selling stockholders;
- the number of shares of our common stock beneficially owned by each such selling stockholder prior to this offering;

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- the percentage (if one percent or more) of our common stock owned by each such selling stockholder prior to this offering;
- the number of shares of our common stock being offered pursuant to this prospectus;
- the number of shares of our common stock owned upon completion of this offering; and
- the percentage (if one percent or more) of common stock owned by each such selling stockholder after this offering.

This table is prepared based on information supplied to us by the selling stockholders or in Schedules 13G and other public documents filed with the SEC, and reflects holdings as of March 15, 2007. As used in this prospectus, the term "selling stockholder" includes each of the selling stockholders listed below, and any donees, pledges, transferees or other successors in interest selling shares received after the date of this prospectus from a selling stockholder as a gift, pledge, or other non-sale related transfer. The number of shares in the column "Number of Shares Being Offered" represents all of the shares that a selling stockholder may offer under this prospectus. Each selling stockholder may sell some, all or none of his or its shares. The number of shares in the column "Shares of Common Stock Beneficially Owned After Offering" assumes that the selling stockholder sells all of the shares covered by this prospectus. We do not know how long the selling stockholders will hold the shares before selling them, and we currently have no agreements, arrangements or understandings with the selling stockholders regarding the sale of any of the shares except an agreement that the selling stockholders would not sell any such shares until April 3, 2007 entered into in connection with the Merger.

Beneficial ownership is determined in accordance with Rule 13d-3(d) promulgated by the SEC under the Securities Exchange Act of 1934, as amended, or the Exchange Act. The percentage of shares beneficially owned prior to the offering is based on 15,700,039 shares of our common stock issued and outstanding as of March 15, 2007.

Except as noted in the footnotes to the table below, no selling stockholder has had, within the past three years, any position, office, or material relationship with us or any of our predecessors or affiliates.

Security Holder	Shares of Common Stock Beneficially Owned Prior to Offering		Number of Shares Being Offered	Shares of Common Stock Beneficially Owned After Offering		
	Number	Percent		Number	Percent	
Entities affiliated with Alta Partners	2,642,583	(1)	16.4	% 2,642,583	*	
Entities affiliated with GIMV NV	2,628,603	(2)	16.3	% 2,628,603	*	
Entities associated with Advent International Corporation	1,560,559	(3)	9.8	% 1,560,559	*	
Johnson & Johnson Development Corporation	709,682	(4)	4.5	% 709,682	*	
Novartis Forschungsstiftung	604,890	(5)	3.8	% 604,890	*	
S.R. One, Limited E	425,755	(6)	2.7	% 425,755	*	
Eisai Co., LTD En	321,683	(7)	2.0	% 321,683	*	
Entities affiliated with NIF Ventures Co., Ltd.	257,346	(8)	1.6	% 257,346	*	
Entities affiliated with Sorrento Ventures	257,346	(9)	1.6	% 257,346	*	
William T. Comer, Ph.D.	201,285	(10)	1.3	% 201,285	*	
Rudolph E. Tanzi, Ph.D.	176,610	(11)	1.1	% 162,400	14,210	*
Evelyn Graham	44,660	(12)	*	32,480	12,180	*
Craig Johnson	44,660	(13)	*	32,480	12,180	*
GC&H Investments	15,299	(14)	*	15,299		*
Peter Davis, Ph.D.	4,872	(15)	*	4,872		*
GATX Ventures, Inc.	1,600	(16)	*	% 1,600		*
TOTAL	9,897,433		57.4	% 9,858,863	38,570	*

* Represents less than 1%.

(1) 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 Alta BioPharma Partners III GmbH & Co. Beteiligungs KG and 13,483 shares held of record and a warrant to purchase 2,541 shares by Alta Embarcadero BioPharma Partners III, LLC. 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. Jean Deleage is a managing director of Alta Partners. Mr. Deleage, a member of our board of directors and a former member of the board of directors of TPTX, disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein.

