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SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

Form 10-K

ANNUAL REPORT UNDER SECTION 13 or 15(d)
OF THE SECURITIES EXCHANGE ACT OF 1934

(Mark One)

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

For the Fiscal Year Ended December 31, 2004

or

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

Commission File Number: 000-29959

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)**

Remi Barbier
President and Chief Executive Officer
416 Browning Way
South San Francisco, CA 94080
(650) 624-8200
(Address, including zip code, or registrant's principal executive offices and telephone number, including area code)

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

Securities registered pursuant to Section 12(g) of the Act: Common Stock, $0.001 par value

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

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

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12-b-2 of Act). Yes ☒ No ☐

The aggregate market value of the voting and non-voting common equity held by non-affiliates was $351,912,625 computed by reference to the last sales price of $8.06 as reported by the Nasdaq National Market System, as of the last business day of the Registrant's most recently completed second fiscal quarter, June 30, 2004.

The number of shares outstanding of the Registrant's common stock on February 11, 2005 was 43,661,616.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement for its 2005 Annual Meeting of Stockholders (the "Proxy Statement"), to be filed with the Securities and Exchange Commission, are incorporated by reference to Part III of this Form 10-K Report.

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PART I

This document contains forward-looking statements that are based upon current expectations that are within the meaning of the Private Securities Reform Act of 1995. We intend 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:

- timing of commencement and completion of enrollment of patients for our clinical trials and the anticipated number of patients to be enrolled;
- expected dates of announcement of achievement of our clinical milestones and results of our clinical trials;
- expansion of our product pipeline;
- future operating losses and anticipated operating and capital expenditures;
- uses of proceeds from our securities offerings.
- the potential benefits of our drug candidates;
- the sufficiency of materials required for the clinical development of our drug candidates;
- the size of the potential market for our products;
- the utility or protection of our intellectual property;
- expected future sources of revenue and capital or increasing cash needs;
- potential competitors or competitive products;
- future market acceptance of our drug candidates;
- expenses increasing substantially or fluctuations in our operating results;
- future expectations regarding trade secrets, technological innovations, licensing agreements and outsourcing of certain business functions;
- anticipated hiring and development of our internal systems and infrastructure;
- the sufficiency of our current resources to fund our operations over the next twelve months; and
- potential future dividends.

Such forward-looking statements involve risks and uncertainties, including, but not limited to, those risks and uncertainties relating to:

- difficulties or delays in development, testing, clinical trials (including patient enrollment), regulatory approval, production and commercialization of our drug candidates;
- unexpected adverse side effects or inadequate therapeutic efficacy of our drug candidates that could slow or prevent product approval (including the risk that current and past results of clinical trials are not indicative of future results of clinical trials);
- the uncertainty of patent protection for our intellectual property or trade secrets;
- potential infringement of the intellectual property rights or trade secrets of third parties;
- pursuing in-license and acquisition opportunities;
- hiring and retaining personnel; and
- our financial position and our ability to obtain additional financing if necessary.

In addition such statements are subject to the risks and uncertainties discussed in the “Risk Factors” section and elsewhere in this document.

Item 1. *Business*

Overview

We are a biopharmaceutical company dedicated to the development of innovative drugs. We specialize in developing safer or more efficacious drugs for use in pain management, particularly in the area of opioid painkillers, which are sometimes referred to as narcotic painkillers. According to IMS Health, sales for opioid painkillers in the United States exceeded $5.6 billion in 2003. We own worldwide commercial rights to all of our drug candidates. We incorporated in Delaware in May 1998.

Our clinical pipeline consists of three proprietary drug candidates. We are developing these three oral, small molecule drugs to treat patients who suffer from severe chronic pain, such as pain associated with advanced osteoarthritis, low-back pain or irritable bowel syndrome, or IBS.

Our novel drug candidates are in multiple Phase III clinical trials. Our drug candidates are:

- Oxytrex™, a new oral opioid painkiller that is currently in two Phase III clinical trials for the treatment of severe chronic pain;
- PTI-901, a drug candidate that is currently in two Phase III clinical trials to treat men and women with IBS; and
- Remoxy™, an anti-abuse version of long-acting oxycodone that is currently in one Phase III clinical trial.

Oxytrex

Oxytrex is an oral opioid painkiller with a novel mechanism of action. We believe Oxytrex could be an effective substitute for oxycodone, a narcotic painkiller widely used today to treat severe chronic pain. Sales of oxycodone exceeded $1.9 billion in 2003. We own worldwide commercial rights to Oxytrex.

Our clinical results to date have shown that Oxytrex provides superior and prolonged pain relief compared to oxycodone. Published pre-clinical results also demonstrate that the technology used in Oxytrex results in a lack of opioid addiction, tolerance or physical dependence in animals. However, for ethical reasons we have not tested these properties in humans and we are not evaluating these properties in our Phase III clinical trials.

We are conducting two large, randomized, double-blinded, placebo-controlled Phase III clinical trials with Oxytrex in patients who suffer from severe chronic pain. Both Phase III clinical trials are being conducted to compare the analgesic efficacy of Oxytrex relative to oxycodone or placebo during a three-month treatment period. The primary endpoints in both clinical trials are similar: analgesic efficacy of Oxytrex, as measured by clinically accepted criteria.

In June 2003, we initiated the first clinical trial to assess the analgesic efficacy of Oxytrex in over 700 patients with severe low-back pain. This trial enrolled patients in over 40 U.S. clinical sites. In September 2004, we successfully completed patient enrollment in this clinical trial. This study remains blinded. We expect to announce results of this clinical trial in the first quarter of 2005.

In March 2004, we initiated a second Phase III clinical trial with Oxytrex. This clinical trial is being conducted to assess the analgesic efficacy of Oxytrex in over 700 patients with severe osteoarthritic pain. This second clinical trial continues to enroll patients in over 40 U.S. clinical sites. We expect to complete patient enrollment in this clinical trial in the second quarter of 2005. We also expect to announce results for this clinical trial in the second half of 2005.

Oxytrex is formulated with two active drug ingredients: oxycodone and low-dose naltrexone. Oxycodone is a strong narcotic painkiller that was developed around 1920 as a substitute for morphine. When used as prescribed, oxycodone can relieve severe chronic pain. We believe we have produced sufficient clinical materials necessary to complete two Phase III clinical trials of Oxytrex. We rely on a limited number of third-party manufacturers to manufacture, fill, label, ship and store Oxytrex.

