PAIN THERAPEUTICS INC
Form S-3
May 11, 2004
Table of Contents

As filed with the Securities and Exchange Commission on May 11, 2004

Registration No. 333-

UNITED STATES

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM S-3

REGISTRATION STATEMENT

Under

The Securities Act of 1933

PAIN THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

Delaware	**91-1911336**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification Number)**

416 Browning Way

South San Francisco, CA 94080

(650) 624-8200

(Address, including zip code, and telephone number, including area code, of registrant s principal executive offices)

Remi Barbier

President, Chief Executive Officer

and Director

Pain Therapeutics, Inc.

416 Browning Way

South San Francisco, CA 94080

(650) 624-8200

(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

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650 Page Mill Road

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Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this Registration Statement.

If the only securities being registered on this Form are being offered pursuant to dividend or interest reinvestment plans, please check the following box. ¨

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box. x

If this Form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, please check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If this Form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering. ¨

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. ¨

CALCULATION OF REGISTRATION FEE

Title of Each Class of Securities to be Registered	Amount to be Registered	Proposed Maximum Offering Price Per Share(1)	Proposed Maximum Aggregate Offering Price(1)	Amount of Registration Fee
Common Stock, $0.001 par value	15,000,000 shares	$7.24	$108,600,000	$13,760

(1) Estimated solely for the purpose of calculating the amount of the registration fee in accordance with Rule 457 under the Securities Act of 1933, as amended, based upon the average of the high and low sales prices of the common stock reported on the Nasdaq National Market on May 3, 2004.

The registrant hereby amends this Registration Statement on such date or dates as may be necessary to delay its effective date until the registrant shall file a further amendment which specifically states that this Registration Statement shall thereafter become effective in accordance with Section 8(a) of the Securities Act of 1933 or until the Registration Statement shall become effective on such date as the Commission acting pursuant to said Section 8(a) may determine.

Table of Contents

The Information in this prospectus is not complete and may be changed. We may not sell these securities until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell securities and is not soliciting an offer to buy securities in any state where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED MAY 7, 2004

PROSPECTUS

15,000,000 Shares

Pain Therapeutics, Inc.

COMMON STOCK

Pain Therapeutics, Inc. may offer shares of its common stock from time to time. We will specify in an accompanying prospectus supplement the terms of any offering. Our common stock is traded on the Nasdaq National Market PTIE. On May 6, 2004 the last reported sale price of our common stock on the Nasdaq National Market was $8.05 per share.

You should read this prospectus, any prospectus supplement and the documents incorporated by reference in this prospectus and any prospectus supplement carefully before you invest. **This prospectus may not be used to offer or sell any securities unless accompanied by a prospectus supplement**.

Investing in our common stock involves a high degree of risk. You should carefully consider the Risk Factors beginning on page 6 of this prospectus before you make an investment decision.

The common stock offered by this prospectus may be offered in amounts, at prices and at terms determined at the time of the offering and may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers. We will set forth the

names of any underwriters or agents in the accompanying prospectus supplement. For additional information on the methods of sale, you should refer to the section entitled Plan of Distribution. The net proceeds we expect to receive from such sale will also be set forth in a prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved these securities or determined if this prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

The date of this prospectus is , 200

Table of Contents

TABLE OF CONTENTS

No person has been authorized to give any information or make any representations in connection with this offering other than those contained or incorporated by reference in this prospectus and any accompanying prospectus supplement in connection with the offering described herein and therein, and, if given or made, such information or representations must not be relied upon as having been authorized by us. Neither this prospectus nor any prospectus supplement shall constitute an offer to sell or a solicitation of an offer to buy offered securities in any jurisdiction in which it is unlawful for such person to make such an offering or solicitation. Neither the delivery of this prospectus or any prospectus supplement nor any sale made hereunder shall under any circumstances imply that the information contained or incorporated by reference herein or in any prospectus supplement is correct as of any date subsequent to the date hereof or of such prospectus supplement.

Table of Contents

SUMMARY

The following summary is qualified in its entirety by the more detailed information, including our consolidated financial statements and related notes, included in this prospectus and incorporated in this prospectus by reference. You should carefully consider the information set forth in this entire prospectus, including the Risk Factors section, the applicable prospectus supplement for such securities and the other documents we refer to and incorporate by reference, including but not limited to the section entitled Risk Factors in our 2003 Annual Report on Form 10-K. Unless the context otherwise requires, the terms Pain Therapeutics, we, us and our refer to Pain Therapeutics, Inc., Inc., a Delaware corporation.

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, using a shelf registration process. Under this shelf process, we may, from time to time, sell up to 15,000,000 shares of our common stock in one or more offerings. Each time we sell common stock, we will provide a prospectus supplement that will contain specific information about the terms of that offering. This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of our common stock, you should refer to the registration statement, including its exhibits. The prospectus supplement may also add, update or change information contained in this prospectus. You should read both this prospectus and any prospectus supplement, including the risk factors, together with the additional information described under the headings Where You Can Find Information and Information Incorporated by Reference.

Pain Therapeutics, Inc.

Overview

We are a biopharmaceutical company that develops novel drugs. Our drugs target severe chronic pain, such as pain associated with advanced osteoarthritis, low-back pain or irritable bowel syndrome. We have three proprietary drug candidates in clinical development: Oxytrex™, Remoxy™ and PTI-901. Our two most advanced drugs, Oxytrex and PTI-901, are in Phase III clinical trials. Remoxy is in Phase I clinical trials in the United Kingdom. We believe the target market for our three drug candidates exceeds $3 billion per year. We currently retain all commercial rights to our drug candidates.

Our Drug Candidates

Oxytrex

Our lead candidate is a novel oral opioid called Oxytrex. Oxytrex is a small molecule drug that is currently in a Phase III clinical program. We are developing Oxytrex to treat severe chronic pain, such as low back, osteoarthritic pain or cancer pain.

If the Food and Drug Administration, or FDA, approves Oxytrex, we believe it could be an effective substitute for oxycodone. Oxycodone is widely used today to treat severe chronic pain. Sales of oxycodone exceed $1.5 billion a year. We own all commercial rights to Oxytrex.

Previous clinical results have shown that Oxytrex provides enhanced pain relief and prolonged pain relief. In a previously announced Phase II study with 350 patients suffering from severe osteoarthritic pain, Oxytrex reduced patients pain scores by over 40% ($p<0.001$ vs. placebo and $p=0.006$ vs. oxycodone) over a 21-day treatment period. By comparison, oxycodone reduced patients pain scores by 24%. Published pre-clinical results also demonstrate that the technology used in Oxytrex results in a lack of opioid addiction, tolerance, physical dependence or withdrawal symptoms in animals.

Table of Contents

The FDA guidelines recommend that we demonstrate the efficacy of Oxytrex in more than one clinical model of pain. We plan to study Oxytrex in at least two Phase III efficacy studies.

In June 2003, we announced the initiation of our first Phase III efficacy study. This randomized, double-blinded study compares the analgesic efficacy of Oxytrex against placebo and oxycodone over a three-month treatment period in up to 700 patients with severe chronic low back pain.

In the first quarter of 2004, we initiated a second Phase III clinical study of Oxytrex. This randomized, double-blinded study will compare the analgesic efficacy of Oxytrex against placebo and oxycodone over a three-month treatment period in up to 700 patients with severe chronic osteoarthritic pain.