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- (2) Includes 1,544,403 shares held of record and a warrant to purchase 286,897 shares held by GIMV NV, 477,704 shares held of record and a warrant to purchase 90,041 shares held by Biotech Fonds Vlaanderen, NV and 193,776 shares held of record and a warrant to purchase 35,782 shares held by Adviesbeheer GIMV Life Sciences NV. GIMV NV, as the parent of each of Biotech Fonds Vlaanderen, NV and Adviesbeheer GIMV Life Sciences NV, 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 of directors and a former member of the board of directors of TPTX, disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein.
- (3) 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; and 2,677 shares held of record and a warrant to purchase 493 shares held by Advent Partners Limited Partnership. Jason Fisherman is a managing director at Advent International. Mr. Fisherman, a member of our board of directors and a former member of the board of directors of TPTX, disclaims beneficial ownership of these shares except to the extent of his pecuniary interest therein. Each fund disclaims beneficial ownership of the others' shares.
- (4) Includes 597,130 shares held of record and a warrant to purchase 112,552 shares.
- (5) Includes 511,018 shares held of record and a warrant to purchase 93,872 shares.
- (6) Includes 360,314 shares held of record and a warrant to purchase 65,441 shares.
- (7) Includes 270,666 shares held of record and a warrant to purchase 51,017 shares.
- (8) Includes 43,306 shares held of record and a warrant to purchase 8,163 shares held by NIF Ventures Co., Ltd.; 79,906 shares held of record and a warrant to purchase 15,061 shares held by Venture Capital Investment Limited Partnership NIF Japan USA Europe Bridge Fund; and 93,320 shares held of record and a warrant to purchase 17,590 shares held by Venture Capital Investment Limited Partnership NIF Global Fund.
- (9) Includes 115,297 shares held of record and a warrant to purchase 21,732 shares held by Sorrento Ventures III, L.P.; 25,309 shares held of record and a warrant to purchase 4,770 shares held by Sorrento Ventures CE, L.P.; and 75,927 shares held of record and a warrant to purchase 14,311 shares held by Sorrento Ventures IV, L.P.
- (10) Dr. Comer is a member of our board of directors and a former member of the board of directors of TPTX. Consists of 174,256 shares held of record and a warrant to purchase 27,029 shares.
- (11) Dr. Tanzi was a member of the board of directors of TPTX. Consists of 162,400 shares held of record and, for purposes of the column entitled 'Shares of Common Stock Beneficially Owned Prior to the Offering' and 'Shares of Common Stock Beneficially Owned After to the Offering,' also includes options to purchase 14,210 shares that are exercisable within 60 days of March 15, 2007.

(12) Ms. Graham is our Chief Operating Officer. Prior to the Merger Ms. Graham was the Chief Operating Officer of TPTX. Consists of 32,480 shares held of record and, for purposes of the column entitled Shares of Common Stock Beneficially Owned Prior to the Offering and Shares of Common Stock Beneficially Owned After to the Offering, also includes options to purchase 12,180 shares that are exercisable within 60 days of March 15, 2007.

(13) Mr. Johnson is our Vice President, Finance and Chief Financial Officer. Prior to the Merger Mr. Johnson was the Vice President, Finance and Chief Financial Officer of TPTX. Consists of 32,480 shares held of record and, for purposes of the column entitled Shares of Common Stock Beneficially Owned Prior to the Offering and Shares of Common Stock Beneficially Owned After to the Offering, also includes options to purchase 12,180 shares that are exercisable within 60 days of March 15, 2007.

(14) Includes 12,930 shares held of record and a warrant to purchase 2,369 shares.

(15) Dr. Davis is a member of our board of directors and a former member of the board of directors of TPTX.

(16) Includes 1,346 shares held of record and a warrant to purchase 254 shares.