PTI-901

PTI-901 is intended to treat men or women who suffer from chronic IBS. If approved by the Food and Drug Administration, or FDA for this indication, we believe PTI-901 will target a market in excess of $1 billion per year. We own worldwide commercial rights to PTI-901.

Chronic IBS is a painful abdominal disorder that leads to major changes in bowel habits. Published presentations estimate that IBS afflicts over 10% of the U.S. population and accounts for about 20% to 50% of referrals to gastroenterology clinics. The causes of IBS are not known and currently there is no cure. 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. Both of these drugs impact gut motility. These motility drugs slow down or speed up the gut, thereby relieving diarrhea or constipation, respectively.

In contrast, we view IBS as a nervous system disorder with gut-related symptoms. We believe an appropriate dose of PTI-901 modulates aberrant neuronal communication within the gut, thus restoring proper bowel function and relieving abdominal pain. In this regard, we believe PTI-901 represents a novel mechanism of action.

Our clinical results to date have shown in a 50-patient open-label study that patients with IBS reported a 76% response rate to PTI-901. This response rate was observed in men and women and occurred without drug-related safety issues.

Based on these results and our discussions with the FDA, we initiated a Phase III program with PTI-901 in November 2003. This program consists of two Phase III clinical trials that are designed to be identical in all respects, except for gender. The first trial plans to enroll 600 women, while the second trial plans to enroll 600 men. Each Phase III clinical trial is randomized double-blinded and placebo-controlled and will assess the clinical effects of a once-daily dose of PTI-901 during a three-month treatment period. The primary endpoint is relief of IBS symptoms as measured by clinically accepted criteria. We expect to announce results for this Phase III clinical trial in women in the second half of 2005. As expected, patient enrollment rates in the Phase III clinical trial for women have been faster than the patient enrollment rate for men. We believe this difference in enrollment rates is due to this disease affecting more women than men.

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

Remoxy

In November 2003, we announced a novel drug candidate that we named Remoxy. Remoxy is being developed as an anti-abuse version of long-acting oral oxycodone. Sales of long-acting oxycodone were approximately $1.9 billion in 2003. We own worldwide commercial rights to Remoxy.

The active drug ingredient in Remoxy is oxycodone. Oxycodone has an abuse potential similar to morphine. The U.S. Drug Enforcement Administration, or the DEA, and the national media have linked illicit oxycodone use to widespread patterns of drug abuse, addiction, diversion and drug overdose. In the United States, drug-abuse related emergency room visits are reported by the Department of Health and Human Service's Drug Abuse Warning Network, or DAWN. DAWN reports 22,000 oxycodone mentions in emergency room visits in 2002, a 450% increase from 4,000 oxycodone mentions in emergency room visits in 1994.

Remoxy's novel formulation is specifically designed to foil abusers who attempt to tamper with the drug in order to induce a powerful euphoric high. Our clinical results to date demonstrate Remoxy is significantly less abusable than Oxycontin®, a brand leader in long-acting oxycodone. During 2004, we announced data from clinical comparisons of the two drugs. In these studies, Oxycontin released significantly more active ingredient than Remoxy in a variety of abuse studies during the time when abusers presumably expect to get high.

We initiated a Phase III clinical program with Remoxy in the United States in December 2004. The first clinical trial in this program is a randomized, double-blinded placebo-controlled, multi-center study being conducted to confirm the efficacy and safety of Remoxy against placebo in approximately 200 patients with moderate-to-severe osteoarthritic pain during a four-week treatment period. We expect to conduct this trial in about 20 clinical sites in the United States. We expect to conduct additional clinical trials of additional formulations of Remoxy in 2005, including at least one additional Phase III clinical trial.

We believe the anti-abuse technology used in Remoxy is applicable to different oral opioid painkillers. Using this platform technology, we may seek to develop anti-abuse versions of one or more additional opioid painkillers.

Remoxy is formulated with Durect Corporation's ORADUR™ 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 ORADUR technology. We plan to formulate and scale-up a 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.

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

Strategy

Our commercial goal is to build a drug franchise in pain management. Our clinical goal is to continue to develop novel drugs that are more effective or safer than drugs used in the clinic today. Our strategy includes the following elements:

Focus 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.

Retain 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. 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.

Outsource 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 can benefit from our core expertise in drug development. Such in-licensing or acquisition opportunities may be in pain management or in other therapeutic areas outside of pain management. We believe this element of our corporate strategy could diversify some of the risks inherent in focusing on a single therapeutic area and could also increase our probability of commercial success.

Our Science and Technology

Our science related to the use of opioid agonists combined with opioid antagonist or the use of agonists alone 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.

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.

We also conduct basic research in collaboration with academic and other partners.

Company sponsored research and development expenditures were $11.4 million, $18.9 million, and $35.0 million in 2002, 2003 and 2004, respectively.

License from Albert Einstein College of Medicine

We have licensed certain technology from Albert Einstein College of Medicine. We have a worldwide exclusive license to the technology and all intellectual rights arising from the technology. Our license rights

terminate upon the expiration of the patents used to protect the technology, which are scheduled to expire no earlier than September 2012. Pursuant to the agreement for the licensed technology, we paid Albert Einstein College of Medicine a one-time licensing fee and are required to pay clinical milestone payments and royalties based on a percentage of net drug sales. If a product is combined with a drug or other substance for which we are paying an additional royalty, the royalty that we pay to Albert Einstein College of Medicine will be reduced by up to one-half of the amount of such additional royalty.

Albert Einstein College of Medicine originally received grants from the U.S. federal government to research some of the technology that we license. The terms of these grants provide the U.S. federal government with a non-exclusive, non-transferable paid-up license to practice inventions made with federal funds. Thus, our licenses are non-exclusive to the extent of the U.S. government's license. If the U.S. government exercises its rights under this license, it could make use of the same technology that we license and the size of our potential market could thereby be reduced.

Our Intellectual Property

We seek to protect our technology by, among other methods, filing and prosecuting U.S. and foreign patents and patent applications with respect to our technology and products and their uses. We plan to prosecute and defend our patent applications, issued patents and proprietary information. Our competitive position and potential future revenues will depend in large part upon our ability to protect our intellectual property from challenges and to enforce our patent rights against potential infringements. If our competitors are able to successfully challenge the validity of our patent rights, based on the existence of prior art or otherwise, they would be able to market products that contain features and clinical benefits similar to those of our products, and demand for our products could decline as a result.

