TITAN PHARMACEUTICALS INC
Form 10-K
March 18, 2013

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the fiscal year ended December 31, 2012

or

¨ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**
For the transition period from to .

Commission file number 000-27436

TITAN PHARMACEUTICALS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**94-3171940**
(State or Other Jurisdiction of Incorporation or Organization)	**(I.R.S. Employer Identification Number)**
400 Oyster Point Blvd., Suite 505, South San Francisco, California	**94080**
(Address of principal executive offices)	**(Zip code)**

Registrant s telephone number, including area code: (650) 244-4990

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

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

Common Stock, $0.001 par value

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

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

Indicate by check mark whether the registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to the filing requirements for the past 90 days. Yes x No ¨

Indicate by check mark whether the registrant has submitted electronically and posted on its corporate Web site, if any, every interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). x Yes ¨ No

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K (§ 229.405 of this chapter) is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. x

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

Large accelerated filer	¨	Accelerated filer	x
Non-accelerated filer	¨	Smaller Reporting Company	¨

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

The aggregate market value of the 64,592,330 shares of voting and non-voting common equity held by non-affiliates of the registrant based on the closing price on June 30, 2012 was $45.2 million.

As of March 11, 2013, 81,811,489 shares of common stock, $.001 par value, of the registrant were issued and outstanding.

DOCUMENTS INCORPORATED BY REFERENCE:

NONE

PART I

NOTE REGARDING FORWARD-LOOKING STATEMENTS

Statements in this Annual Report on Form 10-K or in the documents incorporated by reference herein may contain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Reference is made in particular to the description of our plans and objectives for future operations, assumptions underlying such plans and objectives and other forward-looking terminology such as may, expects, believes, anticipates, intends, expects, projects, or similar terms, variations of such the negative of such terms. Forward-looking statements are based on management s current expectations. Actual results could differ materially from those currently anticipated due to a number of factors, including but not limited to, uncertainties relating to financing and strategic agreements and relationships; difficulties or delays in the regulatory approval process; uncertainties relating to sales, marketing and distribution of our drug candidates that may be successfully developed and approved for commercialization; adverse side effects or inadequate therapeutic efficacy of our drug candidates that could slow or prevent product development or commercialization; dependence on third party suppliers; the uncertainty of protection for our patents and other intellectual property or trade secrets; and competition.

We expressly disclaim any obligation or undertaking to release publicly any updates or revisions to any forward-looking statements contained herein to reflect any change in our expectations or any changes in events, conditions or circumstances on which any such statement is based.

References herein to we, us, Titan, and our company refer to Titan Pharmaceuticals, Inc. unless the context otherwise requires.

Probuphine® and ProNeura are trademarks of our company. This Annual Report on Form 10-K also includes trade names and trademarks of companies other than Titan.

Item 1. Business

Overview

We are a biopharmaceutical company developing proprietary therapeutics for the treatment of serious medical disorders. Our product development programs focus primarily on important pharmaceutical markets with significant unmet medical needs and commercial potential. We are directly developing our product candidates and also utilize corporate, academic and government partnerships as appropriate. Such collaborations have helped to fund product development and have enabled us to retain significant economic interest in our products.

Our principal asset is Probuphine®, the first slow release implant formulation of buprenorphine, designed to maintain a stable, around the clock blood level of the medicine in patients for six months following a single treatment. The clinical and manufacturing development of Probuphine for the treatment of opioid dependence in adult patients is complete. The New Drug Application (NDA) seeking approval for treatment of opioid dependence has been accepted by the United States Food and Drug Administration (FDA) for a Priority Review. Priority Review designation is given to therapies that offer potential major advances in treatment, including improved safety, or provide a treatment where no adequate therapy exists. Based upon the Prescription Drug User Fee Act (PDUFA), the FDA has set a target date of April 30, 2013 for FDA action on the NDA. An FDA advisory committee review has been scheduled for March 21, 2013.

Probuphine is inserted subdermally in a patient s upper arm providing continuous medication, and has the potential to enhance patient compliance to treatment, and limit diversion for illicit use and accidental exposure to the daily dosed formulations. The outpatient treatment of opioid addiction with daily dosed sublingual buprenorphine formulations represents a $1.3 billion market in the U.S., which continues to grow. A transdermal formulation of buprenorphine for the treatment of chronic pain entered the U.S. market in 2011 and Probuphine has the potential to be developed for treating chronic pain as well.

In December 2012, we entered into a license agreement with Braeburn Pharmaceuticals Sprl (Braeburn) that grants Braeburn exclusive commercialization rights to Probuphine® in the United States and Canada. We received a non-refundable up-front license fee of $15.75 million and will receive a $50 million milestone payment upon the approval of the NDA by the FDA. Additionally, we will be eligible to receive up to $130 million upon achievement of specified sales milestones and up to $35 million in regulatory milestones in the event of future NDA submissions and approvals for additional indications, including chronic pain. Titan will receive tiered royalties on net sales of Probuphine ranging from the mid-teens to the low twenties. In addition to the potential milestone payments, Apple Tree Partners IV, Braeburn s parent company, has allocated in excess of $75 million to launch, commercialize and continue the development of Probuphine.

Probuphine is the first product to utilize ProNeura , our novel, proprietary, continuous drug delivery technology. Our ProNeura technology has the potential to be used in developing products for the treatment of other chronic conditions, such as Parkinson s disease, where maintaining stable, around the clock blood levels of a drug can benefit the patient and improve medical outcomes.

Under a sublicense agreement with Novartis Pharma AG (Novartis), we are entitled to royalty revenue of 8-10% of net sales of Fanapt® (iloperidone), an atypical antipsychotic compound being marketed in the U.S. by Novartis for the treatment of schizophrenia, based on a licensed U.S. patent that expires in October 2016 (excluding the potential of a six month pediatric extension). We have entered into several agreements with Deerfield Management (Deerfield), a healthcare investment fund, which entitle Deerfield to most of the future royalty revenues related to Fanapt in exchange for cash and debt considerations, the proceeds from which we have been using to advance the development of Probuphine and for general corporate purposes. We have retained a portion of the royalty revenue from the net sales of Fanapt in excess of specified annual threshold levels; however, based on sales levels to date, it is unlikely that we will receive any revenue from Fanapt in the next several years, if ever.

We operate in only one business segment, the development of pharmaceutical products.

Our Products

Probuphine

We are developing Probuphine for the treatment of opioid dependence. Probuphine is the first product specifically designed for the long-term treatment of opioid dependence and it utilizes ProNeura, our novel, proprietary, long-term drug delivery technology. See Continuous Drug Delivery Technology (ProNeura) below. Probuphine is designed to maintain a stable, around the clock blood level of the drug buprenorphine, an approved agent for the treatment of opioid dependence. If approved, Probuphine is expected to provide six months of medication following a single treatment. Probuphine has been shown to be effective with an acceptable safety profile in the following Phase 3 clinical studies:

- Two six-month, double-blind, placebo-controlled safety and efficacy trials; one of which included an open label, active control (Suboxone). In both studies, Probuphine demonstrated superiority to placebo implants, and in the second study, established non-inferiority in comparison to Suboxone;
- Two six-month, open-label re-treatment safety trials; and
- A pharmacokinetic (relative bioavailability) safety study.

The goal of any therapy for an addictive disorder is to reduce the use of the addictive substance over time and to engage the patient in treatment long enough for therapeutic gains to be consolidated. In a clinical study, the effectiveness of a treatment for opioid dependence is primarily evaluated by testing a patient s urine samples for the presence of illicit opioids over the treatment period. In both placebo-controlled Phase 3 studies of Probuphine, every participant was required to provide urine samples three times a week, essentially on alternate days. Any missed sample was considered a positive result (i.e. urine testing positive for illicit opioid). In these

studies, the primary effectiveness of the treatment with Probuphine (i.e. the primary endpoint) was established by comparing the negative urine results (i.e. urine testing negative for illicit opioid) between the Probuphine and placebo arms using a statistical technique, specifically the cumulative distribution function of negative urines , which basically performs a comparative analysis on the relative proportions of negative urines between treatment groups over the time period of treatment. The patients in the Probuphine arm showed clinically meaningful and a statistically significant difference in the negative urines as compared to the placebo arm in both studies, i.e. the Probuphine patients had statistically more negative results than the placebo arm, demonstrating that the treatment with Probuphine was successful in reducing their usage of illicit opioids as compared to the treatment with placebo. These favorable results for Probuphine were also confirmed by a significant difference over the placebo arm in other secondary measures such as retention in treatment, withdrawal symptoms and craving for opioids, all of which are monitored by clinicians to see if a treatment is providing clinically meaningful benefit to the patients.

Results for the first double-blind, placebo-controlled safety and efficacy study have been published in the Journal of the American Medical Association (JAMA, October 2010).

Patients who completed the controlled studies were eligible for enrollment in the six-month re-treatment studies, which provided data on up to one full year of treatment. The pharmacokinetic safety study has provided important data on the level of buprenorphine in the blood during the treatment period and gives a good profile of the safety of Probuphine. Data from all of these studies was presented at several scientific meetings, including the International Society of Addiction Medicine Annual Meetings in November 2008 and September 2011, the American Society of Addiction Medicine Annual Meetings in May 2009 and 2012, American Society of Addiction Medicine Education Forum in October 2011, and the American College of Neuropharmacology in November 2009 and 2012.

These studies are part of a registration directed program intended to obtain marketing approval of Probuphine for the treatment of opioid dependence in the U.S. and in Europe. We met with the FDA in October 2011 for a pre-NDA meeting and reviewed the clinical development program as well as the chemistry, manufacturing and controls (CMC) aspects of the NDA. Based on this interaction we completed the requirements for an NDA and submitted it to the FDA in October 2012. The NDA seeking approval for the maintenance treatment of opioid dependence has been accepted by the FDA for a Priority Review. Priority Review designation is given to therapies that offer potential major advances in treatment, including improved safety, or provide a treatment where no adequate therapy exists. Based upon the PDUFA requirements, an FDA advisory committee review has been scheduled for March 21, 2013 and the FDA has set a target date of April 30, 2013 for FDA action on the NDA. If approved, Probuphine will be commercialized in the U.S. and Canada by Braeburn. We will seek appropriate commercial partners for Probuphine in other countries, particularly where therapy with daily dosed buprenorphine is already approved.