Oxytrex is formulated with two active drug ingredients: oxycodone and low-dose naltrexone. We believe we have produced sufficient clinical materials necessary to complete two Phase III trials of Oxytrex. We rely on a limited number of third-party manufacturers to manufacture, fill, label, ship or store Oxytrex.

Remoxy

In November 2003, we announced our second novel drug candidate, which we named Remoxy. Remoxy is an abuse-deterrent, long-acting version of oxycodone. Sales of oxycodone exceed $1.5 billion a year. We own all commercial rights to Remoxy.

Oxycodone is a strong narcotic painkiller that is widely used today to treat patients suffering from severe chronic pain. However, oxycodone has an abuse potential similar to morphine. The U.S. Drug Enforcement Agency, or DEA, and the national media have linked illicit oxycodone use to widespread patterns of drug abuse, addiction, diversion and drug overdose. Oxycodone is also the active ingredient in OxyContin©, a branded controlled-release narcotic painkiller. Remoxy s novel capsule formulation is specifically designed to foil abusers who attempt to tamper with the drug in order to induce a powerful euphoric high. Given a choice between prescribing abuse-resistant Remoxy or more easily abusable forms of oxycodone, we believe physicians will choose a less abusable alternative, such as Remoxy.

In November 2003, we filed an Investigational New Drug Application, or IND, for Remoxy with the FDA. The FDA has requested additional information on certain excipients used in formulations of Remoxy. We are responding to the FDA s requests for additional data prior to initiating any clinical studies in the United States.

In January 2004, we initiated a Phase I clinical program of Remoxy in the United Kingdom. Our phase I program is designed to assess the pharmacokinetics and pharmacological profile of several different formulations of Remoxy against placebo and active drug in healthy volunteers.

Remoxy is formulated with Durect Corporation s SABER technology under a joint development and license agreement. Under the terms of our license agreement with Durect, we have exclusive worldwide rights to develop and to commercialize Remoxy and certain other opioid drugs formulated with Durect s SABER technology. We plan to formulate and scale-up a wide range of dosage forms of Remoxy. We reimburse

Durect for formulation and related work, and will make milestone payments based on the achievement of certain technical, clinical or regulatory milestones. We will also pay Durect royalties on related drug sales.

Table of Contents

We believe we can produce sufficient clinical materials necessary to complete our Phase I trials of Remoxy. We rely on Durect Corporation and a limited number of third-party manufacturers to formulate, manufacture, fill, label, ship or store Remoxy.

PTI-901

Our third drug candidate is called PTI-901 and treats Irritable Bowel Syndrome, or IBS. PTI-901 is a proprietary drug candidate that consists of an oral low-dose opioid antagonist. If approved by the FDA to treat men and women with IBS, we believe PTI-901 will target a market in excess of $1 billion per year. We own all commercial rights to PTI-901.

Chronic IBS is a painful abdominal disorder that leads to major changes in bowel habits. IBS causes some patients to have constipation, diarrhea or in some cases both. The causes of IBS are not known, and as yet there is no cure. People with chronic IBS may be unable to attend social events, hold a job, or travel away from home. Over 10 percent of the U.S. population suffers from IBS. For unknown reasons, IBS predominantly affects women.

There are no FDA-approved drugs to treat men with IBS. There are two FDA-approved drugs to treat women with IBS: Lotronex® (GlaxoSmithKline) and Zelnorm® (Novartis). The FDA approved Lotronex® in February 2000 for use in female patients with diarrhea-predominant IBS. The FDA approved Zelnorm® in July 2002 for short-term use by female patients who have constipation-predominant IBS.

We believe PTI-901 represents a novel approach to treat patients with IBS. We believe an appropriate dose of PTI-901 modulates aberrant neuronal communication within the gut, thus restoring proper bowel function and relieving pain in IBS patients.

Results from a 50-patient pilot study with PTI-901 in men and women were announced in May 2003 and presented at the American College of Gastroenterology meeting in October 2003. In this open-label study, patients with IBS reported a 76% response rate to PTI-901. This response rate was observed in both men and women and occurred without drug-related safety issues.

In November 2003, we announced the initiation of a Phase III program with PTI-901. The Phase III program consists of two clinical studies that are identical in all respects, except for gender. One study will enroll 600 women and the other will enroll 600 men, all of whom have been diagnosed with chronic IBS by a gastroenterologist according to clinically accepted criteria. Each Phase III study is randomized, double-blinded and will assess the clinical effect of PTI-901 against placebo during a three-month treatment period.

We believe we have produced sufficient clinical materials necessary to complete two Phase III trials with PTI-901. We rely on a limited number of third-party manufacturers to manufacture, fill, label, ship and store PTI-901.

Strategy

Our commercial goal is to build a franchise in pain management by developing novel drugs that target severe, chronic pain such as pain associated with advanced osteoarthritis, low-back pain or IBS. We intend to achieve this goal by developing proprietary drugs that are more effective or safer than drugs used in the clinic today. Our strategy includes:

Focusing on Clinical Development and Late Stage Products. We believe this focus will enable us to generate product revenues earlier than if we were focused on early-stage research and discovery activities.

Table of Contents

Retaining Significant Rights to Our Drugs. We currently retain worldwide commercialization rights to all of our technology and drug candidates in all markets and indications. In general, we intend to independently develop our drug candidates through late-stage clinical trials. As a result, we expect to capture a greater percentage of the profits from drug sales than we would if we outlicensed our drug candidates earlier in the development process. In market segments that require large or specialized sales forces, such as the market for oxycodone products, we may seek sales and marketing alliances with third parties.

Outsourcing Key Functions. We intend to continue to outsource pre-clinical studies, clinical trials and formulation and manufacturing activities. We believe outsourcing permits significant timesavings and allows for more efficient deployment of our resources.

Pursue In-licensing or Acquisition Opportunities. We intend to evaluate promising drug candidates or technologies to further expand our product pipeline. Our in-licensing strategy consists of evaluating clinical or pre-clinical stage opportunities in therapeutic areas that are related to our core expertise in drug development. We believe this strategy could diversify some of the risks inherent in drug development and increase our probability of commercial success.

Our Science and Technology

Our science was developed at Albert Einstein College of Medicine. It is well known that opioid painkillers produce their pain relieving effect by inhibiting the transmission of pain signals in certain nerve cells in the central nervous system. This inhibition of pain is achieved by inhibiting nerve cells that have opioid receptors on their membranes, via an inhibitory signaling pathway linked to the receptor. Scientists at Albert Einstein College of Medicine, however, have published results suggesting that opioid painkillers also activate an excitatory signaling pathway linked to opioid receptors, thereby stimulating the transmission of pain. This excitatory pathway counteracts pain inhibition and is believed to be a major cause of adverse side effects associated with opioid use, including the development of tolerance and addiction.

We believe that the excitatory pathway of opioid receptors contributes greatly to the adverse effects of chronic opioid use, such as tolerance, physical dependence and addiction. After repeated administration of morphine, oxycodone or other opioid painkillers, increasing doses of opioids are required in order to obtain the same level of pain relief, a process known as tolerance. If chronic opioid treatment is terminated abruptly, withdrawal symptoms rapidly appear. Continued administration of opioids prevents the appearance of withdrawal symptoms, at which point a patient is considered physically dependent. Published results in rodents also show that tolerance and physical dependence can be prevented by coadministration of low-dose naltrexone, an opioid antagonist. We believe low-dose naltrexone blocks the excitatory pathway, thus minimizing tolerance, physical dependence and addiction. In addition, recent pre-clinical work using animal models of addiction suggests that very low doses of opioid antagonists decrease the pleasurable effects and addictive potential of opioid drugs such as morphine or oxycodone.