The focus of our patent strategy is to secure and maintain intellectual property rights to technology for the following categories of our business:

- the clinical use of a low-dose opioid antagonist, either alone or in combination with an opioid painkiller, for pain management and opioid and other addiction;
- the use of a low-dose opioid antagonist to render opioid-based products more effective;
- the clinical use of a low-dose opioid antagonist for the treatment of IBS; and
- the clinical use of a low-dose opioid antagonist, either alone or in combination with any opioid painkiller, for the treatment of other conditions.

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. We may be involved in additional challenges to our intellectual property. An adverse outcome of the reexamination process or any other challenges to our intellectual property 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.

Formulation Agreement

We have an exclusive, worldwide licensing agreement with Durect Corporation. Remoxy is formulated with Durect's ORADUR technology under our agreement with Durect. ORADUR is a patented technology that forms

the basis for a number of oral gel-cap drug candidates, including Remoxy. We plan to complete formulation and scale-up of additional dosage forms of Remoxy to use in late stage clinical trials and commercialization. We have exclusive worldwide rights to develop and to commercialize Remoxy and certain other opioid drugs formulated with Durect's ORADUR technology under our agreement with Durect. We control all of Remoxy's pre-clinical, clinical, commercial manufacturing and sales/marketing activities. 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. We can terminate the agreement without cause and Durect can terminate the agreement only if we do not cure defaults in our obligations under the agreement within a certain period of time.

Manufacturing

We have no manufacturing facilities. We have entered into agreements with and rely upon qualified third parties for the formulation or manufacture of our clinical supplies. These supplies and the manufacturing facilities must comply with DEA regulations and current good manufacturing practices, or GMPs, enforced by the FDA and other government agencies. We plan to continue to outsource formulation, manufacturing and related activities.

In 2005, we plan to continue to develop formulations of Remoxy and manufacture Remoxy to complete our Phase III program. We rely on a limited number of third-party manufacturers to formulate, manufacture, fill, label, ship or store all of our drug candidates.

Government Regulation

Regulation by governmental authorities in the United States and other countries is a significant factor in the manufacture and marketing of pharmaceuticals and in our ongoing research and development activities. All of our products will require regulatory approval by governmental agencies prior to commercialization. In particular, human therapeutic products are subject to rigorous pre-clinical testing and clinical trials and other pre-marketing approval requirements by the FDA and regulatory authorities in other countries. In the United States, various federal, and in some cases state, statutes and regulations also govern or impact upon the manufacturing, safety, labeling, storage, record keeping and marketing of our products. The lengthy process of seeking required approvals and the continuing need for compliance with applicable statutes and regulations require us to spend substantial resources. Regulatory approval, when and if obtained, may be limited in scope which may significantly limit the indicated uses for which our products may be marketed. Further, approved drugs, as well as their manufacturers, are subject to ongoing review and discovery of previously unknown problems with such products that may result in restrictions on their manufacture, sale or use or in their withdrawal from the market.

Applicable FDA regulations treat Oxytrex and PTI-901 as new drugs and require the filing of a New Drug Application, or NDA, and approval by the FDA prior to commercialization in the United States.

The Drug Approval Process

We will be required to complete several activities before we can market any of our drugs for human use in the United States, including:

- pre-clinical studies;
- submission to the FDA of an Investigational New Drug application, or IND, which must become effective before human clinical trials commence;
- adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug candidate;
- submission to the FDA of an NDA; and
- FDA approval of the NDA prior to any commercial sale or shipment of the drug.

Pre-clinical tests include laboratory evaluation of product chemistry and formulation, as well as animal studies to assess the potential safety of the product. Pre-clinical safety tests must be conducted by laboratories that comply with FDA regulations regarding Good Laboratory Practice. We submitted the results of pre-clinical tests to the FDA as part of our INDs prior to commencing clinical trials. We may be required to conduct additional toxicology studies concurrently with the clinical trials.

Based on pre-clinical testing, an IND is filed with the FDA to begin human testing of the drug in the United States. The IND becomes effective if not rejected by the FDA within 30 days. The IND must indicate the results of previous experiments, how, where and by whom the new clinical trials will be conducted, the chemical structure of the compound, the method by which it is believed to work in the human body, any toxic effects of the compound found in the animal studies and how the compound is manufactured. All clinical trials must be conducted in accordance with Good Clinical Practice. In addition, an Institutional Review Board, or IRB, generally comprised of physicians at the hospital or clinic where the proposed studies will be conducted, must review and approve the IND. The IRB also continues to monitor the study. We must submit progress reports detailing the results of the clinical trials to the FDA at least annually. In addition, the FDA may, at any time during the 30-day period or at any time thereafter, impose a clinical hold on proposed or ongoing clinical trials. If the FDA imposes a clinical hold, clinical trials under the IND cannot commence or recommence without FDA authorization and then only under terms authorized by the FDA. An FDA imposed clinical hold on an IND application can result in substantial delay and large, unforeseen expenses, and it may cancel the viability of developing a new drug candidate in the United States.

Clinical trials are typically conducted in three sequential phases that may overlap. Phase I tests typically study a drug's safety profile, and may include the safe dosage range. Phase I clinical trials also determine how a drug is absorbed, distributed, metabolized and excreted by the body, and the duration of its action. In addition, we may, to the extent feasible, assess early indicators of a drug's efficacy in our Phase I trials. In Phase II clinical trials, controlled studies are conducted on volunteer patients with the targeted disease or condition. The primary purpose of these tests is to evaluate the effectiveness of the drug on the volunteer patients as well as to determine a drug's side effect profile. These trials may be conducted concurrently with Phase I clinical trials. In addition, Phase I/II clinical trials may be conducted to evaluate not only the efficacy of the drug on the patient population, but also its safety. During Phase III clinical trials, the drug is studied in an expanded patient population and in multiple sites. Physicians monitor the patients to determine efficacy and to observe and report adverse events that may result from use of the drug.

Our trials are designed to produce clinical information about how our drugs perform compared to placebo or compared to existing opioid drugs where appropriate. We plan to test Oxytrex in several clinical settings of pain in order to support a broad approval by the FDA for use of the drug for the relief of moderate to severe pain. FDA guidelines recommend that we demonstrate Oxytrex's efficacy in more than one clinical presentation of pain, such as arthritis pain or generalized lower back pain. Because clinical models differ in their sensitivity to detect pain, we expect to complete studies in multiple clinical models of pain.