Continuous Drug Delivery Technology (ProNeura)

Our continuous drug delivery system consists of a small, solid rod made from a mixture of ethylene-vinyl acetate (EVA) and a drug substance. The resulting product is a solid matrix that is placed subcutaneously, normally in the upper arm in a simple office procedure, and is removed in a similar manner at the end of the treatment period. The drug substance is released slowly, at continuous levels, through the process of dissolution. This results in a steady rate of release similar to intravenous administration. We believe that such long-term, linear release characteristics are desirable by avoiding peak and trough level dosing that may pose problems for many disease settings.

Our ProNeura technology was developed to address the need for a simple, practical method to achieve continuous long-term drug delivery, and potentially can provide steady drug release on an outpatient basis over extended periods of up to 6-12 months. This technology has been validated with the successful development of Probuphine, and its potential commercialization in the near term is likely to further strengthen the appeal of this

continuous drug delivery system. We continue to seek opportunities to develop this drug delivery technology for other potential treatment applications in which conventional treatment is limited by variability in blood drug levels and poor patient compliance (e.g. treatment of Parkinson disease with dopamine agonists). During 2012, with the support of an SBIR grant, we completed a non-clinical study with long-term delivery of dopamine agonists which supports the potential to develop an implant delivering ropinirole for treating Parkinson s disease. Additional non clinical testing will be required to develop an optimal formulation and evaluating toxicity prior to any clinical testing. We are also evaluating other drugs and disease settings to establish product development programs during 2013.

Fanapt® (iloperidone)

Fanapt (iloperidone) is an atypical antipsychotic approved by the FDA for the treatment of schizophrenia currently being marketed by Novartis in the U.S. Under a sublicense agreement with Novartis, we are entitled to a royalty of 8-10% of net sales, based on a U.S. patent that we licensed from Sanofi-Aventis. The U.S. patent expires in October 2016 (excluding a six-month pediatric extension). Vanda Pharmaceuticals, Inc. (Vanda) owns the development and commercialization rights to the oral and depot formulations of this product for the rest of the world. However, because patent coverage on the compound has now expired in the significant markets outside of the U.S. and no patent term extensions are possible since the product was not approved in these countries prior to patent expiration, we do not expect any royalties on any future sales in such markets.

We have entered into several agreements with Deerfield, which entitle Deerfield to most of the future royalty revenues related to Fanapt in exchange for cash and debt considerations, the proceeds of which have been used to advance the development of Probuphine and for general corporate purposes. We have retained a portion of the royalty revenue from net sales of Fanapt in excess of specified annual threshold levels; however, based on sales levels to date, it is unlikely that we will receive any revenue from Fanapt in the next several years, if ever. We do not incur any ongoing expenses associated with this product.

License Agreements

In December 2012, we entered into a license agreement with Braeburn pursuant to which we granted Braeburn an exclusive right and license to commercialize Probuphine in the United States of America and its territories, including Puerto Rico, and Canada (the Territory). Under the agreement, Braeburn made a non-refundable up-front license fee payment of $15.75 million and agreed to pay us tiered royalties on net sales of Probuphine ranging from the mid-teens to the low twenties. Additionally, we will receive $50 million upon FDA approval of the NDA for Probuphine and at such time ownership of the NDA will transfer to Braeburn. We are also eligible to receive up to an additional $130 million upon the achievement of specified sales milestones and up to $35 million in regulatory milestones. We will retain all of the rights to Probuphine outside the Territory.

In January 1997, we acquired an exclusive worldwide license under U.S. and foreign patents and patent applications relating to the use of iloperidone for the treatment of psychiatric and psychotic disorders and analgesia from Sanofi-Aventis SA (Sanofi-Aventis) (formerly Hoechst Marion Roussel, Inc.). The Sanofi-Aventis agreement provides for the payment of royalties on future net sales and requires us to satisfy certain other terms and conditions, specifically continued diligent product development and commercialization efforts standard for these types of agreements, in order to retain our rights. In November 1997, we granted a worldwide sublicense, exclusive of Japan, to Novartis under which Novartis continued, at its expense, all further development of iloperidone. In April 2001, that sublicense was extended to include Japan. Under this agreement, Novartis agreed to pay Titan a royalty on future net sales of the product equal to 8% of annual worldwide net sales up to $200 million and 10% of annual worldwide net sales above $200 million, in addition to royalty payments owed by us to Sanofi-Aventis. In June 2004, Novartis granted Vanda the worldwide rights to develop and commercialize iloperidone. In October 2009, Vanda and Novartis amended and restated their sub-license agreement whereby Novartis acquired the U.S. and Canadian rights to commercialize Fanapt, the oral formulation of iloperidone approved in the U.S. Novartis also acquired the U.S. and Canadian development and

commercialization rights to the depot formulation previously under development by Vanda and retained the right of first negotiation to co-market Fanapt and the depot formulation in the rest of the world. All of our rights and economic interests in iloperidone, including royalties on sales, remained essentially unchanged under these agreements and, as previously stated, we have entered into several agreements with Deerfield, which entitle Deerfield to the future royalty revenues related to Fanapt in exchange for cash and debt considerations.

In October 1995, we acquired from the Massachusetts Institute of Technology (MIT) an exclusive worldwide license to certain U.S. and foreign patents relating to our continuous drug delivery system that provided for the payment of certain royalties and other payments with respect to based the licensed technology. Because the patent terms have expired, this license was terminated on July 31, 2012 and we have no continuing obligations to MIT with respect to our ProNeura technology.

In July 2005, we entered into an agreement with the University of Iowa Research Foundation. Under this agreement, we received an exclusive worldwide license to patent rights held by the University of Iowa Research Foundation covering the methods of treating biofilm formation, pseudomonas aeruginosa growth, human deficiency virus, and intracellular pathogens and pathogens causing chronic pulmonary infection using gallium maltolate. Under this agreement, we are required to pay a license issuance fee and certain minimum annual royalty payments. In addition, we are required to pay royalties based on net sales of products and processes incorporating the licensed technology. We will evaluate the utility of this license with respect to future product development programs and take action as appropriate.

Patents and Proprietary Rights

Four patent applications have been filed which incorporate the use of specific compounds with the continuous delivery technology, including two applications related to Probuphine for the potential treatment of opioid addiction and chronic pain. In June 2010, the United States Patent and Trademark Office (USPTO) issued a patent covering Probuphine for the treatment of opiate addiction. Titan is the assignee of this patent which claims a method for treating opiate addiction with a subcutaneously implanted device comprising buprenorphine and EVA, a biocompatible copolymer that releases buprenorphine continuously for extended periods of time. This patent will expire in April 2024. Patents have issued in Australia, India, Japan, Mexico and New Zealand. Further prosecution of these applications is currently proceeding at the USPTO and corresponding agencies in Europe, Canada, India and Hong Kong. Patents covering certain dopamine agonist implants have already been issued or allowed in Europe, Japan, Australia, Canada, South Korea, Mexico, New Zealand, South Africa, and Hong Kong, while prosecution of the patent application continues in the U.S., Israel, India and China.

We hold a license from Sanofi-Aventis under certain issued U.S. patents and certain issued foreign patents relating to iloperidone and its methods of use in the treatment of psychiatric disorders, psychotic disorders and analgesia. The term of the U.S. patent that covers certain aspects of our iloperidone product expires in October 2016, excluding a six month extension possible if an approval of pediatric indication is obtained. Limited foreign patent protection remains in Lichtenstein, Georgia, Korea and the Philippines, although no royalty payments are expected from these patents.

We are the licensee from the University of Iowa Research Foundation (UIRF) of two issued U.S. patents (expiring in 2016) relating to methods of use of gallium compounds to inhibit the growth of P. aeruginosa, and the treatment of infections by pathogens causing chronic pulmonary infection. We are also the licensee from UIRF of certain rights to patent applications covering the use of gallium complexes in preventing and also treating bacterial biofilm-based infections, for which patents have issued in Australia, Japan, Mexico, New Zealand, and South Africa, and prosecution in the U.S., Canada, Europe, China, Hong Kong, and India continues.

Competition

The pharmaceutical and biotechnology industries are characterized by rapidly evolving technology and intense competition. Many companies of all sizes, including major pharmaceutical companies and specialized biotechnology companies, are engaged in the development and commercialization of therapeutic agents designed for the treatment of the same diseases and disorders that we target. Many of our competitors have substantially greater financial and other resources, larger research and development staff and more experience in the regulatory approval process. Moreover, potential competitors have or may have patents or other rights that conflict with patents covering our technologies. For risks we face with respect to competition, see Risk Factors We face intense competition.

With respect to Probuphine, Reckitt Benckiser Group, PLC (Reckitt) markets globally a sublingual buprenorphine product (tablet and film formulations) for the treatment of opioid dependence. This product (Subutex®, Suboxone®) which is administered daily, will compete with our six-month implantable product for treating opioid dependence. Reckitt recently announced the discontinuation of the sublingual tablet formulation of Suboxone in favor of the sublingual film formulation which they will continue to market aggressively. In addition, in February 2013, two generic sublingual tablet formulations of Suboxone were approved by the FDA which are expected to compete with Suboxone. Other forms of buprenorphine are also in development by other companies, including intramuscular injections, buccal delivery and intranasally delivered buprenorphine, which also might compete with our product. In 2010, Alkermes, Inc. received FDA approval to market Vivitrol®, a one month depot injection of naltrexone as a maintenance treatment for opioid dependent patients who have successfully achieved abstinence. We are aware of one month depot formulations of buprenorphine in early clinical development for the treatment of opioid dependence, but we are not aware of any six-month formulations being developed other than Probuphine.

Manufacturing

The manufacturing of Probuphine has primarily been conducted at DPT Laboratories, Inc., and we have expanded the manufacturing facility at this contract manufacturer to establish commercial scale capability to support the potential market launch of Probuphine, and ongoing demand following potential approval by the FDA.

Government Regulation

FDA Approval Process

In the United States, pharmaceutical products are subject to extensive regulation by the FDA. The Federal Food, Drug, and Cosmetic Act, or the FDC Act, and other federal and state statutes and regulations, govern, among other things, the research, development, testing, manufacture, storage, recordkeeping, approval, labeling, promotion and marketing, distribution, post-approval monitoring and reporting, sampling, and import and export of pharmaceutical products. Failure to comply with applicable U.S. requirements may subject a company to a variety of administrative or judicial sanctions, such as FDA refusal to approve pending new drug applications, or NDAs, warning letters, product recalls, product seizures, total or partial suspension of production or distribution, injunctions, fines, civil penalties, and criminal prosecution.

