

TITAN PHARMACEUTICALS INC
Form 10-12G
January 14, 2010
Table of Contents

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10

GENERAL FORM FOR REGISTRATION OF SECURITIES

Pursuant to Section 12(b) or (g) of The Securities Exchange Act of 1934

Titan Pharmaceuticals, Inc.

(Exact name of registrant as specified in its charter)

Delaware
State of other jurisdiction of

94-3171940
I.R.S. Employer

incorporation or organization

Identification No.

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

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

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

Common Stock, \$.001 par value

(Title of class)

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 12b2 of the Exchange Act.

Large accelerated filer

Accelerated filer

Non-accelerated filer (Do not check if smaller reporting company)

Smaller reporting company

Table of Contents

EXPLANATORY NOTE

Titan Pharmaceuticals, Inc. has been publicly-traded since our company's initial public offering in January 1996. In December 2008, as part of our efforts to conserve cash, we announced our decision to voluntarily delist from the NYSE Euronext (formerly the American Stock Exchange) and terminate our obligation to file reports under the Securities Exchange Act of 1934 (the Exchange Act). In light of recent favorable developments, in particular the U.S. Food and Drug Administration's approval of Fanapt and our receipt of a grant from the National Institutes for Health for our Probuphine program, our board of directors made a determination to file this registration statement on Form 10 to re-register under the Exchange Act. It is our intention to resume filing all periodic reports under the Exchange Act. In addition, we will seek to have our shares, which are currently quoted on the OTC Pink Sheets system, listed on the OTC Bulletin Board. Our board is taking these actions as part of an ongoing process to evaluate all of the strategic alternatives available to us with the goal of maximizing value for our stockholders.

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

Probuphine®, Spheramine® and ProNeura are trademarks of our company. This Form 10 also includes trade names and trademarks of companies other than Titan.

SPECIAL NOTE REGARDING FORWARD-LOOKING INFORMATION

Statements in this Form 10 or in the documents incorporated by reference herein that are not descriptions of historical facts are forward-looking statements within the meaning of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. 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 terms, and 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 those set forth under Risk Factors including, in particular, risks relating to:

the results of ongoing research and development activities;

uncertainties relating to preclinical and clinical testing, financing and strategic agreements and relationships;

the early stage of products under development;

government regulation;

patent matters; 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.

**Item 1. Business
Overview**

Edgar Filing: TITAN PHARMACEUTICALS INC - Form 10-12G

We are a biopharmaceutical company developing proprietary therapeutics primarily for the treatment of central nervous system (CNS) disorders. We currently have two key assets as described below:

Iloperidone (Fanapt): An atypical antipsychotic approved by the U.S. Food and Drug Administration (FDA) for the treatment of schizophrenia. Novartis Pharma AG (Novartis) has acquired the U.S. and Canadian rights to further develop and commercialize the approved oral formulation, and also further develop and potentially commercialize a depot formulation. Vanda Pharmaceuticals, Inc. (Vanda) has the development and commercialization rights to the oral and

Table of Contents

depot formulations of this product for the rest of the world. We are entitled to a royalty of 8-10% on worldwide net sales for several years based on the remaining life of certain patents, and we anticipate commencement of royalty revenues from sales in the United States during the first half of 2010.

Probuphine: An implant formulation of buprenorphine in Phase 3 clinical development for the treatment of opioid addiction that is capable of maintaining a stable blood level of the drug in patients for six months following a single treatment. We announced positive safety and efficacy results of this product in a placebo controlled Phase 3 study during 2008 and we have now completed approximately half of the overall clinical development program required for registration and potential approval of Probuphine. Recently we have been awarded a \$7.6 million grant from the National Institutes of Health (NIH) that will partially fund the second Phase 3 controlled safety and efficacy study required by the FDA for product registration.

In September 2008, we were notified by Bayer Schering Pharma of the termination of the license agreement for the development and commercialization of Spheramine[®], our proprietary cell therapy product in development for treating Parkinson's disease. Bayer Schering Pharma returned all rights for this product to us and, after further review and analysis of the information, we also decided to discontinue any further activities associated with this product candidate. Subsequently, we terminated our Spheramine license agreement with New York University (NYU) and returned all rights previously granted to us by NYU. Thereafter, to further conserve capital, we also terminated the license agreements for DITPA and gallium maltolate and returned all development and commercialization rights to the respective licensors, except for certain rights from the University of Iowa to potentially use gallium maltolate for the treatment of chronic bacterial infections.