We have designed most Phase II and Phase III clinical trials to date as randomized, double-blind, placebo- controlled, dose-ranging studies. A randomized trial is one in which patients are randomly assigned to the various study treatment arms. A double-blind trial is one in which the patient, the physician and our trial monitor are unaware if the patient is receiving placebo or study drug in order to preserve the integrity of the trial and reduce bias. A placebo-controlled trial is one in which a subset of patients is purposefully given inactive medication.

The FDA publishes industry guidelines specifically for the clinical evaluation of painkillers. We rely in part on these guidelines to design a clinical strategy for the approval of each of our drug candidates. In particular, FDA guidelines recommend that we demonstrate efficacy of our new painkillers in more than one clinical model of pain. Acceptable clinical models of pain include low-back pain or arthritis pain. Upon a clear demonstration of the safety and efficacy of painkillers in multiple clinical models of pain, the FDA has historically approved painkillers with broad indications. Such general purpose labeling often takes the form of "for the management of moderate to severe pain."

We may not successfully complete Phase I, Phase II or Phase III trials within any specified time period, or at all, with respect to any of our drug candidates. Furthermore, we or the FDA may suspend clinical trials at any time in response to concerns that participants are exposed to an unacceptable health risk.

After the completion of clinical trials, if there is substantial evidence that the drug is safe and effective, an NDA is filed with the FDA. The NDA must contain all of the information on the drug gathered to that date, including data from the clinical trials. NDAs are often over 100,000 pages in length.

The FDA reviews all NDAs submitted before it accepts them for filing and may request additional information rather than accepting a NDA for filing. In such an event, the NDA must be resubmitted with the additional information and, again, is subject to review before filing. Once the submission is accepted for filing, the FDA begins an in-depth review of the NDA. Under the Federal Food, Drug and Cosmetic Act, the FDA has 365 days in which to review the NDA and respond to the applicant. The review process is typically extended for significant amounts of time by the FDA requests for additional information or clarification regarding information already provided in the submission. The FDA may refer the application to an appropriate advisory committee, typically a panel of clinicians, for review, evaluation and a recommendation as to whether the application should be approved. The FDA is not bound by the recommendation of an advisory committee. If the FDA's evaluations of the NDA and the manufacturing facilities are favorable, the FDA may issue either an approval letter, or an approvable letter which usually contains a number of conditions that must be met in order to secure final approval of the NDA. When and if those conditions have been met to the FDA's satisfaction, the FDA will issue an approval letter, authorizing commercial marketing of the drug for certain indications. If the FDA's evaluation of the NDA submission or manufacturing facilities is not favorable, the FDA may refuse to approve the NDA or issue a not approvable letter.

If the FDA approves the NDA, the drug becomes available for physicians to prescribe. Periodic reports must be submitted to the FDA, including descriptions of any adverse reactions reported. The FDA may request additional post marketing studies, or Phase IV studies, to evaluate long-term effects of the approved drug.

Other Regulatory Requirements

The FDA mandates that drugs be manufactured in conformity with current GMPs. If the FDA approves any of our drug candidates we will be subject to requirements for labeling, advertising, record keeping and adverse experience reporting. Failure to comply with these requirements could result, among other things, in suspension of regulatory approval, recalls, injunctions or civil or criminal sanctions. We may also be subject to regulations under other federal, state, and local laws, including the Occupational Safety and Health Act, the Environmental Protection Act, the Clean Air Act, national restrictions on technology transfer, and import, export, and customs regulations. In addition, any of our products that contain narcotics will be subject to DEA regulations relating to manufacturing, storage, distribution and physician prescribing procedures. It is possible that any portion of the regulatory framework under which we operate may change and that such change could have a negative impact on our current and anticipated operations.

The Controlled Substances Act imposes various registration, record-keeping and reporting requirements, procurement and manufacturing quotas, labeling and packaging requirements, security controls and a restriction on prescription refills on certain pharmaceutical products. A principal factor in determining the particular requirements, if any, applicable to a product is its actual or potential abuse profile. 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. Any of our drug candidates that contain a scheduled substance will be subject to regulation by the DEA.

Competition

Our success will depend, in part, upon our ability to achieve market share at the expense of existing and established and future products in the relevant target markets. Existing and future products, therapies, technological approaches or delivery systems will compete directly with our products. Competing products may

provide greater therapeutic benefits for a specific indication, or may offer comparable performance at a lower cost. Companies that currently sell generic or proprietary opioid formulations include but are not limited to Roxane Laboratories, Purdue Pharma, Janssen Pharmaceutica, Abbott Laboratories, Cephalon, Endo Pharmaceuticals, Teva Pharmaceuticals, Elkins-Sinn, Watson Laboratories, Ortho-McNeil Pharmaceutical and Forest Pharmaceuticals. Alternative technologies are being developed to increase opioid potency, as well as alternatives to opioid therapy for pain management, several of which are in clinical trials or are awaiting approval from the FDA. Companies that sell drugs to treat IBS include Novartis and GlaxoSmithKline. We believe that a number of other companies are developing new drug candidates to treat IBS.

We compete with fully integrated pharmaceutical companies, smaller 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 drugs already approved by the FDA or in development and operate larger research and development programs in these fields than we do. In addition, many of these competitors, either alone or together with their collaborative partners, have substantially greater financial resources than we do, as well as significantly greater experience in:

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

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

Employees

As of December 31, 2004, we had approximately 31 employees. We engage consultants from time to time to perform services on a per diem or hourly basis.

Available Information

We file electronically with the Securities and Exchange Commission, or SEC, our Annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934. The public may read or copy any materials we file with the SEC at the SEC's Public Reference Room at 450 Fifth Street, NW, Washington, DC 20549. The public may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is http://www.sec.gov.

You may obtain a free copy of our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports on the day of filing with the SEC on our website on the World Wide Web at http://www.paintrials.com, by contacting the Investor Relations Department at our corporate offices by calling 650-824-8200 or by sending an e-mail message to cwaarich@paintrials.com.

Item 2. ***Properties***

We currently lease approximately 10,500 square feet of space in South San Francisco, California, which is used as general office space. We believe that this facility is adequate and suitable for our current needs.

Item 3. ***Legal Proceedings***

We are not a party to any legal proceedings.