Optimal dose ratios of low-dose opioid antagonist to opioid painkiller depend on their specific pharmacology and the mode of administration. Published pre-clinical and clinical dose response studies provide guidance in formulating optimal ratios of low-dose opioid antagonist to opioid painkiller for clinical development.

Table of Contents

Oxytrex is a proprietary combination of two active drug ingredients. The first component is the opioid agonist oxycodone. The second component is an extremely low dose of the opioid antagonist naltrexone. Adding an antagonist to an agonist at usual clinical doses blocks the action of the agonist. This effect is clinically useful, for example, to reverse heroin overdose. At a very low dose, however, studies indicate that this effect is different: a very low-dose of an opioid antagonist can enhance pain relief and attenuate the development of tolerance or addiction. Oxytrex takes advantage of this effect by combining opioid agonists with low doses of opioid antagonists.

PTI-901 is a proprietary drug candidate that consists of oral low-dose opioid antagonist. We use PTI-901 to treat IBS. The precise causes of IBS are unknown. The two FDA-approved drugs attempt to slow down the gastrointestinal tract for diarrhea-predominant IBS in the case of Lotronex®, or speed up the gastrointestinal tract for constipation-predominant IBS in the case of Zelnorm®.

Scientific evidence suggests IBS is a disorder of the nervous system. In this scenario, patients with IBS suffer from aberrant neuronal communication within the gut due to an imbalance of opioid peptides in the gut. Since opioid peptides contribute to the proper function of the gut, an imbalance results in a broad range of gastrointestinal problems, including abdominal pain, diarrhea or constipation. We believe PTI-901 modulates aberrant neuronal communication within the gut, thus restoring proper bowel function and relieving pain in IBS patients.

Company sponsored research and development expenditures were $11.7 million, $11.4 million, $18.9 million and $9.5 million in 2001, 2002 and 2003 and the first three months of 2004, respectively.

We were incorporated in Delaware in May 1998. Our principal executive offices are located at 416 Browning Way, South San Francisco, California 94080 and our telephone number at that address is (650) 624-8200.

Table of Contents

RISK FACTORS

An investment in our securities involves a high degree of risk. You should carefully consider the risks described below before making an investment decision. You should also refer to the other information in this prospectus, including our financial statements and the related notes incorporated by reference into this prospectus. The risks and uncertainties described below are not the only risks and uncertainties we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial also may impair our business operations. If any of the following risks actually occur, our business, results of operations and financial condition could suffer. In that event, the trading price of our common stock could decline, and you may lose all or part of your investment in our common stock. The risks discussed below also include forward-looking statements and our actual results may differ substantially from those discussed in these forward-looking statements.

Risks Relating to our Financial Position and Need for Financing

Our operating history may make it difficult for you to evaluate the success of our business to date and to assess its future viability.

We were founded in May 1998 and are in the development stage. Our operations to date have been limited to organizing and staffing our company, acquiring, developing and securing our technology and undertaking preclinical studies and clinical trials of our drug candidates. We have not yet demonstrated our ability to obtain regulatory approval, formulate and manufacture commercial-scale product or conduct sales and marketing activities. Consequently, any predictions you make about our future success or viability may not be as accurate as they could be if we had a longer operating history.

We have a history of losses and expect to incur substantial losses and negative operating cash flows for the foreseeable future.

We have incurred net losses each year since our inception. As a result of ongoing operating losses, we had an accumulated deficit of $84.4 million as of March 31, 2004. Even if we succeed in developing and commercializing one or more of our drug candidates, we expect to continue to incur substantial losses for the foreseeable future, and we may never become profitable. We anticipate that our expenses will increase substantially in the foreseeable future as we:

- continue to conduct preclinical and clinical trials for our drug candidates, including the Phase III trials of Oxytrex and PTI-901 and formulation activities and Phase I trials of Remoxy;
- seek regulatory approvals for our drug candidates;
- develop, formulate, manufacture and commercialize our drugs;
- implement additional internal systems and develop new infrastructure;
- acquire or in-license additional products or technologies or expand the use of our technology;

maintain, defend and expand the scope of our intellectual property; and

hire additional personnel.

Table of Contents

We will need to generate significant revenues to achieve and maintain profitability. If we cannot successfully develop and commercialize our products, we will not be able to generate such revenues or achieve profitability in the future. Our failure to achieve or maintain profitability could negatively impact the market price of our common stock.

If we cannot raise additional capital on acceptable terms, we may be unable to complete planned additional clinical trials of any or some of our drug candidates.

We have funded all of our operations and capital expenditures with the proceeds from public and private stock offerings. We expect that our current cash, cash equivalent and marketable securities on hand will be sufficient to meet our working capital and capital expenditure needs for at least the next twelve months. However, we may need to raise additional funds sooner and additional financing may not be available on favorable terms, if at all. Even if we succeed in selling additional securities to raise funds, our existing stockholders ownership percentage would be reduced and new investors may demand rights, preferences or privileges senior to those of existing stockholders.

If we determine that we need to raise additional funds and we are not successful in doing so, we may be unable to complete the clinical development of some or all of our drug candidates or to obtain FDA approval of our drug candidates, and we could be forced to discontinue product development, enter into a relationship with a strategic partner earlier than currently intended, reduce sales and marketing efforts and forego attractive business opportunities.

Clinical and Regulatory Risks

If we fail to obtain the necessary regulatory approvals, we will not be allowed to commercialize our drugs, and we will not generate product revenues.

Satisfaction of all regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the drug candidate, and requires the expenditure of substantial resources for research and development and testing. Our research and clinical approaches may not lead to drugs that the FDA considers safe for humans and effective for indicated uses we are studying. The FDA may require us to conduct additional clinical testing, in which case we would have to expend additional time and resources. The approval process may also be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals will:

- delay commercialization of, and product revenues from, our drug candidates; and
- diminish the competitive advantages that we may have otherwise enjoyed.

Even if we comply with all FDA regulatory requirements, we may never obtain regulatory approval for any of our drug candidates. If we fail to obtain regulatory approval of any of our drug candidates we will have fewer saleable products and corresponding lower product revenues. Even if we receive regulatory approval of our products, such approval may involve limitations on the indicated uses or marketing claims we may make for our products. Further, later discovery of previously unknown problems could result in additional regulatory restrictions, including withdrawal of products. The FDA may also require us to commit to perform lengthy post-approval studies, for which we would have to expend

additional resources, which could have an adverse effect on our operating results and financial condition.

Table of Contents

In foreign jurisdictions, we must receive marketing authorizations from the appropriate regulatory authorities before we can commercialize our drugs. Foreign regulatory approval processes generally include all of the aforementioned requirements and risks associated with FDA approval.

If we are unable to design, conduct and complete clinical trials successfully, we will not be able to obtain regulatory approval for our products.

In order to obtain FDA approval of any of our drug candidates, we must submit to the FDA a New Drug Application, or NDA, that demonstrates that the drug candidate is safe and effective in humans for its intended use. This demonstration requires significant research and animal tests, which are referred to as preclinical studies, as well as human tests, which are referred to as clinical trials. Two of our drug candidates, Oxytrex and PTI-901, are in Phase III clinical trials. Remoxy is in Phase I clinical trials.