PLAN OF DISTRIBUTION

The selling stockholders may, from time to time, sell any or all of their shares of common stock on any stock exchange, market or trading facility on which the shares are traded or in private transactions. These sales may be at fixed or negotiated prices. The selling stockholders may use any one or more of the following methods when selling shares:

- on The Nasdaq Global Market (or any other exchange or automated quotation system on which the shares may be listed);
- on the over-the-counter market;
- ordinary brokerage transactions and transactions in which the broker-dealer solicits purchasers;
- block trades in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction;
- purchases by a broker-dealer as principal and resale by the broker-dealer for its account under this prospectus;
- an exchange distribution in accordance with the rules of the applicable exchange;
- through the distribution of the shares by any selling stockholder that is not an individual to its partners, members or stockholders;
- privately negotiated transactions;
- short sales entered into after the effective date of the registration statement of which this prospectus is a part;
- broker-dealers may agree with the selling stockholders to sell a specified number of such shares at a stipulated price per share;

- a combination of any such methods of sale; and
- any other method permitted pursuant to applicable law.

The selling stockholders may also sell shares under Rule 144 or Rule 145(d) under the Securities Act, if available, rather than under this prospectus, provided that they meet the criteria and conform to the requirements of the applicable rule.

Broker-dealers engaged by the selling stockholders may arrange for other brokers-dealers to participate in sales. Broker-dealers may receive commissions or discounts from the selling stockholders (or, if any broker-dealer acts as

agent for the purchaser of shares, from the purchaser) in amounts to be negotiated. The selling stockholders do not expect these commissions and discounts to exceed what is customary in the types of transactions involved. Any profits on the resale of shares of common stock by a broker-dealer acting as principal might be deemed to be underwriting discounts or commissions under the Securities Act. Discounts, concessions, commissions and similar selling expenses, if any, attributable to the sale of shares will be borne by a selling stockholder. The selling stockholders may agree to indemnify any agent, dealer or broker-dealer that participates in transactions involving sales of the shares if liabilities are imposed on that person under the Securities Act.

The selling stockholders may from time to time pledge or grant a security interest in some or all of the shares of common stock owned by them and, if they default in the performance of their secured obligations, the pledgees or secured parties may offer and sell the shares of common stock from time to time under this prospectus after we have filed a supplement to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act supplementing or amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholders also may transfer the shares of common stock in other circumstances, in which case the transferees, pledgees or other successors in interest will be the selling beneficial owners for purposes of this prospectus and may sell the shares of common stock from time to time under this prospectus after we have filed a supplement to this prospectus under Rule 424(b)(3) or other applicable provision of the Securities Act supplementing or amending the list of selling stockholders to include the pledgee, transferee or other successors in interest as selling stockholders under this prospectus.

The selling stockholders and any broker-dealers or agents that are involved in selling the shares of common stock may be deemed to be underwriters within the meaning of the Securities Act in connection with such sales. In such event, any commissions received by such broker-dealers or agents and any profit on the resale of the shares of common stock purchased by them may be deemed to be underwriting commissions or discounts under the Securities Act. Selling stockholders who are underwriters within the meaning of the Securities Act will be subject to the prospectus delivery requirements of the Securities Act. The selling stockholders may indemnify any broker-dealer that participates in transactions involving the sale of the shares against certain liabilities, including liabilities arising under the Securities Act.

The selling stockholders have advised us that they have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their shares of common stock, nor is there an underwriter or coordinating broker acting in connection with a proposed sale of shares of common stock by any selling stockholder. If we are notified by any selling stockholder that any material arrangement has been entered into with a broker-dealer for the sale of shares of common stock, if required, we will file a supplement to this prospectus. If the selling stockholders use this prospectus for any sale of the shares of common stock, they will be subject to the prospectus delivery requirements of the Securities Act.

We have advised the selling stockholders that the anti-manipulation rules of Regulation M under the Exchange Act may apply to sales of our common stock and activities of the selling stockholders and their affiliates. These rules may limit the timing of purchases and sales of the shares by such selling stockholders.

In order to comply with the securities laws of some states, if applicable, the shares of common stock may be sold in these jurisdictions only through registered or licensed brokers or dealers. In addition, in some states the shares may not be sold unless they have been registered or qualified for sale or an exemption from registration or qualification requirements is available and is complied with.