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

There were no matters submitted to a vote of the security holders during the fourth quarter of 2004.

PART II

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

Our common stock is quoted on the Nasdaq National Market under the symbol "PTIE." The following table sets forth the high and low sales prices per share of our common stock as reported on the Nasdaq National Market for the periods indicated.

	Sale Price	
	High	Low
Fiscal 2004:		
First Quarter	$9.86	$5.77
Second Quarter	$9.34	$6.54
Third Quarter	$8.39	$6.22
Fourth Quarter	$8.13	$6.82
Fiscal 2003:		
First Quarter	$3.90	$1.68
Second Quarter	$8.11	$1.68
Third Quarter	$8.95	$5.90
Fourth Quarter	$7.71	$4.44

We currently expect to retain future earnings, if any, for use in the operation and expansion of our business and have not paid and do not anticipate paying any cash dividends in the foreseeable future. As of February 7, 2005, there were approximately 76 holders of record of our common stock.

In 2003, we issued 7,730,500 shares of common stock at $6.50 per share in a follow-on public offering and received approximately $46.7 million after deducting underwriting discounts and related expenses.

In 2004, we registered with the Securities and Exchange Commission and reserved 15,000,000 shares of common stock to be offered via prospectus in amounts, at prices and at terms determined at the time of an offering and may be sold directly by us to investors, through agents designated from time to time, or to or through underwriters or dealers. In 2004, we issued 8,000,000 shares of common stock at $7.25 per share in a follow-on public offering under such registration statement and received approximately $54.5 million after deducting underwriting discounts and related expenses.

From the time of receipt through December 31, 2004, the net proceeds from our public offerings were used for research and development activities, capital expenditures, working capital and other general corporate purposes. As of December 31, 2004, $99.4 million of the proceeds from our public offerings remained available.

The following table summarizes the securities authorized for issuance under our equity compensation plans as of December 31, 2004.

Plan Category	Number of Securities to be Issued Upon Exercise of Outstanding Options, Warrants and Rights	Weighted Average Exercise Price of Outstanding Options, Warrants and Rights	Number of Securities Remaining Available for Future Issuance Under Equity Compensation Plans
Equity compensation plans approved by stockholders	5,334,734	$ 6.94	2,504,206
Equity compensation plans not approved by stockholders	—	—	—
Total	5,334,734	$ 6.94	2,504,206

Item 6. ***Selected Financial Data (in thousands except per share data)***

	Years ended December 31,					May 4, 1998 (inception) through December 31, 2004
	2004	2003	2002	2001	2000	
Statement of operations data:						
Research and development expense	$ 35,093	$ 18,913	$ 11,396	$ 11,668	$ 12,596	$ 93,933
General and administrative expense	3,868	3,338	5,523	5,647	7,710	26,902
Total operating expenses	38,961	22,251	16,919	17,315	20,306	120,835
Operating loss	(38,961)	(22,251)	(16,919)	(17,315)	(20,306)	(120,835)
Interest income	1,185	634	994	2,978	2,826	8,811
Net loss	(37,776)	(21,617)	(15,925)	(14,337)	(17,480)	(112,024)
Return to series C preferred stockholders for beneficial conversion feature	—	—	—	—	(14,231)	(14,231)
Loss available to common stockholders	$ (37,776)	$ (21,617)	$ (15,925)	$ (14,337)	$ (31,711)	$ (126,255)
Basic and diluted loss per common share	$ (1.01)	$ (0.73)	$ (0.59)	$ (0.57)	$ (2.33)	
Weighted average shares used in computing basic and diluted loss per common share	37,267	29,483	27,039	25,332	13,635	

	At December 31,				
	2004	2003	2002	2001	2000
Balance sheet data:					
Cash and cash equivalents	$ 1,379	$ 12,027	$ 50,091	$ 65,274	$ 78,927
Marketable securities	98,018	65,402	55	—	—
Working capital	91,860	74,799	48,146	63,195	77,320
Total assets	101,192	80,513	53,325	68,136	81,147
Total liabilities	7,796	3,951	3,101	2,519	2,452
Stockholders' equity	93,396	76,562	50,224	65,616	78,695

Item 7. ***Management's Discussion and Analysis of Financial Condition and Result of Operations***

This discussion and analysis should be read in conjunction with our financial statements and accompanying notes included elsewhere in this report. Operating results are not necessarily indicative of results that may occur in future periods.

Overview

We are a biopharmaceutical company dedicated to the development of innovative drugs. We specialize in developing safer or more efficacious drugs for use in pain management, particularly in the area of opioid painkillers. U.S. sales of opioid painkillers exceeded $5.6 billion in 2003. We own worldwide commercial rights to all of our drug candidates.

Our clinical pipeline consists of three proprietary drug candidates. We are developing these three oral, small molecule drugs to treat patients who suffer from severe chronic pain, such as pain associated with advanced osteoarthritis, low-back pain or IBS.

Our drug candidates are:

- Oxytrex™, a new oral opioid painkiller that is currently in two Phase III clinical trials for the treatment of severe chronic pain;

- PTI-901, a drug candidate to treat men and women with IBS that is currently in two Phase III clinical trials; and
- Remoxy™, an anti-abuse version of long-acting oxycodone that is currently in one Phase III clinical trial and non-clinical studies.

We have yet to generate any revenues from product sales. We have not been profitable and, since our inception on May 4, 1998 through December 31, 2004, we have recorded an accumulated deficit of approximately $112.0 million. These losses have resulted principally from costs incurred in connection with research and development activities, salaries and other personnel-related costs and general corporate expenses. Research and development activities include costs of preclinical and clinical trials as well as clinical supplies associated with our drug candidates. Salaries and other personnel-related costs include non-cash stock-based compensation associated with options granted to employees and non-employees. Our operating results may fluctuate substantially from period to period as a result of the timing and enrollment rates of clinical trials for our drug candidates and our need for clinical supplies.

We expect to incur significant additional operating losses for the next several years. Our cash requirements for operating activities and capital expenditures will increase substantially in the future as we:

- continue to conduct preclinical and clinical trials for our drug candidates, including the Phase III clinical trials of Oxytrex, PTI-901 and Remoxy as well as formulation and development activities for Remoxy;
- seek regulatory approvals for our drug candidates;
- develop, formulate, manufacture and commercialize our drug candidates;
- 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.