Our Phase III trials may not demonstrate the safety or efficacy of our drug candidates. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful. Results of later clinical trials may not replicate the results of prior clinical trials and pre-clinical testing. FDA guidelines recommend that the efficacy of new painkillers be demonstrated in more than one clinical model of pain. Even if the results of our Phase III trials are positive, we may have to commit substantial time and additional resources to conducting further preclinical and clinical studies before we can submit NDAs or obtain FDA approvals for our drug candidates.

Clinical trials are very expensive and difficult to design and implement, in part because they are subject to rigorous requirements. The clinical trial process is also time consuming. Furthermore, if participating patients in clinical studies suffer drug-related adverse reactions during the course of such trials, or if we or the FDA believe that participating patients are being exposed to unacceptable health risks, we will have to suspend our clinical trials. Failure can occur at any stage of the trials, and we could encounter problems that cause us to abandon clinical trials or to repeat clinical studies.

Even if our clinical trials are completed as planned, their results may not support our product claims. The clinical trials process may fail to demonstrate that our drug candidates are safe and effective for indicated uses. Such failure would cause us to abandon a drug candidate and could delay development of other drug candidates.

If we are unable to satisfy the FDA s request for additional information on Remoxy, we will not be allowed to conduct clinical testing of this product in the United States.

In November 2003, we filed an IND for Remoxy with the FDA. The FDA responded to our IND with a request for additional information on certain excipients used in formulations of Remoxy. We are not able to conduct human clinical studies with Remoxy in the United States until the FDA notifies us that their request for additional information is satisfied. If we are unable to conduct human clinical studies of Remoxy in the United States, we may determine that the commercial opportunity for Remoxy in certain dosage forms is too limited to warrant further investment.

Clinical trial designs that were discussed with authorities prior to their commencement may subsequently be considered insufficient for approval at the time of application for regulatory approval.

We discuss with and obtain guidance from regulatory authorities on certain of our clinical development activities. These discussions are not binding obligations on the part of regulatory authorities. Regulatory authorities may revise previous guidance or decide to ignore previous guidance at any time during the course of our clinical activities or after the completion of our clinical trials. Even with successful clinical safety and efficacy data, we may be required to conduct additional, expensive trials to obtain regulatory approval.

Table of Contents

Developments by competitors may establish standards of care that affect our ability to conduct our clinical trials as planned.

We have conducted clinical trials of our drug candidates comparing our drug candidates to both placebo and other approved drugs. Changes in standards related to clinical trial design could affect our ability to design and conduct clinical trials as planned. For example, regulatory authorities may not allow us to compare our drug candidates to placebo in a particular clinical indication where approved products are available. In that case, both the cost and the amount of time required to conduct a trial could increase.

The DEA limits the availability of the active ingredients in our current drug candidates and, as a result, our quota may not be sufficient to complete clinical trials, meet commercial demand or may result in clinical delays.

The DEA regulates chemical compounds as Schedule I, II, III, IV or V substances, with Schedule I substances considered to present the highest risk of substance abuse and Schedule V substances the lowest risk. Certain active ingredients in our current drug candidates, such as oxycodone, are listed by the DEA as Schedule II or III substances under the Controlled Substances Act of 1970. Consequently, their manufacture, research, shipment, storage, sale and use are subject to a high degree of regulation. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription. Furthermore, the amount of Schedule II substances we can obtain for clinical trials and commercial distribution is limited by the DEA and our quota may not be sufficient to complete clinical trials or meet commercial demand. There is a risk that DEA regulations may interfere with the supply of the drugs used in our clinical trials, and in the future, our ability to produce and distribute our products in the volume needed to meet commercial demand.

Government agencies may establish and promulgate usage guidelines that directly apply to our products.

Government agencies, professional and medical societies, and other groups may establish usage guidelines that apply to our drugs. These guidelines could address such matters as usage and dose, among other factors. Application of such guidelines could limit the use of our drugs.

Conducting clinical trials of our drug candidates exposes us to expensive product liability claims and we may not be able to maintain product liability insurance on reasonable terms or at all.

The risk of product liability is inherent in the testing of pharmaceutical products. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit or terminate testing of one or more of our products. Our inability to obtain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of our products. We currently carry clinical trial insurance but do not carry product liability insurance. We may not be able to obtain such insurance at a reasonable cost, if at all. If our agreements with any future corporate collaborators entitle us to indemnification against product liability losses, such indemnification may not be available or adequate should any claim arise.

Table of Contents

Risks Relating to Commercialization

If physicians and patients do not accept and use our drugs, we will not achieve sufficient product revenues and our business will suffer.

Even if the FDA approves our drugs, physicians and patients may not accept and use them. Acceptance and use of our drugs will depend on a number of factors including:

- perceptions by members of the healthcare community, including physicians, about the safety and effectiveness of our drugs;
- cost-effectiveness of our drugs relative to competing products;
- availability of reimbursement for our products from government or healthcare payers;
- our ability to implement a risk management plan prior to the distribution of any Schedule II drug; and
- effectiveness of marketing and distribution efforts by us and our licensees and distributors, if any.

Because we expect to rely on sales generated by our current lead drug candidates for substantially all of our product revenues for the foreseeable future, the failure of any of these drugs to find market acceptance would harm our business and could require us to seek additional financing.

If we are unable to develop our own sales, marketing and distribution capabilities, or if we are not successful in contracting with third parties for these services on favorable terms, our product revenues could be disappointing.

We currently have no sales, marketing or distribution capabilities. In order to commercialize our products, if any are approved by the FDA, we will either have to develop such capabilities internally or collaborate with third parties who can perform these services for us. If we decide to commercialize any of our drugs ourselves, we may not be able to hire the necessary experienced personnel and build sales, marketing and distribution operations which are capable of successfully launching new drugs and generating sufficient product revenues. In addition, establishing such operations will take time and involve significant expense.

If we decide to enter into co-promotion or other licensing arrangements with third parties, we may be unable to locate acceptable collaborators because the significant number of recent business combinations among pharmaceutical companies has resulted in a reduced number of potential future collaborators. Even if we are able to identify one or more acceptable collaborators, we may not be able to enter into any collaborative arrangements on favorable terms, or at all.

In addition, due to the nature of the market for pain management products, it may be necessary for us to license all or substantially all of our drug candidates to a single collaborator, thereby eliminating our opportunity to commercialize other pain management products independently. If we enter into any collaborative arrangements, our product revenues are likely to be lower than if we marketed and sold our products ourselves.

In addition, any revenues we receive would depend upon our collaborators efforts which may not be adequate due to lack of attention or resource commitments, management turnover, change of strategic focus, further business combinations or other factors outside of our control. Depending upon the terms of our

Table of Contents

collaboration, the remedies we have against an under-performing collaborator may be limited. If we were to terminate the relationship, it may be difficult or impossible to find a replacement collaborator on acceptable terms, or at all.

If we cannot compete successfully for market share against other drug companies, we may not achieve sufficient product revenues and our business will suffer.

The market for our drug candidates is characterized by intense competition and rapid technological advances. If our drug candidates receive FDA approval, they will compete with a number of existing and future drugs and therapies developed, manufactured and marketed by others. Existing or future competing products may provide greater therapeutic convenience or clinical or other benefits for a specific indication than our products, or may offer comparable performance at a lower cost. If our products are unable to capture and maintain market share, we may not achieve sufficient product revenues and our business will suffer.