We have agreed to keep the registration statement of which this prospectus constitutes a part effective with respect to shares of our common stock until the earlier of (1) the date upon which all of the shares of common stock acquired from us, or shares of common stock issuable upon exercise of warrants acquired from us, by such selling stockholders first become eligible for resale pursuant to Rule 145 under the Securities Act without restriction, or (2) the date upon which all of the shares of common stock acquired from us, or shares of common stock issuable upon exercise of warrants acquired from us, by such selling stockholders are sold pursuant to any registration statement filed by us with the SEC.

LEGAL MATTERS

The validity of the securities being offered hereby will be passed upon by Cooley Godward Kronish LLP, San Diego, California. As of the date of this prospectus, Cooley Godward Kronish LLP and a partnership in which interests are owned directly and/or beneficially by partners and employees of Cooley Godward Kronish LLP own 40,171 shares of our common stock and hold warrants exercisable for 2,369 shares of our common stock.

EXPERTS

The consolidated financial statements of TorreyPines Therapeutics, Inc. appearing in TorreyPines Therapeutics, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2006 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon, included therein, and incorporated herein by reference. Such consolidated financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file electronically with the SEC our annual reports on Form 10-K, quarterly interim reports on Form 10-Q, current reports on Form 8-K, and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934, and other information. We make available on or through our website, <http://www.torreypinestherapeutics.com>, free of charge, copies of these reports and other information as soon as reasonably practicable after we electronically file or furnish it to the SEC. You may read and copy any reports, statements or other information that we file with the SEC, at the SEC's public reference room at 100 F Street, N.E., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. Our SEC filings are also available to the public from commercial document retrieval services and on the website maintained by the SEC at <http://www.sec.gov>. Reports, proxy statements and other information concerning TorreyPines also may be inspected at the offices of the National Association of Securities Dealers, Inc., Listing Section, 1735 K Street, Washington, D.C. 20006.

INFORMATION INCORPORATED BY REFERENCE

We incorporate by reference into this prospectus the documents listed below and any future filings we make with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, including any filings after the date of this prospectus but before the end of any offering made under this prospectus. Except as set forth below, the SEC file number for the documents incorporated by reference in this prospectus is 000-25571.

- Annual Report on Form 10-K for the fiscal year ended December 31, 2006 filed on March 29, 2007;
- The description of the Registrant's Common Stock set forth in the Amendment No. 1, Registration Statement on Form 10-SB, filed with the Commission on August 10, 1999.

In addition, all filings that we make with the SEC pursuant to the Exchange Act after the initial filing date of the registration statement, of which this prospectus forms a part, and prior to effectiveness of the registration statement shall be deemed to be incorporated by reference into this prospectus.

Any information in any of the foregoing documents will automatically be deemed to be modified or superseded to the extent that information in this prospectus or in a later filed document that is incorporated or deemed to be incorporated herein by reference modifies or replaces such information.

We also incorporate by reference any future filings (other than current reports furnished under Item 2.02 or Item 7.01 of Form 8-K and exhibits filed on such form that are related to such items) made with the SEC pursuant to

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Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act, until we file a post-effective amendment which indicates the termination of the offering of the securities made by this prospectus. Information in such future filings updates and supplements the information provided in this prospectus. Any statements in any such future filings will automatically be deemed to modify and supersede any information in any document we previously filed with the SEC that is incorporated or deemed to be incorporated herein by reference to the extent that statements in the later filed document modify or replace such earlier statements.

We will provide to each person, including any beneficial owner, to whom a prospectus is delivered, without charge upon written or oral request, a copy of any or all of the documents that are incorporated by reference into this prospectus but not delivered with the prospectus, including exhibits which are specifically incorporated by reference into such documents. If you would like to request documents from us, please send a request in writing or by telephone to us at the following address:

TorreyPines Therapeutics, Inc.
11085 North Torrey Pines Road, Suite 300
La Jolla, CA 92037
(858) 623-5665
Attn: Secretary