Product revenue will depend on our ability to receive regulatory approvals for, and successfully market, our drug candidates. If our development efforts result in regulatory approval and successful commercialization of our drug candidates, we will generate revenue from direct sales of our drugs and/or, if we license our drugs to future collaborators, from the receipt of license fees and royalties from sales of licensed products. We conduct our research and development programs through a combination of internal and collaborative programs. We rely on arrangements with universities, our collaborators, contract research organizations and clinical research sites for a significant portion of our product development efforts.

Since our inception, we have focused all our research and development efforts on the research and development of opioid drugs for the treatment of pain. Research and development expenses related to this project for the period from inception through December 31, 2004 total $93.9 million. The following table summarizes expenses by category for research and development efforts (in thousands):

	Years Ended December 31,			May 4, 1998 (Inception) Through December 31
	2004	2003	2002	2004
Compensation	$ 3,769	$ 3,690	$ 3,097	$ 20,688
Contractor fees [1]	26,605	10,049	5,281	55,016
Supplies [2]	2,575	3,262	2,357	12,121
Other [3]	2,144	1,912	661	6,108
	$35,093	$18,913	$11,396	$ 93,933

(1) Contractor fees generally include expenses for preclinical studies and clinical trials.
(2) Supplies generally include costs for formulation and manufacturing activities.
(3) Other generally includes the allocation of common costs such as facilities.

Our technology has been applied across our portfolio of drug candidates. Data, know-how, personnel, clinical results, research results and other matters related to the research and development of any one of our drug candidates also relate to, and further the development of, our other drug candidates. As a result, costs allocated to a specific drug candidate may not necessarily reflect the actual costs surrounding research and development of that drug candidate due to cross application of the foregoing.

Estimating the dates of completion of clinical development, and the costs to complete development, of our drug candidates would be highly speculative, subjective and potentially misleading. Pharmaceutical products take a significant amount of time to research, develop and commercialize. The clinical trial portion of the development of a new drug alone usually spans several years. We expect to reassess our future research and development plans based on our review of data we receive from our current research and development activities. The cost and pace of our future research and development activities are linked and subject to change.

Critical Accounting Policies

The preparation of our financial statements in accordance with United States generally accepted accounting principles requires us to make estimates and assumptions that affect the reported amounts of assets, liabilities, expenses and interest income in our financial statements and accompanying notes. We evaluate our estimates on an ongoing basis, including those estimates related to contract agreements, research collaborations and investments. We base our estimates on historical experience and various other assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. The following items in our financial statements require significant estimates and judgments:

- *Expenses for clinical trials.* Expenses for clinical trials are incurred from planning through patient enrollment to reporting of the underlying data. We estimate expenses incurred for clinical trials that are in process based on patient enrollment and based on clinical data collection and management. Costs that are associated with patient enrollment are recognized as each patient in the trial completes enrollment. Costs that are based on clinical data collection and management are recognized based on estimates of unbilled goods and services received. In the event of early termination of a clinical trial, we would accrue an amount based on estimates of the remaining non-cancelable obligations associated with winding down the trial.
- *Stock based compensation.* The preparation of the financial statement footnotes requires us to estimate the fair value of stock options granted to employees. While fair value may be readily determinable for awards of stock, market quotes are not available for long-term, nontransferable stock options because these instruments are not traded. We currently use the Black-Scholes option-pricing model to estimate the fair value of employee stock options. However, the Black-Scholes model was developed for use in estimating the fair value of traded options, which have no vesting restrictions and are fully transferable. Option valuation models require the input of highly subjective assumptions, including but not limited to stock price volatility. Because our stock options have characteristics significantly different from those of traded options, and changes to the assumptions used in the Black-Scholes model may materially affect the fair value estimate, in management's opinion, the existing models do not provide a reliable single measure of the fair value of our employee stock options. We are currently evaluating our option valuation methodologies and assumptions in light of current accounting standards related to employee stock options.

Results of Operations

Years Ended December 31, 2004 and 2003

Research and Development

Research and development expense consists primarily of costs of drug development work associated with our drug candidates, including:

- preclinical testing,
- clinical trials,
- clinical supplies and related formulation and design costs, and
- salaries and other personnel-related expenses.

Research and development expense increased to $35.1 million from $18.9 million in the years ended December 31, 2004 and 2003, respectively. The increase was primarily due to the increase in Phase III clinical trials activities for Oxytrex, PTI-901 and Remoxy as well as continued development activities for Remoxy.

We expect research and development expenses to increase over the next several years as we expand our development efforts. Our development efforts should result in our drug candidates progressing through various stages of clinical trials, including our Phase III trials of Oxytrex, PTI-901 and Remoxy. Also, we expect to continue other development efforts on our product candidates. The increase in research and development expenses may fluctuate from period to period due to the timing and scope of our development activities and the results of clinical trials and studies.

General and Administrative

General and administrative expense consists primarily of compensation and other general corporate expenses. General and administrative expense increased to $3.9 million from $3.3 million in the years ended December 31, 2004 and 2003, respectively, primarily due an increase in non-cash stock-based compensation expense. We expect general and administrative expenses to increase over the next several years in connection with precommercialization and commercialization activities for our product candidates. The increase may fluctuate from period to period due to the timing and scope of these activities and the results of clinical trials and studies.

Interest Income

Interest income increased to $1.2 million from $0.6 million in the years ended December 31, 2004 and 2003, respectively, primarily due to increases in average balances of marketable securities. We expect our interest income to decrease during 2005 as we use cash to fund our operations.

Years Ended December 31, 2003 and 2002

Research and Development

Research and development expense consists primarily of drug development work associated with our drug candidates, including costs of preclinical studies, clinical trials, clinical supplies and related formulation and design costs and salaries and other personnel related expenses. Research and development expense increased to $18.9 million from $11.4 million in the years ended December 31, 2003 and 2002, respectively. The $7.5 million increase in expense was primarily due to the development costs related to our new drug candidate Remoxy as well as for the ongoing development and Phase III programs for Oxytrex and PTI-901.

General and Administrative

General and administrative expense consists primarily of compensation and other general corporate expenses as well as non-cash stock based compensation. General and administrative expense decreased to $3.3 from $5.5 million for the year ended December 31, 2003 and 2002, respectively. The decrease in general and administrative expense resulted primarily from lower non-cash equity related expense as well as a reclassification of certain occupancy and other expenses to research and development.