We will compete for market share against fully integrated pharmaceutical companies or other companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have opioid painkillers already approved or in development. In addition, many of these competitors, either alone or together with their collaborative partners, operate larger research and development programs and have substantially greater financial resources than we do, as well as significantly greater experience in:

- developing drugs;
- conducting preclinical testing and human clinical trials;
- obtaining FDA and other regulatory approvals of drugs;
- formulating and manufacturing drugs; and
- launching, marketing, distributing and selling drugs.

Our ability to generate product revenues will be diminished if we fail to obtain acceptable prices or an adequate level of reimbursement for our products from healthcare payers.

Our ability to commercialize our drugs, alone or with collaborators, will depend in part on the extent to which reimbursement will be available from:

- government and health administration authorities;

private health maintenance organizations and health insurers; and

other healthcare payers.

Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Healthcare payers, including Medicare, health maintenance organizations and managed care organizations, are challenging the prices charged for medical products and services and/or are seeking pharmacoeconomic data to justify formulary acceptance and reimbursement practices. Government and other healthcare payers increasingly are attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for drugs, and by refusing, in some cases, to provide coverage for uses of approved products for disease indications for which the FDA has or has not granted labeling approval. Third-party insurance

Table of Contents

coverage may not be available to patients for any products we discover and develop, alone or with collaborators. If government and other healthcare payers do not provide adequate coverage and reimbursement levels for our products, market acceptance of them could be limited.

Risks Relating to our Intellectual Property

If we are unable to protect our intellectual property our competitors could develop and market products with similar features that may reduce demand for our products.

Our success, competitive position and potential future revenues will depend in part on our ability to protect our intellectual property. If we, Albert Einstein College of Medicine or our other collaborators fail to file, prosecute or maintain certain patents, our competitors could market products that contain features and clinical benefits similar to those of our products, and demand for our products could decline as a result. In January 2003, the U.S. Patent and Trademark Office, or PTO, disclosed that a law firm for an unidentified third-party filed requests for an Ex Parte Reexamination related to certain claims on patents we exclusively licensed from Albert Einstein College of Medicine. In each of the reexaminations, the PTO issued a first/initial office action and responses to those office actions were filed. In certain of the reexaminations, the PTO issued second/final office actions in which the PTO affirmed the patentability of certain claims related to uses of our drugs under development while maintaining rejections with respect to other claims, and responses to those office actions have been filed. Reexamination certificates have been issued in certain of the proceedings confirming the patentability of the claims. We cannot provide any assurance as to the outcome of the remaining ongoing PTO proceedings. An adverse outcome of the reexamination process could result in loss of claims of these patents that pertain to certain drugs we currently have under development and could have a material adverse impact on our future revenues.

We intend to file additional patent applications relating to our technology, products and processes. We may direct Albert Einstein College of Medicine or our collaborators to file additional patent applications relating to the licensed technology or we may do so ourselves. However, our competitors may challenge, invalidate or circumvent any of our current or future patents. These patents may also fail to provide us with meaningful competitive advantages.

We may become involved in expensive litigation or other legal proceedings related to our existing intellectual property rights, including patents.

We expect that we will rely upon trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. Others may independently develop substantially equivalent proprietary information or be issued patents that may prevent the sale of our products or know-how or require us to license such information and pay significant fees or royalties in order to produce our products.

Our technology could infringe upon claims of patents owned by others. If we were found to be infringing on a patent held by another, we might have to seek a license to use the patented technology. In that case, we might not be able to obtain such a license on terms acceptable to us, or at all. If a legal action were to be brought against us or our licensors, we could incur substantial defense costs, and any such action might not be resolved in our favor. If such a dispute were to be resolved against us, we could have to pay the other party large sums of money and our use of our technology and the testing, manufacture, marketing or sale of one or more of our proposed products could be restricted or prohibited.

Table of Contents

Risks Relating to our Business and Strategy

Competition for qualified personnel in the pharmaceutical industry is intense, and if we are not successful in attracting and retaining qualified personnel, we could experience delays in completing necessary clinical trials, in the regulatory approval process or in formulating, manufacturing, marketing and selling our potential products.

We will need to hire additional qualified personnel with expertise in clinical research, preclinical testing, government regulation, formulation and manufacturing and sales and marketing. We compete for qualified individuals with numerous biopharmaceutical companies, universities and other research institutions.

Competition for such individuals, particularly in the San Francisco Bay area, is intense, and our search for such personnel may not be successful. Attracting and retaining qualified personnel will be critical to our success.

Law enforcement concerns over diversion of opioids and social issues around abuse of opioids may make the regulatory approval process very difficult for our drug candidates.

Media stories regarding the diversion of opioids and other controlled substances are commonplace. Law enforcement agencies or regulatory agencies may apply policies that seek to limit the availability of opioids. Such efforts may adversely affect the regulatory approval process for our drug candidates.

Developments by competitors may render our products or technologies obsolete or non-competitive.

Alternative technologies and products are being developed to improve or replace the use of opioids for pain management, several of which are in clinical trials or are awaiting approval from the FDA. In addition, the active ingredients in nearly all opioid drugs are available in generic form. Drug companies that sell generic opioid drugs represent substantial competition. Many of these organizations competing with us have substantially greater capital resources, larger research and development staffs and facilities, greater experience in drug development and in obtaining regulatory approvals and greater manufacturing and marketing capabilities than we do. These organizations also compete with us to attract qualified personnel and partners for acquisitions, joint ventures or other collaborations.

Business interruptions could limit our ability to operate our business.

Our operations as well as those of our collaborators on which we depend are vulnerable to damage or interruption from computer viruses, human error, natural disasters, electrical and telecommunication failures, international acts of terror and similar events. We have not established a formal disaster recovery plan and our back-up operations and our business interruption insurance may not be adequate to compensate us for losses we may suffer. A significant business interruption could result in losses or damages incurred by us and require us to cease or curtail our operations.

Table of Contents

Risks Relating to Manufacturing

If third-party manufacturers of our drug candidates fail to devote sufficient time and resources to our concerns, or if their performance is substandard, our clinical trials and product introductions may be delayed and our costs may be higher than expected.

We have no manufacturing facilities and have limited experience in drug product development and commercial manufacturing. We lack the resources and expertise to formulate, manufacture or test the technical performance of our drug candidates. We currently rely on a limited number of experienced personnel and a small number of contract manufacturers and other vendors to formulate, test, supply, store and distribute drug supplies for our clinical trials. Our reliance on a limited number of vendors exposes us to the following risks, any of which could delay our clinical trials, and, consequently, FDA approval of our drug candidates and commercialization of our products, result in higher costs, or deprive us of potential product revenues:

Contract commercial manufacturers, their sub-contractors or other third parties we rely on, may encounter difficulties in achieving the volume of production needed to satisfy clinical needs or commercial demand, may experience technical issues that impact quality, and may experience shortages of qualified personnel to adequately staff production operations.

Our contract manufacturers could default on their agreements with us to provide clinical supplies or meet our requirements for commercialization of our products.

The use of alternate manufacturers may be difficult because the number of potential manufacturers that have the necessary governmental licenses to produce narcotic products is limited. Additionally, the FDA and the DEA must approve any alternative manufacturer of our product before we may use the alternative manufacturer to produce our supplies. It may be difficult or impossible for us to find a replacement manufacturer on acceptable terms quickly, or at all. Our contract manufacturers and vendors may not perform as agreed or may not remain in the contract manufacturing business for the time required to successfully produce, store and distribute our products.