Our Products

The following table provides a summary status of our products:

Product	Potential Indication(s)	Phase of Development	Marketing Rights
Iloperidone (Fanapt)	Schizophrenia, psychosis	Approved in U.S. for schizophrenia	Novartis U.S. and Canada Vanda - Rest of the world Titan
Probuphine	Opioid addiction	Phase 3	

Iloperidone (Fanapt) was approved by the FDA in May 2009 for the treatment of schizophrenia and Novartis has acquired the rights to commercialize it in the U.S. and Canada. Novartis announced that it commenced commercial launch of Fanapt in January 2010.

Probuphine is currently in Phase 3 clinical development and although it has demonstrated efficacy in one controlled Phase 3 study, additional development is necessary prior to registration and it may still not be successfully developed or commercialized. Titan has been awarded a \$7.6 million grant by the NIH in partial support of the second controlled Phase 3 study, however we will require significant further capital to support this and other clinical studies, manufacturing development, testing, and regulatory clearances prior to commercialization. We may experience unanticipated problems relating to product development and cannot predict whether we will successfully develop and commercialize any products.

Iloperidone (Fanapt)

Iloperidone (Fanapt) is our novel, proprietary product approved in the U.S. on May 6, 2009 for the treatment of adult patients with schizophrenia. The Phase 3 clinical development was conducted initially by our sub-licensee, Novartis, and completed by Novartis' sub-licensee, Vanda. In July 2008, Vanda received a non-approval letter from the FDA requesting additional information about the product. Vanda addressed the questions asked by the FDA and provided additional clarification following which the FDA granted marketing approval as noted above. The approval was supported by two placebo-controlled Phase 3 clinical studies comparing Fanapt to placebo and active control in patients with schizophrenia, as well as safety data from more than 3,000 patients. Fanapt , a mixed dopamine D2 / serotonin 5HT2A receptor antagonist belonging to the class of atypical antipsychotics, will be commercialized in the U.S. and Canada by Novartis and the development of a depot formulation will also be pursued by Novartis. Vanda has commercialization rights for the rest of the world for the oral formulation and the

Table of Contents

depot formulations, although Novartis has the first option to negotiate an agreement to co-market both these products in the rest of the world. Based on the terms of our sub-license agreement with Novartis we are entitled to royalty revenue of 8% of annual worldwide net sales up to \$200 million and 10% of annual worldwide net sales above \$200 million. We do not incur any expenses associated with this product.

Probuphine

We are developing Probuphine for the treatment of opioid addiction. Probuphine is the first product to utilize our novel, proprietary long-term drug delivery technology (See Continuous Drug Delivery Technology below). Probuphine is designed to provide continuous, long-term therapeutic levels of the drug buprenorphine, an approved agent for the treatment of opioid addiction. Probuphine has been shown to be safe and effective in the three Phase 3 studies that have been completed to date, specifically:

A six-month, double-blind, placebo-controlled safety and efficacy trial;

A six-month, open-label re-treatment safety trial; and

A pharmacokinetic safety study.

Top-line results for the first double-blind, placebo-controlled safety and efficacy study were initially released in July 2008. These data indicated that Probuphine showed a clinically and statistically significant difference over placebo by consistently meeting the primary and secondary endpoints as highlighted below:

Cumulative distribution function of % negative urines:

weeks 1-16: Probuphine>placebo; p= 0.0361 (primary endpoint)

weeks 17-24: Probuphine>placebo; p= 0.0004

weeks 1-24: Probuphine>placebo; p= 0.0117

Difference in mean % negative urines:

weeks 1-16: Probuphine>placebo; p= 0.0253

weeks 17-24: Probuphine>placebo; p= 0.0006

Treatment retention over 24 weeks: Probuphine>placebo; p< 0.0001

Patient-rated opioid withdrawal over 24 weeks: Probuphine>placebo; p= 0.0005

Edgar Filing: TITAN PHARMACEUTICALS INC - Form 10-12G

Clinician-rated opioid withdrawal over 24 weeks: Probuphine > placebo; p= 0.0008

Opioid craving 24 weeks: Probuphine > placebo; p= 0.0006

Global severity of opioid addiction:

Patient rated: Probuphine > placebo; p=0.0021

Physician rated: Probuphine > placebo; p=0.0086

Treatment with Probuphine was well tolerated in this clinical study.