Pharmaceutical product development in the U.S. typically involves preclinical laboratory and animal tests, the submission to the FDA of either a notice of claimed investigational exemption or an investigational new drug application, or IND, which must become effective before clinical testing may commence, and adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug for each indication for which FDA approval is sought. Satisfaction of FDA pre-market approval requirements typically takes many years and the actual time required may vary substantially based upon the type, complexity, and novelty of the product or disease.

Preclinical tests include laboratory evaluation of product chemistry, formulation, and toxicity, as well as animal trials to assess the characteristics and potential safety and efficacy of the product. The conduct of the preclinical tests must comply with federal regulations and requirements, including good laboratory practices. The results of preclinical testing are submitted to the FDA as part of an IND along with other information, including information about product chemistry, manufacturing and controls, and a proposed clinical trial protocol. Long term preclinical tests, such as animal tests of reproductive toxicity and carcinogenicity, may continue after the IND is submitted.

Clinical trials involve the administration of the investigational new drug to healthy volunteers or patients under the supervision of a qualified investigator. Clinical trials must be conducted: (i) in compliance with federal regulations; (ii) in compliance with good clinical practice, or GCP, an international standard meant to protect the rights and health of patients and to define the roles of clinical trial sponsors, administrators, and monitors; as well as (iii) under protocols detailing the objectives of the trial, the parameters to be used in monitoring safety, and the effectiveness criteria to be evaluated. Each protocol involving testing on U.S. patients and subsequent protocol amendments must be submitted to the FDA as part of the IND.

The FDA may order the temporary, or permanent, discontinuation of a clinical trial at any time, or impose other sanctions if it believes that the clinical trial either is not being conducted in accordance with FDA requirements or presents an unacceptable risk to the clinical trial patients. The study protocol and informed consent information for patients in clinical trials must also be submitted to an institutional review board, or IRB, for approval. An IRB may also require the clinical trial at the site to be halted, either temporarily or permanently, for failure to comply with the IRB s requirements, or may impose other conditions.

Clinical trials to support NDAs for marketing approval are typically conducted in three sequential phases, but the phases may overlap. In Phase 1, the initial introduction of the drug into healthy human subjects or patients, the drug is tested to assess metabolism, pharmacokinetics, pharmacological actions, side effects associated with increasing doses, and, if possible, early evidence on effectiveness. Phase 2 usually involves trials in a limited patient population to determine the effectiveness of the drug for a particular indication, dosage tolerance, and optimum dosage, and to identify common adverse effects and safety risks. If a compound demonstrates evidence of effectiveness and an acceptable safety profile in Phase 2 evaluations, Phase 3 trials are undertaken to obtain the additional information about clinical efficacy and safety in a larger number of patients, typically at geographically dispersed clinical trial sites, to permit FDA to evaluate the overall benefit-risk relationship of the drug and to provide adequate information for the labeling of the drug.

After completion of the required clinical testing, an NDA is prepared and submitted to the FDA. FDA approval of the NDA is required before marketing of the product may begin in the U.S. The NDA must include the results of all preclinical, clinical, and other testing and a compilation of data relating to the product s pharmacology, chemistry, manufacture, and controls. The cost of preparing and submitting an NDA is substantial.

Once the submission is accepted for filing, the FDA begins an in-depth review. Priority review can be applied to drugs that the FDA determines offer major advances in treatment, or provide a treatment where no adequate therapy exists. The FDA may refer applications for novel drug products, or drug products which present difficult questions of safety or efficacy, to an advisory committee typically a panel that includes clinicians and other experts for review, evaluation, and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee, but it generally follows such recommendations. Before approving an NDA, the FDA will typically inspect one, or more, clinical sites to assure compliance with GCP. Additionally, the FDA will inspect the facility or the facilities at which the drug is manufactured. FDA will not approve the product unless compliance with current good manufacturing practice, or GMP a quality system regulating manufacturing is satisfactory and the NDA contains data that provide substantial evidence that the drug is safe and effective in the indication studied.

After the FDA evaluates the NDA and the manufacturing facilities, it issues either an approval letter or a complete response letter. A complete response letter generally outlines the deficiencies in the submission and

may require substantial additional testing, or information, in order for the FDA to reconsider the application. If, or when, those deficiencies have been addressed to the FDA s satisfaction in a resubmission of the NDA, the FDA will issue an approval letter.

An approval letter authorizes commercial marketing of the drug with specific prescribing information for specific indications. As a condition of NDA approval, the FDA may require a risk evaluation and mitigation strategy, or REMS, to help ensure that the benefits of the drug outweigh the potential risks. REMS can include medication guides, communication plans for healthcare professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring, and the use of patient registries. The requirement for a REMS can materially affect the potential market and profitability of the drug. Moreover, product approval may require substantial post-approval testing and surveillance to monitor the drug s safety or efficacy. Once granted, product approvals may be withdrawn if compliance with regulatory standards is not maintained or problems are identified following initial marketing.

The Hatch-Waxman Act

In seeking approval for a drug through an NDA, applicants are required to list with the FDA each patent whose claims cover the applicant s product. Upon approval of a drug, each of the patents listed in the application for the drug is then published in the FDA s Approved Drug Products with Therapeutic Equivalence Evaluations, commonly known as the Orange Book. Drugs listed in the Orange Book can, in turn, be cited by potential competitors in support of approval of an abbreviated new drug application, or ANDA. An ANDA provides for marketing of a drug product that has the same active ingredients in the same strengths and dosage form as the listed drug and has been shown through bioequivalence testing to be therapeutically equivalent to the listed drug. Other than the requirement for bioequivalence testing, ANDA applicants are not required to conduct, or submit results of, pre-clinical or clinical tests to prove the safety or effectiveness of their drug product. Drugs approved in this way are commonly referred to as generic equivalents to the listed drug, and can often be substituted by pharmacists under prescriptions written for the original listed drug.

The ANDA applicant is required to certify to the FDA concerning any patents listed for the approved product in the FDA s Orange Book. Specifically, the applicant must certify that: (i) the required patent information has not been filed; (ii) the listed patent has expired; (iii) the listed patent has not expired, but will expire on a particular date and approval is sought after patent expiration; or (iv) the listed patent is invalid or will not be infringed by the new product. A certification that the new product will not infringe the already approved product s listed patents, or that such patents are invalid, is called a Paragraph IV certification. If the applicant does not challenge the listed patents, the ANDA application will not be approved until all the listed patents claiming the referenced product have expired. The ANDA application also will not be approved until any non-patent exclusivity listed in the Orange Book for the referenced product has expired. Federal law provides a period of five years following approval of a drug containing no previously approved active ingredients during which ANDAs for generic versions of those drugs cannot be submitted, unless the submission contains a Paragraph IV challenge to a listed patent - in which case the submission may be made four years following the original product approval. Federal law provides for a period of three years of exclusivity during which the FDA cannot grant effective approval of an ANDA based on the approval of a listed drug that contains previously approved active ingredients but is approved in a new dosage form, route of administration or combination, or for a new use; the approval of which was required to be supported by new clinical trials conducted by, or for, the applicant.

Section 505(b)(2) New Drug Applications

Most drug products obtain FDA marketing approval pursuant to an NDA or an ANDA. A third alternative is a special type of NDA, commonly referred to as a Section 505(b)(2) NDA, enables the applicant to rely, in part, on the FDA s previous approval of a similar product, or published literature, in support of its application. Section 505(b)(2) permits the filing of an NDA where at least some of the information required for approval comes from studies not conducted by, or for, the applicant and for which the applicant has not obtained a right of

reference. If the 505(b)(2) applicant can establish that reliance on the FDA s previous approval is scientifically appropriate, it may eliminate the need to conduct certain preclinical or clinical studies of the new product. The FDA may also require companies to perform additional studies or measurements to support the change from the approved product. The FDA may then approve the new product candidate for all, or some, of the label indications for which the referenced product has been approved, as well as for any new indication sought by the Section 505(b)(2) applicant.

Advertising and Promotion

Once an NDA is approved, a product will be subject to certain post-approval requirements. For instance, the FDA closely regulates the post-approval marketing and promotion of drugs, including standards and regulations for direct-to-consumer advertising, off-label promotion, industry-sponsored scientific and educational activities and promotional activities involving the internet.

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

Adverse Event Reporting and GMP Compliance

Adverse event reporting and submission of periodic reports is required following FDA approval of an NDA. The FDA also may require post-marketing testing, known as Phase 4 testing, risk minimization action plans, and surveillance to monitor the effects of an approved product, or the FDA may place conditions on an approval that could restrict the distribution or use of the product. In addition, quality-control, drug manufacture, packaging, and labeling procedures must continue to conform to current good manufacturing practices, or cGMPs, after approval. Drug manufacturers and certain of their subcontractors are required to register their establishments with FDA and certain state agencies. Registration with the FDA subjects entities to periodic unannounced inspections by the FDA, during which the agency inspects manufacturing facilities to assess compliance with cGMPs. Accordingly, manufacturers must continue to expend time, money, and effort in the areas of production and quality-control to maintain compliance with cGMPs. Regulatory authorities may withdraw product approvals or request product recalls if a company fails to comply with regulatory standards, if it encounters problems following initial marketing, or if previously unrecognized problems are subsequently discovered.

Pediatric Information

Under the Pediatric Research Equity Act, or PREA, NDAs or supplements to NDAs must contain data to assess the safety and effectiveness of the drug for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the drug is safe and effective. The FDA may grant full or partial waivers, or deferrals, for submission of data. Unless otherwise required by regulation, PREA does not apply to any drug for an indication for which orphan designation has been granted.

The Best Pharmaceuticals for Children Act, or BPCA, provides NDA holders a six-month extension of any exclusivity patent or non-patent for a drug if certain conditions are met. Conditions for exclusivity include the FDA s determination that information relating to the use of a new drug in the pediatric population may produce health benefits in that population, the FDA making a written request for pediatric studies, and the applicant agreeing to perform, and reporting on, the requested studies within the statutory timeframe. Applications under the BPCA are treated as priority applications, with all of the benefits that designation confers.