If any third-party manufacturer makes improvements in the manufacturing process for our products, we may not own, or may have to share, the intellectual property rights to such innovation.

We rely on third-party commercial drug manufacturers for drug supply.

Approved third-party commercial drug manufacturers may subsequently be stopped from producing, storing, shipping or testing our drug products due to their non-compliance with federal, state or local regulations. Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the DEA, and corresponding state and foreign government agencies to ensure strict compliance with good manufacturing practice and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers compliance with these regulations and standards.

Table of Contents

If we cannot formulate and scale-up a wide range of dosage forms of Remoxy, we might determine that the commercial opportunity for Remoxy is too limited to warrant further investment in clinical testing and development.

We plan to formulate and scale-up a wide range of dosage forms of Remoxy. We may not be able to successfully complete our formulation or scale-up activities or we may determine that the commercial opportunity for Remoxy in certain dosage forms is too limited to warrant further investment.

Risks Relating to our Collaboration Agreements

If outside collaborators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard, our regulatory submissions and our product introductions may be delayed.

We depend on independent investigators and collaborators, such as universities and medical institutions, to conduct our clinical trials under agreements with us. These collaborators are not our employees and we cannot control the amount or timing of resources that they devote to our programs. These investigators may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. If outside collaborators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard, the approval of our regulatory submissions and our introductions of new drugs will be delayed.

Our collaborators may also have relationships with other commercial entities, some of which may compete with us. If outside collaborators assist our competitors to our detriment, the approval of our regulatory submissions will be delayed and the sales from our products will be less than expected.

Our collaborative agreements may not succeed or may give rise to disputes over intellectual property or other issues.

Our strategy to focus on development of novel drug candidates discovered by third parties requires us to enter into license agreements with such third parties. In addition, we may enter into collaborative agreements to commercialize our products. Such agreements are generally complex and contain provisions that could give rise to legal disputes. Such disputes can delay the development of potential new drug products, or can lead to lengthy, expensive litigation or arbitration. Other factors relating to collaborative agreements may adversely affect the success of our drug candidates, including:

- the development of parallel products by our collaborators or by a competitor;
- arrangements with collaborative partners that limit or preclude us from developing certain products or technologies;
- premature termination of a collaborative agreement; or

failure by a collaborative partner to devote sufficient resources to the development of our potential products.

Table of Contents

Risks Relating to an Investment in our Common Stock

Our stock price has been volatile and could experience a sudden decline in value.

Our common stock has experienced significant price and volume fluctuations and may continue to experience volatility in the future. You may not be able to sell your shares quickly or at the latest market price if trading in our stock is not active or the volume is low. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

- results of our preclinical and clinical trials;
- publicity regarding actual or potential medical results relating to products under development by us or others;
- announcements of technological innovations or new commercial products by us or others;
- developments in patent or other proprietary rights by us or others;
- comments or opinions by securities analysts or major stockholders;
- future sales of our common stock by existing stockholders;
- regulatory developments or changes in regulatory guidance;
- litigation or threats of litigation;
- economic and other external factors or other disaster or crises;
- the departure of any of our officers, directors or key employees;
- period-to-period fluctuations in financial results; and
- limited daily trading volume.

The National Association of Securities Dealers, Inc., or NASD, and the SEC have adopted certain new rules. If we were unable to continue to comply with the new rules, we could be delisted from trading on such market, and thereafter trading in our common stock, if any, would be conducted through the over-the-counter market or on the Electronic Bulletin Board of the NASD. As a consequence of such delisting, an

investor would likely find it more difficult to dispose of, or to obtain quotations as to the price of, our common stock. Delisting of our common stock could also result in lower prices per share of our common stock than would otherwise prevail.

Volatility in the stock prices of other companies may contribute to volatility in our stock price.

The stock market in general, and the Nasdaq National Market and the market for technology companies in particular, have experienced significant price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. Further, there has been particular volatility in the market prices of securities of early stage and development stage life sciences companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in the market price of a company s

Table of Contents

securities, securities class action litigation has often been instituted. A securities class action suit against us could result in substantial costs, potential liabilities and the diversion of management s attention and resources.

Our stock ownership is concentrated, and our officers, directors and principal stockholders can exert significant control over matters requiring stockholder approval.

Due to their combined stock holdings, our officers, directors and principal stockholders (stockholders holding greater than 5% of our common stock) acting collectively may have the ability to exercise significant influence over matters requiring stockholder approval including the election of directors and approval of significant corporate transactions. In addition, this concentration of ownership may delay or prevent a change in control of the Company and may make some transactions more difficult or impossible to complete without the support of these stockholders.

Our operating results may fluctuate from quarter to quarter and this fluctuation may cause our stock price to decline.

Our quarterly operating results have fluctuated in the past and are likely to fluctuate in the future. Factors contributing to these fluctuations include, among other items, the timing and enrollment rates of clinical trials for our drug candidates, our need for clinical supplies and the re-measurement of certain deferred stock compensation. Thus, quarter-to-quarter comparisons of our operating results are not indicative of what we might expect in the future. As a result, in some future quarters our operating results may not meet the expectations of securities analysts and investors, which could result in a decline in the price of our stock.

There may not be an active, liquid trading market for our common stock.

There is no guarantee that an active trading market for our common stock will be maintained on the Nasdaq National Market. Investors may not be able to sell their shares quickly or at the latest market price if trading in our stock is not active.

Our charter documents contain provisions that may prevent or delay removal of incumbent management or a change of control.

Provisions of our amended and restated certificate of incorporation and amended and restated bylaws may have the effect of deterring or delaying attempts by our shareholders to remove or replace management, engage in proxy contests and effect changes in control. These provisions include:

- a classified board so that only one third of the board of directors is elected each year;
- elimination of cumulative voting in the election of directors;

procedures for advance notification of shareholder nominations and proposals;

the ability of our board of directors to amend our bylaws without shareholder approval; and

the ability of our board of directors to issue up to 10,000,000 shares of preferred stock without shareholder approval upon the terms and conditions and with the rights, privileges and preferences as the board of directors may determine.

Table of Contents

In addition, as a Delaware corporation, we are subject to Delaware law, including Section 203 of the Delaware General Corporation Law. In general, Section 203 prohibits a Delaware corporation from engaging in any business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder unless certain specific requirements are met as set forth in Section 203.

These provisions, alone or together, could have the effect of deterring or delaying changes in incumbent management, proxy contests or changes in control.

Table of Contents

DISCLOSURE REGARDING FORWARD-LOOKING STATEMENTS

In addition to the other information contained or incorporated by reference in this prospectus, you should carefully consider the risk factors disclosed in this prospectus or any prospectus supplement when evaluating an investment in our common stock. This prospectus contains forward-looking statements that are based upon current expectations that are within the meaning of the Private Securities Reform Act of 1995. It is the Company s intent that such statements be protected by the safe harbor created thereby.

Forward-looking statements involve risks and uncertainties and our actual results and the timing of events may differ significantly from the results discussed in the forward-looking statements. Examples of such forward-looking statements include, but are not limited to:

- statements about future operating losses and anticipated operating and capital expenditures;
- statements about the potential benefits of our drug candidates;
- statements relating to the timing, substance, sufficiency of materials required for or anticipated results of our clinical development of our drug candidates;
- statements about the size of the potential market for our products;
- statements about upcoming announcements by the Company;
- statements relating to the utility of our intellectual property;
- statements about expected future sources of revenue and capital;
- statements about potential competitors or products;
- statements about future market acceptance of our drug candidates;
- statements about expenses increasing substantially or fluctuating;
- statements about future expectations regarding trade secrets, technological innovations, licensing agreements and outsourcing of certain business functions;
- statements about anticipated hiring;

statements about the sufficiency of our current resources to fund our operations over the next twelve months;

statements about increasing cash requirements; statements about fluctuations in our operating results;

statements about potential future dividends; and

statements about development of our internal systems and infrastructure.