The six month re-treatment study and the pharmacokinetic safety study have also provided important data on the safety of Probuphine. Data from all of these studies have been presented at the International Society of Addiction Medicine 2008 Annual Meeting in November 2008, and the American Society of Addiction Medicine 2009 Annual Meeting in May 2009.

These studies are part of a registration directed program intended to obtain marketing approval of Probuphine for the treatment of opioid addiction in Europe and the U.S. The Phase 3 program includes additional clinical studies, including a second controlled Phase 3 study which has received a \$7.6 million award from the NIH. This NIH grant will support approximately half of the expenses associated with this study and we will need additional funding to complete this clinical study and the overall development program. If adequate additional funding is available in a timely manner, the clinical study may commence patient enrollment in March/April 2010. We continue to have discussions with the FDA relating to finalizing the Probuphine clinical development program and the chemistry and manufacturing controls (CMC) which is necessary prior to any product registration.

Table of Contents

In June 2004, we announced final results from a pilot clinical study that evaluated the safety, pharmacokinetics and preliminary efficacy of Probuphine in the treatment of opioid-addicted patients. The results were presented at the Annual Meeting of the International Society of Addiction Medicine in Helsinki, and demonstrated that all 12 patients switched from daily sublingual buprenorphine therapy to Probuphine, had maintenance of therapeutic benefit for a period of six months following a single treatment of Probuphine. Treatment with Probuphine was well tolerated in this clinical study, with no significant adverse events.

Continuous Drug Delivery Technology

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 diffusion. This results in a constant 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 poses problems for many CNS and other therapeutic agents.

Our continuous drug delivery technology was developed to address the need for a simple, practical method to achieve continuous long-term drug delivery, and potentially can provide controlled drug release on an outpatient basis over extended periods of up to 6-12 months. In addition to Probuphine, which is our first product in clinical testing to utilize our proprietary continuous drug delivery technology, 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.

Sponsored Research and License Agreements

We are a party to several agreements with research institutions, companies, universities and other entities for the performance of research and development activities and for the acquisition of licenses relating to such activities. Expenses under these agreements totaled approximately \$239,000, \$378,000, and \$690,000 in the years ended December 31, 2008, 2007, and 2006, respectively.

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 in order to retain our rights, all of which have been met to date.

In November 1997, we granted a worldwide sublicense, except 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. Novartis will make our milestone and royalty payments to Sanofi-Aventis during the life of the Novartis agreement, and will also pay Titan a royalty on future net sales of the product.

In June 2004, Vanda acquired from Novartis the worldwide rights to develop and commercialize iloperidone. Under its agreement with Novartis, Vanda proceeded with and funded the iloperidone Phase III development program. All of our rights and economic interests in iloperidone, including royalties on sales of iloperidone, remained essentially unchanged under the agreement.

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 agreed to fund and continue the development of this formulation. Further, Novartis has also retained the right of first negotiation to co-market Fanapt and the depot formulation in the rest of the world. Our royalty interest in iloperidone remains unchanged, and Titan is entitled to royalty revenue of 8% of annual worldwide net sales up to \$200 million and 10% of annual worldwide net sales above \$200 million for several years based on the remaining life of certain patents. We anticipate commencement of royalty revenues from U.S. sales during the first half of 2010.

Table of Contents

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. The exclusive nature of the MIT license is subject to certain conditions regarding timely performance of product development activities. We must also satisfy certain other usual terms and conditions set forth in the MIT license in order to retain our license rights, including payments of royalties based on sales of products and processes incorporating the licensed technology, as well as a percentage of income derived from sublicenses of the licensed technology.

In August 2000, through the acquisition of GeoMed, Inc., we acquired an exclusive worldwide license to make, use and sell products developed under the patent rights to the compositions and application of gallium complexes. We subsequently acquired additional rights to gallium; however, between December 2008 and March 2009, as part of our ongoing efforts to conserve cash, we terminated all of the license agreements with the exception of an agreement we entered into in July 2005 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.