Interest Income

Interest income decreased to $0.6 million from $1.0 million for the years ended December 31, 2003 and 2002, respectively. The decrease in interest income is primarily the result of lower average balances of cash and cash equivalents and marketable securities as well as lower returns on the investment of our cash and cash equivalents and marketable securities.

Liquidity and Capital Resources

Since inception, we have financed our operations primarily through public and private securities offerings. We intend to continue to use the proceeds from these offerings to fund research and development activities, capital expenditures, working capital requirements and other general corporate purposes. As of December 31, 2004, cash, cash equivalents and marketable securities were $99.4 million.

In October 2004, we issued 8 million shares of common stock at a price of $7.25 per share in a follow-on public offering and received approximately $54.5 million in net proceeds after deducting underwriting discounts and commissions. Our other financing activities provided $0.3 million in the year ended December 31, 2004, primarily from the exercise of stock options issued under our 1998 Stock Plan.

Net cash used in operating activities was $32.6 million for the year ended December 31, 2004 compared to $20.5 million for the year ended December 31, 2003. Cash used in operating activities in both years related primarily to the funding of operating losses.

Our investing activities to purchase property, equipment and leasehold improvements used cash of $0.2 million for the year ended December 31, 2004. Other investing activities for the year ended December 31, 2004 consisted primarily of the purchase and sale of marketable securities. We expect to continue to invest in our infrastructure to support our operations.

We lease approximately 10,500 square feet of general office space. In addition to office space, we also lease equipment pursuant to operating leases. Our leases expire at various dates through 2010. Under the terms of our real property and equipment leases, annual minimum lease payments are as follows as of December 31, 2004 (in thousands):

	2005	2006	2007	2008	2009	2010 and Thereafter	Total
Minimum lease payments	$187	$191	$187	$196	$206	$ 160	$1,127

We have license agreements that require us to make milestone payments upon the successful achievement of milestones, including clinical milestones. Our formulation agreement with Durect Corporation obligates us to make certain milestone payments upon achieving clinical milestones and regulatory milestones. We believe the amount of each of these milestone payments will be immaterial within the period such milestone is achieved. Our license agreements also require us to pay certain royalties to our licensors if we succeed in fully commercializing products under these license agreements. All of these potential future payments are cancelable as of December 31, 2004.

Since our inception we have used cash of $91.2 million in operating activities and have an accumulated deficit of approximately $112.0 million. We expect to incur significant additional losses for the next several years and expect our cash requirements to increase in the future. The amount and timing our future cash

requirements will depend on regulatory and market acceptance of our drug candidates and the resources we devote to researching and developing, formulating, manufacturing, commercializing and supporting our products. We believe that our current resources should be sufficient to fund our operations for at least the next twelve months. We may seek additional future funding through public or private financing within this timeframe, if such funding is available and on terms acceptable to us.

RISK FACTORS

Our future operating results may vary substantially from anticipated results due to a number of factors, many of which are beyond our control. The following discussion highlights some of these factors and the possible impact of these factors on future results of operations. You should carefully consider these factors before making an investment decision. If any of the following factors actually occur, our business, financial condition or results of operations could be harmed. In that case, the price of our common stock could decline, and you could experience losses on your investment.

Risks Relating to our Financial Position and Need for Financing

Our operating history may make it difficult for you to evaluate 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 our drug candidates on a commercial scale 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 $112.0 million as of December 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 clinical trials of Oxytrex, PTI-901 and Remoxy as well as formulation and development activities for Remoxy;
- seek regulatory approvals for our drug candidates;
- develop, formulate, manufacture and commercialize our drug candidates;
- 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.

We will need to generate significant revenues to achieve and maintain profitability. If we cannot successfully develop, obtain regulatory approval for and commercialize our drug candidates, we will not be able to generate such revenues or achieve profitability in the future. Our failure to achieve or maintain profitability would have a material adverse impact on the market price of our common stock.

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

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 equivalents 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 within such twelve-month period or thereafter 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 raise additional capital through strategic alliance and license arrangements, we may have to trade our rights to our technology, intellectual property or drug candidates to others in such arrangements on terms that may not be favorable to us.

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 seek or obtain FDA approval of our drug candidates. We then could be forced to discontinue product development, enter into a relationship with a strategic partner earlier than currently intended, reduce sales and marketing efforts or 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 drug candidates, 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 and would likely delay the date of potentially receiving regulatory approval. In particular, the FDA may require additional toxicology studies for certain excipients used in Remoxy or any of our other drug candidates. 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, which would have an adverse effect on our operating results and financial condition.

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 for any of our drug candidates we will have fewer saleable products, if any, and corresponding lower product revenues, if any. Even if we receive regulatory approval of our drug candidates, such approval may involve limitations on the indications and conditions of use or marketing claims we may make for our products. Further, later discovery of previously unknown problems or adverse events could result in additional regulatory restrictions, including withdrawal of products. The FDA may also require us to commit to perform lengthy Phase IV 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.

In jurisdictions outside the United States, we must receive marketing authorizations from the appropriate regulatory authorities before we can commercialize our drugs. Regulatory approval processes outside the United States 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 drug candidates.

In order to obtain FDA approval for 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. Oxytrex, PTI-901 and Remoxy are in Phase III clinical trials in the United States.

Our Phase III clinical 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. This means that even if one of our Phase III clinical trials demonstrates positive results for our drug candidates, we are likely to have to demonstrate positive results in one or more additional Phase III clinical trials prior to receiving broad label FDA approval for treatment of severe chronic pain. Even if the results of our Phase III clinical 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 or terminate 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.

In addition, completion of clinical trials can be delayed by numerous factors, including:

- delays in identifying and agreeing on acceptable terms with prospective clinical trial sites;
- slower than expected rates of patient recruitment and enrollment;
- increases in time required to complete monitoring of patients during or after participation in a trial; and
- unexpected need for additional patient-related data.

Any of these delays, if significant, could impact the timing, approval and commercialization of our drug candidates and could significantly increase our overall costs of drug development.

Even if our clinical trials are completed as planned, their results may not support our expectations or intended marketing 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.

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.

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 Drug Enforcement Administration, or DEA, limits the availability of the active ingredients in certain of our current drug candidates and, as a result, our quota may not be sufficient to complete clinical trials, or to 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 under the Controlled Substances Act of 1970. Consequently, their manufacture, research, shipment, storage, sale and use are subject to a high degree of oversight and 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 drug candidates.