Table of Contents

USE OF PROCEEDS

Unless otherwise indicated in a prospectus supplement, the net proceeds from the sale of securities offered by this prospectus will be used for general corporate purposes and working capital requirements. We may also use a portion of the net proceeds to fund possible investments in and acquisitions of complementary businesses, partnerships, minority investments, products or technologies. Currently, there are no commitments or agreements regarding such acquisitions or investments that are material. Pending their ultimate use, we intend to invest the net proceeds in money market funds, commercial paper and governmental and non-governmental debt securities with maturities of up to three years.

Table of Contents

PLAN OF DISTRIBUTION

We may sell our common stock:

- through one or more underwriters or dealers;
- through agents;
- directly to one or more purchasers; or
- through a combination of the above.

If underwriters are used in the sale, they will acquire the common stock for their own account and may resell the stock from time to time in one or more transactions at a fixed public offering price. The obligations of the underwriters to purchase the common stock will be subject to the conditions set forth in the applicable underwriting agreement. We may offer the common stock to the public through underwriting syndicates represented by managing underwriters or by underwriters without a syndicate. Each prospectus supplement will identify any underwriter, dealer or agent, and describe any compensation received by them from us. Any initial public offering price and any discounts or concessions allowed or reallowed or paid to dealers may be changed from time to time.

Underwriters, dealers or agents may receive compensation in the form of discounts, concessions or commissions from us or our purchasers as their agents in connection with the sale of the common stock. These underwriters, dealers or agents may be considered to be underwriters under the Securities Act. As a result, discounts, commissions or profits on resale received by underwriters, dealers or agents may be treated as underwriting discounts and commissions.

Underwriters or agents and their associates may be customers of, engage in transactions with or perform services for us in the ordinary course of business. We will describe in the prospectus supplement, naming the underwriter, the nature of any such relationship.

We may grant underwriters who participate in the distribution of the common stock an option to purchase additional securities to cover over-allotments, if any, in connection with the distribution. We will identify the amount of any such over-allotment option in the applicable prospectus supplement.

We will name any agent involved in the offering and sale of common stock and we will describe any commissions we will pay the agent and the terms of any agency relationship in the prospectus supplement. We may authorize agents or underwriters to solicit offers by certain types of institutional investors to purchase common stock from us at the public offering price set forth in the prospectus supplement pursuant to delayed delivery contracts providing for payment and delivery on a specified date in the future. We will describe the conditions to these contracts and the commissions we must pay for solicitation of these contracts in the prospectus supplement.

We may distribute the common stock from time to time in one or more transactions:

- at a fixed price or prices, which may be changed from time to time;
- at market prices prevailing at the time of sale;
- at prices related to prevailing market prices; and
- at negotiated prices.

A prospectus supplement or supplements will describe the method of distribution of each distribution of common stock in the applicable prospectus supplement.

Table of Contents

We may determine the price or other terms of the common stock offered under this prospectus by use of an electronic auction. We will describe how any auction will determine the price or any other terms, how potential investors may participate in the auction and the nature of the underwriters obligations in the related supplement to this prospectus.

Underwriters, dealers and agents may be entitled to indemnification by us against certain civil liabilities, including liabilities under the Securities Act, or to contribution with respect to payments made by the underwriters, dealers or agents, under agreements between us and the underwriters, dealers and agents.

In connection with the offering of the common stock, certain persons participating in such offering may engage in transactions that stabilize, maintain or otherwise affect the market price, including over-allotment, stabilizing transactions, short covering transactions and penalty bids in accordance with Regulation M under the Exchange Act. Over-allotment involves sales in excess of the offering size, which create a short position. Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum. Short covering transactions involve purchases of the common stock in the open market after the distribution is completed to cover short positions. Penalty bids permit the underwriters to reclaim a selling concession from a dealer when the common stock originally sold by the dealer is purchased in a covering transaction to cover short positions. Those activities may cause the price of the common stock to be higher than it would otherwise be. If commenced, the underwriters may discontinue any of the activities at any time.

Any underwriters who are qualified market makers on the Nasdaq National Market may engage in passive market making transactions in the common stock on the Nasdaq National Market in accordance with Rule 103 of Regulation M, during the business day prior to the pricing of the offering, before the commencement of offers or sales of the common stock. Passive market makers must comply with applicable volume and price limitations and must be identified as passive market makers. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for such security; if all independent bids are lowered below the passive market maker s bid, however, the passive market maker s bid must then be lowered when certain purchase limits are exceeded.

To the extent required, this prospectus may be amended and supplemented from time to time to describe a specific plan of distribution.

Table of Contents

LEGAL MATTERS

The validity of common stock offered hereby will be passed upon by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California.

EXPERTS

The financial statements of Pain Therapeutics, Inc. at December 31, 2003 and 2002, and for each of the two years in the period ended December 31, 2003 and for the period from May 4, 1998 (inception) through December 31, 2003, appearing in Pain Therapeutics, Inc. s Annual Report (Form 10-K) for the year ended December 31, 2003, have been audited by Ernst & Young LLP, independent auditors, as set forth in their report thereon included therein and incorporated herein by reference which, as to the period from May 4, 1998 (inception) through December 31, 2001, is based in part on the report of KPMG LLP, independent auditors. The financial statements referred to above are included in reliance upon such reports given on the authority of such firms as experts in accounting and auditing.

The financial statements of Pain Therapeutics, Inc. for the year ended December 31, 2001 have been incorporated by reference in the registration statement in reliance upon the report of KPMG LLP, independent auditors, incorporated by reference herein and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and current reports, proxy statements and other information with the SEC. We have filed with the SEC a registration statement on Form S-3 under the Securities Act with respect to the shares of common stock we are offering under this prospectus. This prospectus does not contain all of the information set forth in the registration statement and the exhibits to the registration statement. For further information with respect to us and the securities we are offering under this prospectus, we refer you to the registration statement and the exhibits and schedules filed as a part of the registration statement. You may read and copy the registration statement, as well as our reports, proxy statements and other information, at the SEC s public reference room at 450 Fifth Street, N.W., Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference rooms. Our SEC filings are also available at the SEC s web site at http://www.sec.gov.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference into this prospectus the information we filed with the SEC. This means that we can disclose important information by referring you to those documents. The information incorporated by reference is considered to be a part of this prospectus. Information that we file later with the SEC will automatically update and supersede this information. We incorporate by reference the documents listed below and any future filings made by us with the SEC under Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act (other than reports or portions furnished under Items 9 or 12 of Form 8-K) until we complete our offering of the common stock:

our annual report on Form 10-K for the fiscal year ended December 31, 2003;

our quarterly report on Form 10-Q for the fiscal quarter ended March 31, 2004; and

the description of our common stock contained in our Registration Statement on Form 8-A, filed with the Securities and Exchange Commission on March 15, 2000, and any further amendment or report filed hereafter for the purpose of updating any such description.

Table of Contents

Copies of documents incorporated by reference, excluding exhibits except to the extent such exhibits are specifically incorporated by reference, are available from us without charge, upon oral or written request to:

Pain Therapeutics, Inc.