Patents and Proprietary Rights

We hold a license from Sanofi-Aventis under certain issued U.S. patents and certain foreign patents relating to iloperidone and its methods of use. Our license is exclusive for 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 2011, however it is anticipated that based on provisions of the Hatch-Waxman Act, the market exclusivity period for Fanapt will be extended by five years to 2016. The method of use patent covering the depot formulation will expire in 2020 assuming no further extensions. Prosecution of various divisional and continuation applications and their foreign counterparts continues satisfactorily, although it is uncertain whether additional patents will be granted.

We are the exclusive licensee under the MIT license to two U.S. patents relating to a long-term drug delivery system, with patent terms expiring in 2009, and certain European patents with patent terms expiring in 2008 and 2010. These dates do not include possible term extensions. Four additional 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. We have received a Notice of Allowance from the United States Patent and Trademark Office (PTO) for certain claims regarding the use of Probuphine for the treatment of opioid addiction. Further prosecution of these applications are currently proceeding at the U.S. PTO and corresponding agencies in other countries. The U.S. patent related to the use of Probuphine for the treatment of opioid addiction will provide market exclusivity up to 2023.

We are the licensee of certain issued U.S. and foreign patents and patent applications relating to methods of use to inhibit the growth of P. aeruginosa, and to treat infections by pathogens causing chronic pulmonary infections. The two issued U.S. patents have terms expiring in 2016. The date does not include a possible term extension. We have additionally licensed applications covering the use of gallium complexes in treating and preventing bacterial biofilm-based infections. In 2009 patents were issued in South Africa and in Mexico relating to this application

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

Table of Contents

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, Inc. received FDA approval in 2002 for a sublingual buprenorphine product for the treatment of opioid addiction. This product, to be administered daily, will compete with our six-month implantable product for opioid addiction. The FDA previously approved Orphan Drug designation, expiring in 2009, for Reckitt Benckiser's sublingual buprenorphine for the treatment of opioid addiction. Other forms of buprenorphine are also in development by other companies, including intramuscular injections and intranasally delivered buprenorphine, which also might compete with our product.

Several products categorized as atypical antipsychotics that will compete with Fanapt are already on the market. These products include Risperdal sold by Janssen Pharmaceuticals, Zyprexa sold by Eli Lilly, Clozaril sold by Novartis, Seroquel sold by AstraZeneca, Geodon sold by Pfizer, and Abilify sold by Bristol-Myers Squibb. Competition among these companies is already intense and iloperidone will face significant competition. The success of Fanapt will depend on how it can be differentiated from products already on the market on the basis of efficacy, side-effect profile, cost, availability of formulations and dose requirements, among other things.

Manufacturing

We utilize contract manufacturing organizations to manufacture our products for pre-clinical studies and clinical trials. While we have not introduced any products on the commercial market to date, at such time as we are ready to do so we will need to allocate additional resources to the manufacture of these products. We do not have the facilities to manufacture these products in-house nor do we intend to establish our own manufacturing operation at this time. We currently plan to pursue collaborative arrangements regarding the manufacture of any products that we may successfully develop.

Government Regulation

In order to obtain FDA approval of a new drug, a company generally must submit proof of purity, potency, safety and efficacy, among other regulatory standards. In most cases, such proof entails extensive clinical and pre-clinical laboratory tests.

The procedure for obtaining FDA approval to market a new drug involves several steps. Initially, the manufacturer must conduct pre-clinical animal testing to demonstrate that the product does not pose an unreasonable risk to human subjects in clinical studies. Upon completion of such animal testing, an Investigational New Drug application, or IND, must be filed with the FDA before clinical studies may begin. An IND application consists of, among other things, information about the proposed clinical trials. Among the conditions for clinical studies and IND approval is the requirement that the prospective manufacturer's quality control and manufacturing procedures conform to current Good Manufacturing Practices (cGMP), which must be followed at all times. Once the IND is approved (or if the FDA does not respond within 30 days), the clinical trials may begin.

Human clinical trials on drugs are typically conducted in three sequential phases, although the phases may overlap. Phase I trials typically consist of testing the product in a small number of healthy volunteers or patients, primarily for safety in one or more doses. During Phase II, in addition to safety, dose selection and efficacy of the product is evaluated in up to several hundred patients and sometimes more. Phase III trials typically involve additional testing for safety and confirmation of efficacy in an expanded patient population at multiple test sites. The FDA may order the temporary or permanent discontinuation of a clinical trial at any time.