Physician Drug Samples

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

Controlled Substances

Manufacturers of controlled substances, including buprenorphine, are also subject to the licensing, quota, and regulatory requirements of the Controlled Substances Act. Failure to comply with the Controlled Substances Act and the regulations promulgated thereunder could subject companies to loss or suspension of those licenses and to civil or criminal penalties.

Anti-Kickback, False Claims Laws & The Prescription Drug Marketing Act

In addition to FDA restrictions on marketing of pharmaceutical products, several other types of state and federal laws have been applied to restrict certain marketing practices in the pharmaceutical industry in recent years. These laws include anti-kickback statutes and false claims statutes. The federal healthcare program anti-kickback statute prohibits, among other things, knowingly and willfully offering, paying, soliciting or receiving remuneration to induce; or in return for; purchasing, leasing, ordering or arranging for the purchase, lease or order of any healthcare item or service reimbursable under Medicare, Medicaid, or other federally financed healthcare programs. This statute has been interpreted to apply to arrangements between pharmaceutical manufacturers on the one hand and prescribers, purchasers, and formulary managers on the other. Violations of the anti-kickback statute are punishable by imprisonment, criminal fines, civil monetary penalties, and exclusion from participation in federal healthcare programs. Although there are a number of statutory exemptions and regulatory safe harbors protecting certain common activities from prosecution or other regulatory sanctions, the exemptions and safe harbors are drawn narrowly, and practices that involve remuneration intended to induce prescribing, purchases, or recommendations may be subject to scrutiny if they do not qualify for an exemption or safe harbor.

Federal false claims laws prohibit any person from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid. Recently, several pharmaceutical and other healthcare companies have been prosecuted under these laws for allegedly inflating drug prices they report to pricing services, which in turn were used by the government to set Medicare and Medicaid reimbursement rates, and for allegedly providing free product to customers with the expectation that the customers would bill federal programs for the product. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws. The majority of states also have statutes or regulations similar to the federal anti-kickback law and false claims laws, which apply to items and services reimbursed under Medicaid and other state programs, or, in several states, apply regardless of the payor.

Foreign Regulatory Issues

Sales of pharmaceutical products outside the United States are subject to foreign regulatory requirements that vary widely from country to country. Whether or not FDA approval has been obtained, approval of a product by a comparable regulatory authority of a foreign country must generally be obtained prior to the commencement of marketing in that country. Although the time required to obtain such approval may be longer or shorter than that required for FDA approval, the requirements for FDA approval are among the most detailed in the world and FDA approval generally takes longer than foreign regulatory approvals.

Employees

At December 31, 2012, we had 13 full-time employees, 2 part-time employees and several consultants.

Item 1A. Risk Factors

FDA approval of Probuphine may be delayed.

At December 31, 2012, we had cash of approximately $18.1 million, which, together with the FDA s reimbursement of the $2.0 million NDA filing fee, we believe is sufficient to fund our current operations through June 2014. In the event that the FDA issues a complete response letter requiring additional clinical and manufacturing development prior to approval that would require expenditures in excess of certain amounts specified in our agreement with Braeburn, Braeburn will have the right to either terminate the agreement or, in the event the FDA ultimately approves Probuphine for sale in the U.S., reduce the amount of the $50 million milestone payment payable to us by the amount of our obligations for the additional development expenses.

If Braeburn were to terminate the agreement, we would not have sufficient funds available to us to complete the FDA approval process and commercialize Probuphine and, as a result, our business and prospects would be materially adversely impacted. Furthermore, continuation of our current Parkinson s disease development program and the initiation of any additional programs will depend upon our receipt of the $50 million milestone payment and if such payment is not received or is significantly reduced our ability to fund any new product development programs will be materially impaired.

FDA approval of Probuphine may be denied.

The FDA has targeted April 30, 2013 for FDA action on the Probuphine NDA that we submitted in October 2012. The FDA may deny approval of Probuphine for many reasons, including:

- we may be unable to demonstrate to the satisfaction of the FDA that Probuphine is safe and effective for the treatment of opioid dependence in adults;
- the FDA may disagree with our interpretation of data from non-clinical studies or clinical trials;
- we may be unable to demonstrate that Probuphine s clinical and other benefits outweigh any safety or other perceived risks; or
- the FDA may fail to approve the manufacturing processes or facilities of the third-party manufacturers with which we have contracted.

If Probuphine fails to receive FDA approval, our business and prospects will be materially adversely impacted.

The timing and amount of revenues from Probuphine, if any, will be wholly dependent on the efforts of third parties.

We have granted an exclusive license to Braeburn for the commercialization of Probuphine in the United States and Canada. If approved by the FDA, Braeburn will be solely responsible for the marketing, manufacture and commercialization of Probuphine in the Territory and, accordingly, the timing and amount of any royalty revenues or sales milestones we receive from this product will be wholly dependent upon Braeburn s ability to successfully launch and commercialize this product in the Territory. Braeburn is a recently formed company and does not have a track record upon which investors can rely on making an investment decision. Additionaly, our ability to generate revenues in the Territory from any additional indications for Probuphine, including chronic pain, depends on Braeburn s ability to successfully develop, obtain regulatory approvals for and commercialize the product for additional indications. We do not have control over the amount and timing of resources that Braeburn will dedicate to these efforts, none of which have commenced to date. We will be similarly dependent on the development, regulatory and marketing efforts of third parties with respect to revenues, if any, from sales of Probuphine outside the Territory. To date, we have not entered into any collaborative arrangements or granted any rights with respect to Probuphine in the rest of the world.

If Probuphine or any other product candidate that we may successfully develop does not achieve broad market acceptance among physicians, patients, healthcare payors and the medical community, the revenues that it generates from their sales will be limited.

Even if Probuphine or any other product candidate we may in the future develop receives regulatory approval, they may not gain market acceptance among physicians, patients, healthcare payors and the medical community. Coverage and reimbursement of our product candidates by third-party payors, including government payors, generally is also necessary for commercial success. The degree of market acceptance of any approved products will depend on a number of factors, including:

- the efficacy and safety as demonstrated in clinical trials;
- the clinical indications for which the product is approved;
- acceptance by physicians, operators of hospitals and clinics and patients of the product as a safe and effective product;
- the potential and perceived advantages of the product over alternative treatments;
- the safety of the product in broader patient groups, including its use outside of approved indications;
- the cost of treatment in relation to alternative treatments;
- the availability of adequate reimbursement and pricing by third parties and government authorities;
- the prevalence and severity of adverse events;
- the effectiveness of sales and marketing efforts; and
- unfavorable publicity relating to the product.

If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, hospitals and clinics, healthcare payors and patients, we may not generate significant revenue from such products.

We must comply with extensive government regulations.

The research, development, manufacture labeling, storage, record-keeping, advertising, promotion, import, export, marketing and distribution of pharmaceutical products are subject to an extensive regulatory approval process by the FDA in the U.S. and comparable health authorities in foreign markets. The process of obtaining required regulatory approvals for drugs is lengthy, expensive and uncertain. Approval policies or regulations may change and the FDA and foreign authorities have substantial discretion in the pharmaceutical approval process, including the ability to delay, limit or deny approval of a product candidate for many reasons. Despite the time and expense invested in clinical development of product candidates, regulatory approval is never guaranteed. Regulatory approval may entail limitations on the indicated usage of a drug, which may reduce the drug s market potential. Even if regulatory clearance is obtained, post-market evaluation of the products, if required, could result in restrictions on a product s marketing or withdrawal of the product from the market, as well as possible civil and criminal sanctions. Of the large number of drugs in development, only a small percentage successfully complete the regulatory approval process and are commercialized.

We are dependent upon key collaborative relationships and license agreements.

We will rely significantly on the resources of third parties to market and commercialize Probuphine, if approved, as well as any other products we may develop. For example, our ability to ultimately derive revenues from Probuphine in the Territory is dependent upon Braeburn implementing a successful marketing program for the treatment of opioid dependence in adults and pursuing development and commercialization of the product for other indications. Beyond any contractual rights, we cannot control the amount or timing of resources that any

existing or future corporate partner devotes to product development and commercialization efforts for our product candidates. We depend on our ability to maintain existing collaborative relationships, to develop new collaborative relationships with third parties and potentially to acquire or in-license additional products and technologies for the development of new product candidates.

Our dependence on third party collaborators and license agreements subjects us to a number of risks, including:

- our collaborators may not comply with applicable regulatory guidelines with respect to developing or commercializing our products, which could adversely impact sales or future development of our products;
- we and our collaborators could disagree as to future development plans and our collaborators may delay, fail to commence or stop future clinical trials or other development; and
- there may be disputes between us and our collaborators, including disagreements regarding the license agreements, that may result in the delay of or failure to achieve developmental, regulatory and commercial objectives that would result in milestone or royalty payments and/or the delay or termination of any future development or commercialization of our products.

In addition, collaborators may, to the extent permitted by our agreements, develop products that divert resources from our products, preclude us from entering into collaborations with their competitors or terminate their agreements with us prematurely. Moreover, disagreements could arise with our collaborators or strategic partners over rights to our intellectual property and our rights to share in any of the future revenues from products or technologies resulting from use of our technologies, or our activities in separate fields may conflict with other business plans of our collaborators.

We face risks associated with third parties conducting preclinical studies and clinical trials of our products; as well as our dependence on third parties to manufacture any products that we may successfully develop.

We depend on third-party laboratories and medical institutions to conduct preclinical studies and clinical trials for our products and other third-party organizations to perform data collection and analysis, all of which must maintain both good laboratory and good clinical practices. We also depend upon third party manufacturers for the production of any products we may successfully develop to comply with current Good Manufacturing Practices of the FDA, which are similarly outside our direct control. If third party laboratories and medical institutions conducting studies of our products fail to maintain both good laboratory and clinical practices, the studies could be delayed or have to be repeated. Similarly, if the manufacturers of any products we develop in the future fail to comply with current Good Manufacturing Practices of the FDA, we may be forced to cease manufacturing such product until we have found another third party to manufacture the product.

We face risks associated with product liability lawsuits that could be brought against us.

Our liability insurance coverage may not be sufficient to cover claims that may be made against us in the event that the use or misuse of our product candidates causes, or merely appears to have caused, personal injury or death. Any claims against us, regardless of their merit, could severely harm our financial condition, strain our management and other resources or destroy the prospects for commercialization of the product which is the subject of any such claim.