416 Browning Way

South San Francisco, California 94080

United States of America

Attn: Investor Relations

(650) 624-8200

Table of Contents

PART II

INFORMATION NOT REQUIRED IN THE PROSPECTUS

Item 14. Other Expenses of Issuance and Distribution

The aggregate estimated expenses to be paid by the registrant in connection with this offering are as follows:

Securities and Exchange Commission registration fee	$ 13,760
Accounting fees and expenses	15,000
Legal fees and expenses	25,000
Printing Fees	5,000
Miscellaneous	6,240
Total	$ 65,000

Item 15. Indemnification of Directors and Officers of Pain Therapeutics, Inc.

Under Section 145 of the Delaware General Corporation Law, we can indemnify any person who is, or is threatened to be made, a party to any threatened, pending or completed legal action, suit or proceeding, whether civil, criminal, administrative or investigative other than action by us or on our behalf, by reason of the fact that such person is or was one of our officers or directors, or is or was serving at our request as a director, officer, employee or agent of another corporation or enterprise. The indemnity may include expenses including attorneys fees, judgments, fines and amounts paid in settlement actually and reasonably incurred by such person in connection with such action, suit or proceeding, provided that such officer or director acted in good faith and in a manner he or she reasonably believed to be in or not opposed to our best interests, and, for criminal proceedings, had no reasonable cause to believe his or her conduct was illegal. Under Delaware law, we may also indemnify officers and directors in an action by us or on our behalf under the same conditions, except that no indemnification is permitted without judicial approval if the officer or director is adjudged to be liable to us in the performance of his or her duty. Where an officer or director is successful on the merits or otherwise in the defense of any action referred to above, we must indemnify him or her against the expenses which such officer or director actually and reasonably incurred.

Our amended and restated certificate of incorporation contains a provision to limit the personal liability of our directors for violations of their fiduciary duty. This provision eliminates each director s liability to us or our stockholders for monetary damages to the fullest extent permitted by Delaware law. The effect of this provision is to eliminate the personal liability of directors for monetary damages for actions involving a breach of their fiduciary duty of care, including any such actions involving gross negligence.

Our amended and restated bylaws provide for indemnification of our officers and directors to the fullest extent permitted by applicable law.

We have also entered into indemnification agreements with our directors and officers. The indemnification agreements provide indemnification to our directors and officers under certain circumstances for acts or omissions which may not be covered by directors and officers liability

insurance. We have also obtained directors and officers liability insurance, which insures against liabilities that our directors or officers may incur in such capacities.

Table of Contents

Item 16. Exhibits

The following exhibits are filed herewith or incorporated by reference herein:

EXHIBIT INDEX

Exhibit Number	Description of Document
1.1	Form of Underwriting Agreement. (1)
5.1	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation. (1)
23.1	Consent of Ernst & Young LLP, independent auditors.
23.2	Consent of KPMG LLP, independent auditors.
23.3	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in Exhibit 5.1).
24.1	Power of Attorney of certain directors and officers of Pain Therapeutics, Inc. (included on the signature page hereof).

(1) To be filed by amendment or as an exhibit to a current report of the registrant on Form 8-K and incorporated herein by reference.

Item 17. Undertakings

(A) The undersigned registrant hereby undertakes:

(a) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(1) to include any prospectus required by Section 10(a)(3) of the Securities Act;

(2) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the SEC pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than a 20 percent change in the maximum aggregate offering price set forth in the Calculation of Registration Fee table in the effective registration statement; and

(3) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

provided, *however*, that paragraphs (1)(i) and (1)(ii) do not apply if the registration statement is on Form S-3, Form S-8 or Form F-3, and the information required to be included in a post-effective amendment by those paragraphs is contained in periodic reports filed with or furnished to the SEC by the registrant pursuant to Section 13 or 15(d) of the Exchange Act that

are incorporated by reference in the registration statement.

Table of Contents

(b) That, for the purpose of determining any liability under the Securities Act, each post-effective amendment shall be deemed to be a new registration statement relating to the securities it offers, and the offering of the securities at that time shall be deemed to be the initial bona fide offering thereof.

(c) To remove from registration by means of a post-effective amendment any of the securities being registered that remain unsold at the termination of this offering.

(B) That, for purposes of determining any liability under the Securities Act, each filing of the registrant s annual report pursuant to section 13(a) or section 15(d) of the Exchange Act (and, where applicable, each filing of an employee benefit plan s annual report pursuant to section 15(d) of the Exchange Act) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

(C) Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the SEC this form of indemnification is against public policy as expressed in the Securities Act and is, therefore, unenforceable. In the event that a claim for indemnification against these liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer or controlling person of the registrant in the successful defense of any action, suit or proceeding) is asserted by a director, officer or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question whether such indemnification by it is against public policy as expressed in the Securities Act and will be governed by the final adjudication of this issue.

Table of Contents

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3, and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California on May 7, 2004.

PAIN THERAPEUTICS, INC.

By: /s/ Remi Barbier

Remi Barbier
Chief Executive Officer and President

Table of Contents

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Remi Barbier and Peter S. Roddy, his or her true and lawful agent, proxy and attorney-in-fact, each acting alone, with full power of substitution and resubstitution, for him or her and in his or her name, place and stead, in any and all capacities, to (i) act on, sign, and file with the SEC any and all amendments (including post-effective amendments) to this registration statement together with all schedules and exhibits thereto, (ii) act on, sign and file such certificates, instruments, agreements and other documents as may be necessary or appropriate in connection therewith, (iii) act on and file any supplement to any prospectus included in this registration statement or any such amendment or any subsequent registration statement filed pursuant to Rule 462(b) under the Securities Act, and (iv) take any and all actions which may be necessary or appropriate to be done, as fully for all intents and purposes as he or she might or could do in person, hereby approving, ratifying and confirming all that such agent, proxy and attorney-in-fact or any of his substitutes may lawfully do or cause to be done by virtue thereof.

Pursuant to the requirements of the Securities Act, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated:

Signature	Title	Date
/s/ Remi Barbier Remi Barbier	Chief Executive Officer, President (Principal Executive Officer) and Director	May 7, 2004
/s/ Peter S. Roddy Peter S. Roddy	Chief Financial Officer (Principal Financial and Accounting Officer)	May 7, 2004
/s/ Nadav Friedmann, M.D., Ph.D. Nadav Friedmann, M.D., Ph.D.	Director	May 7, 2004
/s/ Robert Z. Gussin, Ph.D. Robert Z. Gussin, Ph.D.	Director	May 7, 2004
/s/ Vernon R. Loucks, Jr. Vernon R. Loucks, Jr.	Director	May 7, 2004
/s/ Michael J. O Donnell Michael J. O Donnell	Director	May 7, 2004
/s/ Sanford R. Robertson Sanford R. Robertson	Director	May 7, 2004

Table of Contents

EXHIBIT INDEX

Exhibit Number	Description
1.1	Form of Underwriting Agreement.(1)
5.1	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation. (1)
23.1	Consent of Ernst & Young LLP, independent auditors.
23.2	Consent of KPMG LLP, independent auditors.
23.3	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in Exhibit 5.1).
24.1	Power of Attorney of certain directors and officers of Pain Therapeutics, Inc. (included on signature page hereof).

(1) To be filed by amendment or as an exhibit to a current report of the registrant of Form 8-K and incorporated herein by reference.