The results of the pre-clinical and clinical testing on new drugs, if successful, are submitted to the FDA in the form of a New Drug Application (NDA). The NDA approval process requires substantial time and effort and there can be no assurance that any approval will be granted on a timely basis, if at all. The FDA may refuse to approve an NDA if applicable regulatory requirements are not satisfied. Product approvals, if granted, may be withdrawn if compliance with regulatory standards is not maintained or problems occur following initial marketing.

Table of Contents

The FDA may also require post-marketing testing and surveillance of approved products, or place other conditions on their approvals. These requirements could cause it to be more difficult or expensive to sell the products, and could therefore restrict the commercial applications of such products. Product approvals may be withdrawn if compliance with regulatory standards is not maintained or if problems occur following initial marketing. With respect to patented products or technologies, delays imposed by the governmental approval process may materially reduce the period during which we will have the exclusive right to exploit such technologies.

In May 2009, in recognition of the significant number (almost weekly) of telephonic and in-person meetings attended by the members of our board of directors to help manage the company during the period from January to May 2009, each member of the board of directors was awarded a stock option grant to purchase 100,000 shares of common stock with immediate vesting.

We believe we are in compliance with all material applicable regulatory requirements. However, see **Risk Factors** We must comply with extensive government regulations for additional risks we face regarding regulatory requirements and compliance.

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, 2009, we had four employees and several consultants. See **Risk Factors** We may not be able to retain our key management and scientific personnel.

Item 1A. Risk Factors

The timing and amount of royalty revenues from iloperidone (Fanapt) will be wholly dependent on the efforts of third parties.

We do not have any role in the marketing, manufacture or commercialization of iloperidone (Fanapt). The timing and amount of royalty revenues we receive from the sale of this product will be wholly dependent upon the ability of Novartis to successfully launch and commercialize this product in the United States and Canada and on the ability of Vanda or others to sell this product in other countries. Similarly, our ability to realize any royalty revenue relating to the depot formulation of the product will depend on the ability of Novartis to successfully complete the development and regulatory approval process and implement the marketing program necessary to commercialize this product. While Novartis has announced that it launched commercial sales of Fanapt in January 2010, which would result in royalty payments to us during the following quarter, Novartis may experience unanticipated problems that delay, perhaps materially, product sales and our receipt of revenues.

Our available capital is sufficient to fund our operations only through September 2010 and we do not have the funds needed to continue the Probuphine program.

At September 30, 2009, we had cash and cash equivalents of \$0.7 million, which we believe is sufficient, together with the proceeds of a private placement and debt financing completed in December 2009 and the NIH grant, to sustain our planned operations through September 2010, at which time we expect to be generating revenues from royalties on the sale of Fanapt. We do not currently have sufficient capital to fully fund the Probuphine program and we cannot be certain that the requisite funds will be available, from royalty revenues or otherwise, to continue that program.

Table of Contents

Probuphine is in the development stage and may not be successfully developed or commercialized.

Probuphine, which is in Phase 3 clinical development, will require significant further capital expenditures, development, testing, and regulatory clearances prior to commercialization. Even if we are able to obtain the requisite funding to continue this program, the results of preclinical and clinical studies to date are not necessarily indicative of whether a product will demonstrate safety and efficacy in large patient populations to the satisfaction of the regulatory authorities in the U.S. and elsewhere. Of the large number of drugs in development, only a small percentage successfully complete the FDA regulatory approval process and are commercialized.

To date, we have experienced setbacks in some of our other product development efforts. For example, the results of a study evaluating the EKG profile of patients taking iloperidone led to a significant delay in the development of that product, a vaccine product formerly under development failed to meet the study's primary endpoint, and a study of one of our products in a combination treatment was discontinued as a result of an interim safety analysis. We may continue to experience unanticipated problems relating to product development, testing, regulatory compliance, manufacturing, marketing and competition, and our costs and expenses could exceed current estimates. We cannot predict whether we will successfully develop and commercialize Probuphine or any other product.

We must comply with extensive government regulations.