We may be unable to protect our patents and proprietary rights.

Our future success will depend to a significant extent on our ability to:

- obtain and keep patent protection for our products and technologies on an international basis;
- enforce our patents to prevent others from using our inventions;

maintain and prevent others from using our trade secrets; and

operate and commercialize products without infringing on the patents or proprietary rights of others.

We cannot assure you that our patent rights will afford any competitive advantages, and these rights may be challenged or circumvented by third parties. Further, patents may not be issued on any of our pending patent applications in the U.S. or abroad. Because of the extensive time required for development, testing and regulatory review of a potential product, it is possible that before a potential product can be commercialized, any related patent may expire or remain in existence for only a short period following commercialization, reducing or eliminating any advantage of the patent. If we sue others for infringing our patents, a court may determine that such patents are invalid or unenforceable. Even if the validity of our patent rights is upheld by a court, a court may not prevent the alleged infringement of our patent rights on the grounds that such activity is not covered by our patent claims.

In addition, third parties may sue us for infringing their patents. In the event of a successful claim of infringement against us, we may be required to:

pay substantial damages;

stop using our technologies and methods;

stop certain research and development efforts;

develop non-infringing products or methods; and

obtain one or more licenses from third parties.

If required, we cannot assure you that we will be able to obtain such licenses on acceptable terms, or at all. If we are sued for infringement, we could encounter substantial delays in development, manufacture and commercialization of our product candidates. Any litigation, whether to enforce our patent rights or to defend against allegations that we infringe third party rights, will be costly, time consuming, and may distract management from other important tasks.

We also rely in our business on trade secrets, know-how and other proprietary information. We seek to protect this information, in part, through the use of confidentiality agreements with employees, consultants, advisors and others. Nonetheless, we cannot assure you that those agreements will provide adequate protection for our trade secrets, know-how or other proprietary information and prevent their unauthorized use or disclosure. To the extent that consultants, key employees or other third parties apply technological information independently developed by them or by others to our proposed products, disputes may arise as to the proprietary rights to such information, which may not be resolved in our favor.

We face intense competition.

Competition in the pharmaceutical and biotechnology industries is intense. We face, and will continue to face, competition from numerous companies that currently market, or are developing, products for the treatment of the diseases and disorders we have targeted. Many of these entities have significantly greater research and development capabilities, experience in obtaining regulatory approvals and manufacturing, marketing, financial and managerial resources than we have. We also compete with universities and other research institutions in the development of products, technologies and processes, as well as the recruitment of highly qualified personnel. Our competitors may succeed in developing technologies or products that are more effective than the ones we have under development or that render our proposed products or technologies noncompetitive or obsolete. In addition, our competitors may achieve product commercialization or patent protection earlier than we will.

Healthcare reform and restrictions on reimbursements may limit our financial returns.

Braeburn s ability to commercialize Probuphine in the Territory and our ability or the ability of any future collaborators to commercialize Probuphine outside the Territory or to commercialize any other products we may

successfully develop will depend in part on the extent to which government health administration authorities, private health insurers and other organizations will reimburse consumers for the cost of these products. These third parties are increasingly challenging both the need for and the price of new drug products. Significant uncertainty exists as to the reimbursement status of newly approved therapeutics. Adequate third party reimbursement may not be available for our own or our collaborator s drug products to enable us or them to maintain price levels sufficient to realize an appropriate return on their and our investments in research and product development.

We may not be able to retain our key management and scientific personnel.

As a company with a limited number of personnel, we are highly dependent on the services of our executive management and scientific staff, in particular Sunil Bhonsle and Marc Rubin, our President and Executive Chairman, respectively, and our Executive Vice President and Chief Development Officer, all of whom are parties to employment agreements with us. The loss of one or more of such individuals could substantially impair ongoing research and development programs and could hinder our ability to obtain corporate partners. Our success depends in large part upon our ability to attract and retain highly qualified personnel. We compete in our hiring efforts with other pharmaceutical and biotechnology companies, as well as universities and nonprofit research organizations, and we may not be successful in our efforts to attract and retain personnel.

Our stock price has been and will likely continue to be volatile.

Our stock price has experienced substantial fluctuations and could continue to fluctuate significantly due to a number of factors, including:

- variations in our anticipated or actual operating results or prospects;
- sales of substantial amounts of our common stock;
- announcements about us or about our competitors, including introductions of new products;
- litigation and other developments relating to our patents or other proprietary rights or those of our competitors;
- conditions in the pharmaceutical or biotechnology industries;
- governmental regulation and legislation; and
- change in securities analysts estimates of our performance, or our failure to meet analysts expectations.

Our common stock is deemed to be a penny stock, which may make it more difficult for investors to sell their shares due to suitability requirements.

Our common stock is subject to Rule 15g-1 through 15g-9 under the Securities Exchange Act of 1934, as amended (the Exchange Act), which imposes certain sales practice requirements on broker-dealers which sell our common stock to persons other than established customers and accredited investors (generally, individuals with a net worth in excess of $1,000,000 or annual incomes exceeding $200,000 (or $300,000 together with their spouses)). For transactions covered by this rule, a broker-dealer must make a special suitability determination for the purchaser and have received the purchaser s written consent to the transaction prior to the sale. This rule adversely affects the ability of broker-dealers to sell our common stock and the ability of our stockholders to sell their shares of common stock.

Additionally, our common stock is subject to the SEC regulations for penny stock. Penny stock includes any equity security that is not listed on a national exchange and has a market price of less than $5.00 per share, subject to certain exceptions. The regulations require that prior to any non-exempt buy/sell transaction in a penny stock, a disclosure schedule set forth by the SEC relating to the penny stock market must be delivered to the

16

purchaser of such penny stock. This disclosure must include the amount of commissions payable to both the broker-dealer and the registered representative and current price quotations for the common stock. The regulations also require that monthly statements be sent to holders of penny stock that disclose recent price information for the penny stock and information of the limited market for penny stocks. These requirements adversely affect the market liquidity of our common stock.

Our net operating losses and research and development tax credits may not be available to reduce future federal and state income tax payments.

At December 31, 2012, we had federal net operating loss and tax credit carryforwards of $215.7 million and $7.6 million, respectively, and state net operating loss and tax credit carryforwards of $146.7 million and $7.8 million, respectively, available to offset future taxable income, if any. Current federal and state tax laws include substantial restrictions on the utilization of net operating loss and tax credits in the event of an ownership change and we cannot assure you that our net operating loss and tax carryforwards will continue to be available.

Item 2. Properties

Our executive offices are located in approximately 9,255 square feet of office space in South San Francisco, California that we occupy under a three-year operating lease expiring in June 2013. It is our intention to renew this lease for a multi-year period prior to June 2013, and continue to be based in South San Francisco.

Item 3. Legal Proceedings

We are currently not a party to any material legal or administrative proceedings and are not aware of any pending or threatened legal or administrative proceedings against us.

PART II

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

(a) Price Range of Securities

Since June 2, 2010, our common stock has been quoted on the OTC Bulletin Board under the symbol TTNP.OB. The following table sets forth, for the periods indicated, the high and low sales prices per share of our common stock as reported by the OTC Bulletin Board. The quotations reflect inter-dealer prices without retail markups, markdowns, or commissions and may not represent actual transactions. For current price information, stockholders are urged to consult publicly available sources.

	High	Low
Fiscal 2012		
Fourth Quarter	$ 1.23	$ 0.76
Third Quarter	$ 1.05	$ 0.65
Second Quarter	$ 1.13	$ 0.65
First Quarter	$ 1.40	$ 1.05
Fiscal 2011		
Fourth Quarter	$ 1.78	$ 1.06
Third Quarter	$ 2.08	$ 1.30
Second Quarter	$ 2.22	$ 1.30
First Quarter	$ 1.81	$ 1.17

(b) Approximate Number of Equity Security Holders

As of March 15, 2013, there were approximately 141 record holders of our common stock.

(c) Dividends

We have never paid a cash dividend on our common stock and anticipate that for the foreseeable future any earnings will be retained for use in our business and, accordingly, do not anticipate the payment of cash dividends.

Performance Graph

The information contained in the Performance Graph shall not be deemed to be soliciting material or filed with the SEC or subject to the liabilities of Section 18 of the Securities Exchange Act of 1934, as amended (the Exchange Act), except to the extent that we specifically incorporate it by reference into a document filed under the Securities Act of 1933, as amended (the Securities Act), or the Exchange Act.

The following graph compares the cumulative total stockholder return on our common stock with the cumulative total stockholder return of (i) the NYSE MKT Index, and (ii) a peer group index consisting of companies reporting under the Standard Industrial Classification Code 2834 (Pharmaceutical Preparations). The graph assumes $100 invested on December 31, 2007 and assumes dividends reinvested. Measurement points are at the last trading day of the fiscal years ended December 31, 2008, 2009, 2010, 2011 and 2012. The stock price performance on the following graph is not necessarily indicative of future stock price performance.

COMPARE CUMULATIVE TOTAL RETURN

AMONG TITAN PHARMACEUTICALS, INC., NYSE MKT INDEX AND

SIC CODE INDEX

Item 6. Selected Financial Data.

The selected financial data presented below summarizes certain financial data which has been derived from and should be read in conjunction with our consolidated financial statements and notes thereto included in the section beginning on page F-1. See also Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations.

	Years Ended December 31,				
	2012	2011	2010	2009	2008
	(in thousands, except per share data)				
Statement of Operations Data:					
Total revenue	$ 7,117	$ 4,068	$ 10,093	$ 79	$ 73
Operating expenses:					
Research and development	10,610	11,206	12,855	2,456	16,235
General and administrative	4,877	3,368	3,263	3,438	9,756
Other income (expense), net	(6,810)	(4,697)	(809)	(71)	484
Net loss	(15,180)	(15,203)	(6,834)	(5,886)	(25,434)
Gain on retirement of preferred stock upon dissolution of subsidiary			1,241		
Net loss applicable to common stockholders	$ (15,180)	$ (15,203)	$ (5,593)	$ (5,886)	$ (25,434)
Basic and diluted net loss per common share	$ (0.23)	$ (0.26)	$ (0.09)	$ (0.10)	$ (0.44)
Shares used in computing:					
Basic and diluted net loss per common share	66,509	59,324	59,248	58,473	58,285

	As of December 31,				
	2012	2011	2010	2009	2008
	(in thousands)				
Balance Sheet Data:					
Cash	$ 18,102	$ 5,406	$ 3,180	$ 3,300	$ 4,672
Working capital (deficit)	2,042	4,839	(706)	2,069	2,759
Total assets	24,827	10,217	4,752	3,726	5,668
Total stockholders (deficit) equity	(23,128)	(20,079)	(6,053)	(1,448)	1,793

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

Forward-Looking Statements

Statements in the following discussion and throughout this report that are not historical in nature are forward-looking statements within the meaning of Section 27A of the Securities Act and Section 21E of the Exchange Act. You can identify forward-looking statements by the use of words such as expect, anticipate, estimate, may, will, should, intend, believe, and similar expressions. Although we believe the expe reflected in these forward-looking statements are reasonable, such statements are inherently subject to risk and we can give no assurances that our expectations will prove to be correct. Actual results could differ from those described in this report because of numerous factors, many of which are beyond our control. These factors include, without limitation, those described under Item 1A Risk Factors. We undertake no obligation to update these forward-looking statements to reflect events or circumstances after the date of this report or to reflect actual outcomes. Please see Note Regarding Forward-Looking Statements at the beginning of this Annual Report on Form 10-K.

The following discussion of our financial condition and results of operations should be read in conjunction with our consolidated financial statements and the related notes thereto and other financial information appearing elsewhere in this Annual Report on Form 10-K.

Overview

We are a biopharmaceutical company developing proprietary therapeutics for the treatment of serious medical disorders. Our product development programs focus primarily on important pharmaceutical markets with significant unmet medical needs and commercial potential. We are directly developing our product candidates and also utilize corporate, academic and government partnerships as appropriate. Such collaborations have helped to fund product development and have enabled us to retain significant economic interest in our products.

Our principal asset is Probuphine®, the first slow release implant formulation of buprenorphine, designed to maintain a stable, around the clock blood level of the medicine in patients for six months following a single treatment. The clinical and manufacturing development of Probuphine for the treatment of opioid dependence in adult patients is complete. The NDA seeking approval for treatment of opioid dependence has been accepted by the FDA for a Priority Review. Priority Review designation is given to therapies that offer potential major advances in treatment, including improved safety, or provide a treatment where no adequate therapy exists. Based upon the PDUFA, the FDA has set a target date of April 30, 2013 for FDA action on the NDA. An FDA advisory committee review has been scheduled for March 21, 2013.

In December 2012, we entered into a license agreement with Braeburn that grants Braeburn exclusive commercialization rights to Probuphine® in the United States and Canada. We received a non-refundable up-front license fee of $15.75 million (approximately $15.0 million, net of expenses) and will receive a $50 million milestone payment upon the approval of the NDA by the FDA. Additionally, we will be eligible to receive up to $130 million upon achievement of specified sales milestones and up to $35 million in regulatory milestones in the event of future NDA submissions and approvals for additional indications, including chronic pain. We will receive tiered royalties on net sales of Probuphine ranging from the mid-teens to the low twenties. In addition to the potential milestone payments, Apple Tree Partners IV, Braeburn s parent company, has allocated in excess of $75 million to launch, commercialize and continue the development of Probuphine.

Probuphine is the first product to utilize ProNeura , our novel, proprietary, continuous drug delivery technology. Our ProNeura technology has the potential to be used in developing products for the treatment of other chronic conditions, such as Parkinson s disease, where maintaining stable, around the clock blood levels of a drug can benefit the patient and improve medical outcomes.

Under a sublicense agreement with Novartis, we are entitled to royalty revenue of 8-10% of net sales of Fanapt® (iloperidone), an atypical antipsychotic compound being marketed in the U.S. by Novartis for the

treatment of schizophrenia, based on a licensed U.S. patent that expires in October 2016 (excluding the potential of a six month pediatric extension). We have entered into several agreements with Deerfield, a healthcare investment fund, which entitle Deerfield to most of the future royalty revenues related to Fanapt in exchange for cash and debt considerations, the proceeds from which we have been using to advance the development of Probuphine and for general corporate purposes. We have retained a portion of the royalty revenue from the net sales of Fanapt in excess of specified annual threshold levels; however, based on sales levels to date, it is unlikely that we will receive any revenue from Fanapt in the next several years, if ever.

Critical Accounting Policies and the Use of Estimates

The preparation of our financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in our consolidated financial statements and accompanying notes. Actual results could differ materially from those estimates. We believe the following accounting policies for the years ended December 31, 2012 and 2011 to be applicable:

Revenue Recognition

We generate revenue principally from royalty payments, collaborative research and development arrangements, technology licenses, and government grants. Consideration received for revenue arrangements with multiple components is allocated among the separate units of accounting based on their respective selling prices. The selling price for each unit is based on vendor-specific objective evidence, or VSOE, if available, third party evidence if VSOE is not available, or estimated selling price if neither VSOE nor third party evidence is available. The applicable revenue recognition criteria are then applied to each of the units.

Revenue is recognized when the four basic criteria of revenue recognition are met: (1) a contractual agreement exists; (2) transfer of technology has been completed or services have been rendered; (3) the fee is fixed or determinable; and (4) collectibility is reasonably assured. For each source of revenue, we comply with the above revenue recognition criteria in the following manner:

Royalties earned are based on third-party sales of licensed products and are recorded in accordance with contract terms when third-party results are reliably measurable and collectibility is reasonably assured. Pursuant to certain license agreements, we earn royalties on the sale of Fanapt by Novartis in the U.S. As described in Note 8, Royalty Liability, we are obligated to pay royalties on such sales to Sanofi-Aventis and Deerfield. As we have no performance obligations under the license agreements, we have recorded the royalties earned, net of royalties we are obligated to pay, as revenue in our Consolidated Statement of Operations.

Collaborative arrangements typically consist of non-refundable and/or exclusive technology access fees, cost reimbursements for specific research and development spending, and various milestone and future product royalty payments. If the delivered technology does not have stand-alone value or if we do not have objective or reliable evidence of the fair value of the undelivered component, the amount of revenue allocable to the delivered technology is deferred. Non-refundable upfront fees with stand-alone value that are not dependent on future performance under these agreements are recognized as revenue when received, and are deferred if we have continuing performance obligations and have no evidence of fair value of those obligations. Cost reimbursements for research and development spending are recognized when the related costs are incurred and when collections are reasonably expected. Payments received related to substantive, performance-based at-risk milestones are recognized as revenue upon achievement of the clinical success or regulatory event specified in the underlying contracts, which represent the culmination of the earnings process. Amounts received in advance are recorded as deferred revenue until the technology is transferred, costs are incurred, or a milestone is reached.

Technology license agreements typically consist of non-refundable upfront license fees, annual minimum access fees or royalty payments. Non-refundable upfront license fees and annual minimum payments received with separable stand-alone values are recognized when the technology is transferred or accessed, provided that the technology transferred or accessed is not dependent on the outcome of our continuing research and development efforts.

Government grants, which support our research efforts in specific projects, generally provide for reimbursement of approved costs as defined in the notices of grants. Grant revenue is recognized when associated project costs are incurred.

Share-Based Payments

We recognize compensation expense for all share-based awards made to employees and directors. The fair value of share-based awards is estimated at the grant date based on the fair value of the award and is recognized as expense, net of estimated pre-vesting forfeitures, ratably over the vesting period of the award. We use the Black-Scholes option pricing model to estimate the fair value method of our awards. Calculating stock-based compensation expense requires the input of highly subjective assumptions, including the expected term of the share-based awards, stock price volatility, and pre-vesting forfeitures. We estimate the expected term of stock options granted for the years ended December 31, 2012, 2011 and 2010 based on the historical experience of similar awards, giving consideration to the contractual terms of the share-based awards, vesting schedules and the expectations of future employee behavior. We estimate the volatility of our common stock at the date of grant based on the historical volatility of our common stock. The assumptions used in calculating the fair value of stock-based awards represent our best estimates, but these estimates involve inherent uncertainties and the application of management judgment. As a result, if factors change and we use different assumptions, our stock-based compensation expense could be materially different in the future. In addition, we are required to estimate the expected pre-vesting forfeiture rate and only recognize expense for those shares expected to vest. We estimate the pre-vesting forfeiture rate based on historical experience. If our actual forfeiture rate is materially different from our estimate, our stock-based compensation expense could be significantly different from what we have recorded in the current period.

Income Taxes

We make certain estimates and judgments in determining income tax expense for financial statement purposes. These estimates and judgments occur in the calculation of certain tax assets and liabilities, which arise from differences in the timing of recognition of revenue and expense for tax and financial statement purposes.

As part of the process of preparing our consolidated financial statements, we are required to estimate our income taxes in each of the jurisdictions in which we operate. This process involves us estimating our current tax exposure under the most recent tax laws and assessing temporary differences resulting from differing treatment of items for tax and accounting purposes.

We assess the likelihood that we will be able to recover our deferred tax assets. We consider all available evidence, both positive and negative, expectations and risks associated with estimates of future taxable income and ongoing prudent and feasible tax planning strategies in assessing the need for a valuation allowance. If it is not more likely than not that we will recover our deferred tax assets, we will increase our provision for taxes by recording a valuation allowance against the deferred tax assets that we estimate will not ultimately be recoverable.

Clinical Trial Accrual

We also record accruals for estimated ongoing clinical trial costs. Clinical trial costs represent costs incurred by clinical research organizations, (CROs), and clinical sites. These costs are recorded as a component of research and development expenses. Under our agreements, progress payments are typically made to

investigators, clinical sites and CROs. We analyze the progress of the clinical trials, including levels of patient enrollment, invoices received and contracted costs when evaluating the adequacy of accrued liabilities. Significant judgments and estimates must be made and used in determining the accrued balance in any accounting period. Actual results could differ from those estimates under different assumptions. Revisions are charged to expense in the period in which the facts that give rise to the revision become known. The actual clinical trial costs for the Probuphine studies conducted in the past three years have not differed materially from the estimated projection of expenses.

Warrants Issued in Connection with Equity Financing

We generally account for warrants issued in connection with equity financings as a component of equity, unless there is a deemed possibility that we may have to settle warrants in cash. For warrants issued with deemed possibility of cash settlement, we record the fair value of the issued warrants as a liability at each reporting period and record changes in the estimated fair value as a non-cash gain or loss in the Condensed Consolidated Statements of Operations and Comprehensive Loss.