The research, development, manufacture and marketing of pharmaceutical products are subject to an extensive regulatory approval process by the FDA and other regulatory agencies in the U.S. and other countries. The process of obtaining required regulatory approvals for drugs, including conducting preclinical and clinical testing to determine safety and efficacy, is lengthy, expensive and uncertain. Even after such time and expenditures, we may not obtain necessary regulatory approvals for clinical testing or for the manufacturing or marketing of any products. We have limited experience in obtaining FDA approval. 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. Our business will be seriously harmed if our regulatory submissions are delayed or we cancel plans to make submissions for proposed products for any of the following reasons:

unanticipated preclinical testing or clinical trial reports;

failure to reach agreement with the FDA regarding study protocols or endpoints;

changes in regulations or the adoption of new regulations;

unanticipated enforcement of existing regulations;

unexpected technological developments; and

developments by our competitors.

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 will 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.

Table of Contents

We face risks associated with clinical trial liability claims in the event that the use or misuse of our product candidates results in personal injury or death.

We face an inherent risk of clinical trial liability claims in the event that the use or misuse of our product candidates results in personal injury or death. Our clinical liability insurance coverage may not be sufficient to cover claims that may be made against us. 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

Table of Contents

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.

Our ability or the ability of our collaborators to commercialize drug products, if any, may 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. 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 shares are currently quoted in the OTC Pink Sheets and we cannot predict whether our shares will ever trade on the OTC Bulletin Board or any national securities exchange.

Our shares are currently quoted in the OTC Pink Sheets. Many institutional investors have investment policies which prohibit them from trading in stocks on the OTC Pink Sheets. As a result, shares quoted on the OTC Pink Sheets generally have limited trading volume and exhibit a wide spread between the bid/ask quotations than stock traded on national exchanges. We anticipate having a registered broker-dealer file a Form 15c211 with the Financial Industry Regulatory Authority that would permit our common stock to be quoted for trading on the OTC Bulletin Board, but we cannot be sure that such an effort would be successful. As a result, an investment in our common stock may be illiquid and investors may not be able to liquidate their investment readily or at all when they desire to sell.

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;

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.

Table of Contents

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 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 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.

As a result of the de-registration of our securities, we are currently ineligible to use Form S-3 to register securities, which may adversely affect our cost of future capital.

We are currently ineligible to use Form S-3 to register securities for sale by us or for resale by other security holders and will not be eligible until we have timely filed all periodic reports under the Exchange Act for at least 12 calendar months. In the meantime, we would need to use Form S-1 to register securities with the SEC for capital raising transactions or issue such securities in private placements, in either case, increasing the costs of raising capital during this period.

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, 2008, we had federal net operating loss and tax credit carryforwards of \$231.9 million and \$7.3 million, respectively, and state net operating loss and tax credit carryforwards of \$110.2 million and \$6.5 million, respectively. 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. We have not performed a change of ownership analysis since 1999 and, accordingly, some or all of our net operating loss and tax credit carryforwards may not be available to offset future taxable income, if any. Even if the carryforwards are available, they may be subject to annual limitations, lack of future taxable income, or future ownership changes that could result in the expiration of the carryforwards before they are utilized.

Table of Contents**Item 2. Financial Information****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 and with Management's Discussion and Analysis of Financial Condition and Results of Operations below.

	Nine Months ended		Years Ended December 31,				
	September 30, (unaudited)		2008	2007	2006	2005	2004
	2009	2008	(in thousands, except per share data)				
Statement of Operations Data:							
Total revenue	\$ 53	\$ 73	\$ 73	\$ 24	\$ 32	\$ 89	\$ 31
Operating expenses:							
Research and development	1,707	12,810	16,235	12,244	11,620	17,770	20,415
Acquired/in-process research and development(1)							759
General and administrative	2,443	7,086	9,756	6,213	4,859	5,370	5,237
Other income (expense), net	(7)	516	484	786	710	589	376
Net loss	\$ (4,104)	\$ (19,307)	\$ (25,434)	\$ (17,647)	\$ (15,737)	\$ (22,462)	\$ (26,004)
Basic and diluted net loss per share	\$ (0.07)	\$ (0.33)	\$ (0.44)	\$ (0.41)	\$ (0.42)	\$ (0.69)	\$ (0.83)
Shares used in computing:							
Basic and diluted net loss per share	58,291	58,284	58,285	42,998	37,902	32,635	31,381

(1)