Liquidity and Capital Resources

	2012	2011	2010
		(in thousands)	
As of December 31:			
Cash	$ 18,102	$ 5,406	$ 3,180
Working capital	$ 2,042	$ 4,839	$ (706)
Current ratio	1.1:1	1.9:1	0.9:1
Years Ended December 31:			
Cash (used in) provided by operating activities	$ 1,830	$ (14,476)	$ (4,657)
Cash used in investing activities	$ (1,154)	$ (234)	$ (28)
Cash provided by financing activities	$ 12,020	$ 16,936	$ 4,565

We have funded our operations since inception primarily through sales of our debt and equity securities, as well as with proceeds from warrant and option exercises, corporate licensing and collaborative agreements, and government-sponsored research. At December 31, 2012, we had approximately $18.1 million of cash compared to approximately $5.4 million at December 31, 2011.

Our operating activities provided approximately $1.8 million during the year ended December 31, 2012. This consisted primarily of the net loss for the period of approximately $15.2 million, approximately $0.3 million related to the non-cash interest expense on our royalty liability and approximately $1.4 million related to net changes in operating assets and liabilities. This was offset in part by approximately $14.4 million related to deferred revenue in connection with the license agreement with Braeburn, approximately $1.8 million related to net non-cash losses on changes in the fair value of warrants, non-cash charges of approximately $17,000 related to depreciation, and approximately $2.6 million related to stock-based compensation expenses. Uses of cash in operating activities were primarily to fund product development programs and administrative expenses. The license agreement with Sanofi-Aventis require us to pay royalties on future product sales. In addition, in order to maintain license and other rights while products are under development, we must comply with customary licensee obligations, including the payment of patent-related costs, annual minimum license fees, meeting project-funding milestones and diligent efforts in product development. The aggregate commitments we have under these agreements, including minimum license payments, for the next 12 months is approximately $3,000. See Item 1. Business License Agreements.

Net cash used in investing activities of approximately $1.2 million during the year ended December 31, 2012 primarily related to purchases of equipment.

Net cash provided by financing activities of approximately $12.0 million during the year ended December 31, 2012 consisted of approximately $7.5 million of net proceeds from the sale of common stock and warrants, net of issuance costs and $4.9 million of net proceeds from the exercise of warrants to purchase common stock. This was offset in part by payments of approximately $0.4 million related to payments on our long-term debt.

On March 15, 2011, we entered into several agreements with entities affiliated with Deerfield pursuant to which Deerfield agreed to provide $20.0 million in funding to us. Funding occurred on April 5, 2011. Pursuant to the terms of a facility agreement, we issued Deerfield 8.5% promissory notes in the aggregate principal amount of $20.0 million. We paid Deerfield a facility fee of $0.5 million and issued them warrants to purchase 6,000,000 shares of our common stock (the Deerfield Warrants). Deerfield has the right to have the long-term debt repaid at 110% of the principal amount in the event we complete a major transaction, which includes, but is not limited to, a merger or sale of our company or the sale of Fanapt or Probuphine. Under a royalty agreement, in exchange for $3.0 million that was recorded as royalty liability, we agreed to pay Deerfield 2.5% of the aggregate royalties on net sales of Fanapt, subsequent to the funding date, constituting a portion of the royalty revenue we receive from Novartis. The agreements with Deerfield also provide us with the option to repurchase the royalty rights for $40.0 million.

On April 5, 2011, we used approximately $7.6 million of proceeds from the Deerfield funding to repay Oxford Financing Corporation in full, including required final payments aggregating $480,000.

On November 14, 2011, we entered into several agreements with Deerfield pursuant to which we agreed to pay them a substantial portion of the remaining future royalties on the sales of Fanapt in exchange for $5.0 million in cash that was recorded as royalty liability, a $10.0 million reduction in the principal amount owed to Deerfield under the existing facility agreement and a revised principal repayment schedule of $2.5 million per year for four years commencing in April 2013 to retire the remaining long-term debt of $10.0 million. Deerfield is entitled to the balance of our portion of the royalties on Fanapt (5.5% to 7.5% of net sales, net of the 2.5% we previously agreed to pay to Deerfield) up to specified threshold levels of net sales of Fanapt and 40% of the royalties above the threshold level. We retain 60% of the royalties on net sales of Fanapt above the threshold levels, subject to an agreement that half of any such retained royalties will go towards repayment of our outstanding debt to Deerfield. Funding of the transaction took place on November 25, 2011.

In February 2013, we amended the terms of the Deerfield Warrants, which are currently exercisable at $1.25 per share, to permit payment of the exercise price through the reduction of the outstanding loan. In February and March 2013, Deerfield exercised an aggregate of 6,000,000 warrants resulting in a reduction of our outstanding indebtedness to Deerfield of $7.5 million and, accordingly, the Deerfield debt will be fully repaid upon payment of $2.5 million in April 2013.

On April 9, 2012, we entered into subscription agreements with certain institutional investors for the purchase and sale, in a registered direct offering, of (i) 6,517,648 shares of our common stock (the Shares), (ii) six-year warrants to purchase 6,517,648 shares of common stock (the Series A Warrants) and (iii) six-month warrants to purchase 6,517,648 shares of common stock (the Series B Warrants and, together with the Series A Warrants, the Warrants) for gross proceeds of $5,540,000. The closing of the sale of the Shares and Warrants occurred on April 13, 2012 and April 18, 2012. Net proceeds were approximately $5.0 million. Prior to their expiration, Series B Warrants to purchase 5,761,765 shares of our common stock were exercised resulting in gross proceeds to us of approximately $4.9 million.

On September 12, 2012, we entered into a stock purchase and option agreement with an affiliate of Braeburn pursuant to which we sold 3,400,000 shares of our common stock for an aggregate purchase price of $4.25 million, or $1.25 per share, and agreed to an exclusive option period for execution of the proposed license agreement.

On December 13, 2012, we entered into a license agreement with Braeburn pursuant to which we granted Braeburn an exclusive right and license to commercialize Probuphine® in the Territory. We will retain all of the rights to Probuphine® outside the Territory. In consideration of the rights granted to Braeburn under the license agreement, Braeburn paid to us an upfront, non-refundable license fee of $15.75 million (approximately $15.0 million, net of expenses). Upon FDA approval of the NDA for Probuphine®, Braeburn will be required to make a $50 million milestone payment to us and ownership of the NDA will transfer to Braeburn. We are also eligible to receive up to an additional $130 million upon the achievement of specified sales milestones and up to $35 million in regulatory milestones. Braeburn will also pay us tiered royalties ranging from the mid-teens to the low twenties.

We believe that our working capital at December 31, 2012, together with the FDA s reimbursement of the NDA filing fee, is sufficient to fund our planned operations through June 2014. In the event that the FDA issues a complete response letter requiring us to conduct additional clinical studies that would require expenditures in excess of certain amounts specified in our agreement with Braeburn, Braeburn will have the right to either terminate the agreement or reduce the amount of the $50 million milestone payment payble to us in the event the FDA ultimately approves Probuphine. If Braeburn were to terminate the agreement, we would not have sufficient funds available to us to complete the FDA approval process and commercialize Probuphine and, as a result, our business and prospects would be materially adversely impacted. Furthermore, continuation of our current Parkinson s disease development program and the initiation of any additional programs will depend upon our receipt of the $50 million milestone payment and if such payment is not received or is significantly reduced our ability to fund any new product development programs will be materially impaired and we may need to obtain additional financing, either through the sale of debt or equity securities, to continue our Probuphine program and other product development activities. If we are unable to complete a debt or equity offering, or otherwise obtain sufficient financing when and if needed, we may be required to reduce, defer or discontinue one or more of our product development activities.

The following table sets forth the aggregate contractual cash obligations as of December 31, 2012 (in thousands):

		Payments Due by Period			
Contractual obligations	**Total**	**< 1 year**	**1-3 years**	**3-5 years**	**5 years+**
Operating leases	$ 121	$ 121	$	$	$
Debt obligation(1)	11,771	3,262	5,885	2,624	
Total contractual cash obligations	$ 11,892	$ 3,383	$ 5,885	$ 2,624	$

(1) Excludes payments related to the royalty liability with Deerfield under the March 2011 and November 2011 Royalty Agreements.

Results of Operations

Year Ended December 31, 2012 Compared to Year Ended December 31, 2011

Our net loss applicable to common stockholders for 2012 was approximately $15.2 million, or approximately $0.23 per share, compared to our net loss applicable to common stockholders of approximately $15.2 million, or approximately $0.26 per share, for 2011. Our net loss for 2012 includes a non-cash loss of approximately $1.8 million resulting from increases in the fair value of warrants issued as part of the March 2011 Deerfield transaction and the April 2012 financing transaction.

We generated royalty revenues during 2012 of approximately $4.8 million compared to approximately $3.6 million during 2011. We generated grant revenues during 2012 of approximately $42,000 compared to approximately $0.5 million during 2011. We generated licensing revenues of approximately $2.3 million during 2012. The licensing revenue consisted of approximately $1.7 million related to the premium paid on our common

stock as part of the September 2012 stock purchase and option agreement with an affiliate of Braeburn and approximately $0.6 million related to the amortization of the non-refundable up-front license fee of $15.75 million (approximately $15.0 million, net of expenses) related to our licensing agreement with Braeburn. There were no revenues from licensing agreements in 2011. Royalty revenues during 2012 and 2011 consisted of royalties on sales of Fanapt. Grant revenues during 2012 and 2011 consisted of proceeds from NIH grants related to our Probuphine and ProNeura related programs.

Research and development expenses for 2012 were approximately $10.6 million compared to approximately $11.2 million in 2011, a decrease of approximately $0.6 million, or 5%. The decrease in research and development costs was primarily associated with a decrease in external research and development expenses related to the Phase 3 clinical trials of our Probuphine product which were completed in 2011. This was offset by expenses related to the preparation and submission of an NDA for a Probuphine product with the FDA in October 2012. External research and development expenses include direct expenses such as clinical research organization charges, investigator and review board fees, patient expense reimbursements and contract manufacturing expenses. During 2012, our external research and development expenses relating to our Probuphine product development program were approximately $5.4 million compared to approximately $7.7 million for 2011. Other research and development expenses include internal operating costs such as clinical research and development personnel-related expenses, clinical trials-related travel expenses, and allocation of facility and corporate costs. As a result of the risks and uncertainties inherently associated with pharmaceutical research and development activities described elsewhere in this report, we are unable to estimate the specific timing and future costs of our clinical development programs or the timing of material cash inflows, if any, from our products or product candidates.

General and administrative expenses for 2012 were approximately $4.9 million, compared to approximately $3.4 million in 2011, an increase of approximately $1.5 million, or 44%. The increase in general and administrative expenses was primarily related to increases in non-cash stock compensation costs of approximately $0.8 million, employee-related costs of approximately $0.3 million, consulting and professional fees of approximately $0.3 million, fees paid to members of our board of Directors of approximately $0.1 million and facilities-related costs of approximately $0.1 million. This was offset in part by decreases in travel-related costs of approximately $0.1 million.

Net other expense for 2012 was approximately $6.8 million, compared to approximately $4.7 million in 2011. The increase in net other expense during 2012 was primarily related to interest expense, net of approximately $4.9 million on the Deerfield long-term debt and a $1.8 million non-cash loss related to increases in the fair value of the warrants issued to Deerfield and the warrants issued as part of the April 2012 financing transaction.

Year Ended December 31, 2011 Compared to Year Ended December 31, 2010

Our net loss applicable to common stockholders for 2011 was approximately $15.2 million, or approximately $0.26 per share, compared to our net loss applicable to common stockholders of approximately $5.6 million, or approximately $0.09 per share, for 2010. Our net loss for 2011 includes a non-cash gain of $1.9 million resulting from changes in the fair value of warrants issued as part of the March 2011 Deerfield transaction.

We generated royalty revenues during 2011 of approximately $3.6 million compared to approximately $2.5 million during 2010. We generated grant revenues during 2011 of approximately $0.5 million compared to approximately $7.6 million during 2010. We generated no revenues from licensing agreements in 2011 compared to approximately $24,000 during 2010. Royalty revenues during 2011 and 2010 consisted of royalties on sales of Fanapt. Grant revenues during 2011 and 2010 consisted of proceeds from the NIH grants related to our Probuphine and ProNeura related programs.

Research and development expenses for 2011 were approximately $11.2 million compared to approximately $12.9 million in 2010, a decrease of approximately $1.7 million, or 13%. The decrease in research and development costs was primarily associated with a decrease in external research and development expenses related to the Phase 3 clinical trials of our Probuphine product which were completed in 2011. External research and development expenses include direct expenses such as clinical research organization charges, investigator and review board fees, patient expense reimbursements and contract manufacturing expenses. During 2011, our external research and development expenses relating to our Probuphine product development program were approximately $7.7 million compared to approximately $10.1 million for 2010. Other research and development expenses include internal operating costs such as clinical research and development personnel-related expenses, clinical trials-related travel expenses, and allocation of facility and corporate costs. As a result of the risks and uncertainties inherently associated with pharmaceutical research and development activities described elsewhere in this report, we are unable to estimate the specific timing and future costs of our clinical development programs or the timing of material cash inflows, if any, from our products or product candidates.

General and administrative expenses for 2011 were approximately $3.4 million, compared to approximately $3.3 million in 2010, an increase of approximately $0.1 million, or 3%. The increase in general and administrative expenses was primarily related to increases in non-cash stock compensation costs of approximately $0.3 million, employee-related costs of approximately $0.3 million, marketing-related costs of approximately $0.2 million . This was offset in part by decreases in legal fees of approximately $0.3 million, consulting and professional fees of approximately $0.3 million, and facilities-related costs of $0.1 million.

Net other expense for 2011 was approximately $4.7 million, compared to approximately $0.8 million in 2010. The increase in net other expense during 2011 was primarily related to interest expense of approximately $6.2 million on the Deerfield long-term debt and $0.2 million of interest expense related to the Oxford loans. This was offset in part by a $1.9 million non-cash gain related to decreases in the fair value of the Deerfield warrants.

Year Ended December 31, 2010 Compared to Year Ended December 31, 2009

Our net loss applicable to common stockholders for 2010 was approximately $5.6 million, or approximately $0.09 per share, compared to our net loss applicable to common stockholders of approximately $5.9 million, or approximately $0.10 per share, for 2009. Our net loss for 2010 includes a non-cash gain of $1.2 million resulting from the retirement of preferred stock upon dissolution of Ingenex, Inc., our majority-owned subsidiary.

We generated royalty revenues during 2010 of approximately $2.5 million. We had no royalty revenue during 2009. We generated grant revenues during 2010 of approximately $7.6 million. We had no grant revenue during 2009. We generated revenues of $24,000 from licensing agreements in 2010 compared to approximately $79,000 during 2009. Royalty revenues during 2010 consisted of royalties on sales of Fanapt. Grant revenues during 2010 consisted of proceeds from the NIH grants related to our Probuphine and ProNeura related programs.

Research and development expenses for 2010 were approximately $12.9 million compared to approximately $2.5 million in 2009, an increase of approximately $10.4 million, or 416%. The increase in research and development costs was primarily associated with an increase in external research and development expenses related to the initiation and ongoing expenses of the Phase 3 clinical trials related to our Probuphine product. External research and development expenses include direct expenses such as clinical research organization charges, investigator and review board fees, patient expense reimbursements and contract manufacturing expenses. During 2010, our external research and development expenses relating to our Probuphine product development program were approximately $10.1 million compared to approximately $0.7 million for 2009. Other research and development expenses include internal operating costs such as clinical research and development personnel-related expenses, clinical trials-related travel expenses, and allocation of facility and corporate costs. As a result of the risks and uncertainties inherently associated with pharmaceutical research and development

activities described elsewhere in this report, we are unable to estimate the specific timing and future costs of our clinical development programs or the timing of material cash inflows, if any, from our products or product candidates.

General and administrative expenses for 2010 were approximately $3.3 million, compared to approximately $3.4 million in 2009, a decrease of approximately $0.1 million, or 3%. The decrease in general and administrative expenses was primarily related to decreases in non-cash stock compensation costs of approximately $0.7 million and facilities-related costs of $0.5 million. This was offset in part by increases in employee-related costs of approximately $0.2 million, legal fees of approximately $0.5 million, and consulting and professional fees of approximately $0.3 million.

Net other expense for 2010 was approximately $0.8 million compared to approximately $71,000 in 2009. Net other expense in 2010 consisted primarily of interest expense of approximately $0.7 million and loan fees of approximately $0.1 million resulting from our loans with Oxford and tax-related expenses of approximately $6,000. Net other expense in 2009 consisted primarily of financing-related expenses of approximately $60,000, interest expense of approximately $9,000 and tax-related expenses of approximately $10,000 offset by interest income of approximately $2,000 and net gain of approximately $6,000 resulting from the sale of certain assets.

Off-Balance Sheet Arrangements

We have never entered into any off-balance sheet financing arrangements and we have never established any special purpose entities. We have not guaranteed any debt or commitments of other entities or entered into any options on non-financial assets.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

We held no marketable securities at December 31, 2012 and 2011.

Item 8. Consolidated Financial Statements and Supplementary Data.

The response to this item is included in a separate section of this Report. See Index to Consolidated Financial Statements on Page F-1.

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

None.

Item 9A. Controls and Procedures.

(a) *Evaluation of Disclosure Controls and Procedures*: Our principal executive and financial officers reviewed and evaluated the effectiveness of our disclosure controls and procedures (as defined in Exchange Act Rule 13a-15(e)) as of the end of the period covered by this Annual Report on Form 10-K. Based on that evaluation, our principal executive and financial officers concluded that our disclosure controls and procedures are effective in timely providing them with material information relating to the Company, as required to be disclosed in the reports we file under the Exchange Act.

(b) *Management s Annual Report on Internal Control Over Financial Reporting*:

Internal control over financial reporting refers to the process designed by, or under the supervision of, our Principal Executive Officer and Principal Financial Officer, and effected by our board of directors, management and other personnel, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles, and includes those policies and procedures that:

(1) Pertain to the maintenance of records that in reasonable detail accurately and fairly reflect the transactions and dispositions of our assets;

(2) Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that our receipts and expenditures are being made only in accordance with authorization of our management and directors; and

(3) Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisitions, use or disposition of our assets that could have a material effect on the financial statements.

Internal control over financial reporting cannot provide absolute assurance of achieving financial reporting objectives because of its inherent limitations. Internal control over financial reporting is a process that involves human diligence and compliance and is subject to lapses in judgment and breakdowns resulting from human failures. Internal control over financial reporting also can be circumvented by collusion or improper management overrides. Due to such limitations, there is a risk that material misstatements may not be prevented or detected on a timely basis by internal control over financial reporting. However, these inherent limitations are known features of the financial reporting process. Therefore, it is possible to design into the process safeguards to reduce, though not eliminate, this risk. Management is responsible for establishing and maintaining adequate internal control over financial reporting for the company.

Management has used the framework set forth in the report entitled *Internal Control Integrated Framework* published by the Committee of Sponsoring Organizations of the Treadway Commission, known as COSO, to evaluate the effectiveness of the Company s internal control over financial reporting. Based on this assessment, management has concluded that our internal control over financial reporting was effective as of December 31, 2012.

The attestation report concerning the effectiveness of our internal controls over financial reporting as of December 31, 2012 issued by OUM & Co. LLP, an independent registered public accounting firm, appears in Item 8 of this Annual Report on Form 10-K.

(c) *Changes in Internal Control Over Financial Reporting*: There were no changes in our internal control over financial reporting (as defined in Rules 13(a)-15(f) and 15(d)-15(f) under the Securities Act of 1934) during our most recent fiscal quarter that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

PART III

Item 10. Directors; Executive Officers and Corporate Governance

Set forth below are the name, age and position and a brief account of the business experience of each of our executive officers and directors:

Name	Age	Office	Director Since
Marc Rubin (1)	58	Executive Chairman of the Board	November 2007
Sunil Bhonsle	63	President and Director	February 2004
Victor J. Bauer (2)(3)	77	Director	November 1997
Eurelio M. Cavalier (1)(3)(4)	80	Director	September 1998
Hubert E. Huckel (1)(2)(3)	81	Director	October 1995
M. David MacFarlane (2)(4)	72	Director	May 2002
Ley S. Smith (1)(2)(4)	78	Director	July 2000

(1) Member of Executive Committee
(2) Member of Audit Committee