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

Conducting clinical trials of our drug candidates or potential commercial sales of a drug candidate may expose 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. If we successfully commercialize one or more of our drug candidates, we may face product liability claims, regardless of FDA approval for commercial manufacturing and sale. 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.

If we receive regulatory approval for our drug candidates, we and our collaborators will also be subject to ongoing FDA obligations and continued regulatory review, such as continued safety reporting requirements, and we and our collaborators may also be subject to additional FDA post-marketing obligations or new regulations, all of which may result in significant expense and limit our ability to commercialize our potential drugs.

Any regulatory approvals that we receive for our drug candidates may also be subject to limitations on the indicated uses for which the drug may be marketed or contain requirements for potentially costly post-marketing follow-up studies. In addition, if the FDA approves any of our drug candidates, the labeling, packaging, adverse event reporting, storage, advertising, promotion and record keeping for the drug will be subject to extensive regulatory requirements. The subsequent discovery of previously unknown problems with the drug, including adverse events of unanticipated severity or frequency, may result in restrictions on the marketing of the drug, and could include withdrawal of the drug from the market.

The FDA's policies may change and additional government regulations may be enacted that could prevent or delay regulatory approval of our drug candidates. We cannot predict the likelihood, nature or extent of adverse

government regulation that may arise from future legislation or administrative action, either in the United States or abroad. If we are not able to maintain regulatory compliance, we may be subject to fines, suspension or withdrawal of regulatory approvals, product recalls, seizure of products, operating restrictions and criminal prosecution. Any of these events could prevent us from marketing our drugs and our business could suffer.

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;
- published studies demonstrating the 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, or at all, 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 number of potential collaborators is limited and because of competition from others for similar alliances with potential 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 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 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. We currently have not generated pharmacoeconomic data on any of our products. 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. Adequate third-party insurance 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 our product candidates 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. As of February 2005, Reexamination Certificates have been issued resolving the majority of the proceedings by confirming the patentability of the claims of the patents and adding new claims to several patents. In addition, Notices of Intent to Issue Reexamination Certificates have been issued in the remaining proceedings.

We may be involved in additional challenges to our intellectual property. An adverse outcome of the reexamination process or any other challenges to our intellectual property 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.

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.

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 or compliance with applicable and strictly enforced regulations governing the manufacture of pharmaceutical products, 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 contract 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.

Our employees and consultants are generally subject to confidentiality or other agreements with their former employers and they may inadvertently or otherwise violate those agreements.

Many of our employees and consultants were previously employed at universities or biotechnology or pharmaceutical companies. While we require our employees and consultants to honor any agreements they may have entered into prior to working with us, we may be subject to claims that we inadvertently or otherwise used or disclosed trade secrets or other confidential information belonging to former employers. Failure to defend such claims could result in loss of valuable rights or personnel, which in turn could harm or prevent commercialization of our drug candidates. Successful defense against such claims can be expensive and might distract us from our execution of our strategies.

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. Our competitors may market less expensive or more effective drugs that would compete with our product candidates

or reach market with competing drugs before we are able to reach market with our drug candidates. 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.

Risks Relating to Manufacturing

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.

In addition, even if we enter into long-term supply arrangements with third-party suppliers, we cannot control changes in strategy by third-party suppliers that affect their ability or willingness to continue to supply our drug products on acceptable terms.

If our drug supply for one of our drug candidates was interrupted, our operations could be negatively affected.

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. If we unsuccessful in our formulation or scale-up activities with Remoxy, our future sales may be less than expected and our operations may suffer.

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.

We may not succeed at in-licensing drug candidates or technologies to expand our product pipeline.

We may not successfully in-license drug candidates or technologies to expand our product pipeline. The number of such candidates or technologies may be limited. Competition among large pharmaceutical companies and biopharmaceutical companies for promising drug candidates or technologies is intense because such companies generally desire to expand their product pipelines through in-licensing.

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.

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 or delays in 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 Securities and Exchange Commission, or 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 the NASDAQ National Market, or Nasdaq, 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.

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 stockholders 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 our board of directors is elected each year;
- elimination of cumulative voting in the election of directors;
- procedures for advance notification of stockholder nominations and proposals;
- the ability of our board of directors to amend our bylaws without stockholder approval; and
- the ability of our board of directors to issue up to 10,000,000 shares of preferred stock without stockholder approval upon the terms and conditions and with the rights, privileges and preferences as our board of directors may determine.

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.

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

The stock market in general, Nasdaq 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 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 share 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.

Publicly available information regarding stockholders' ownership may not be comprehensive because the SEC does not require certain large stockholders to publicly disclose their stock ownership positions.

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 clinical, financial or operating results may not meet the expectations of securities analysts and investors that 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 Nasdaq. Investors may not be able to sell their shares quickly or at the latest market price if trading in our stock is not active.

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

The primary objective of our cash investment activities is to preserve principal while at the same time maximizing the income we receive from our investments without significantly increasing risk. Some of the securities that we invest in may be subject to market risk. This means that a change in prevailing interest rates may cause the principal amount of the investment to fluctuate. For example, if we hold a security that was issued with a fixed interest rate at the then-prevailing rate and the interest rate later rises, the principal amount of our investment will probably decline. A hypothetical 50 basis point increase in interest rates would not have a material effect on the fair value of our available-for-sale securities at December 31, 2004. To minimize this risk in the future, we intend to maintain our portfolio of cash equivalents and marketable securities in a variety of securities, including commercial paper, government and non-government debt securities and/or money market funds that invest in such securities. We have no holdings of derivative financial or commodity instrument. As of December 31, 2004, our investments consisted of available-for-sale investments in corporate and government notes and obligations or in money market accounts and checking funds with variable, market rates of interest.

Item 8. ***Financial Statements and Supplementary Data***

INDEX TO FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
Pain Therapeutics, Inc.

We have audited management's assessment, included in the accompanying Management's Annual Report on Internal Control Over Financial Reporting included in Item 9A, that Pain Therapeutics, Inc. maintained effective internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission (the COSO criteria). Pain Therapeutics, Inc.'s management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting. Our responsibility is to express an opinion on management's assessment and an opinion on the effectiveness of Pain Therapeutics, Inc. internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, evaluating management's assessment, testing and evaluating the design and operating effectiveness of internal control, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A company's internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and directors of the company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, management's assessment that Pain Therapeutics, Inc. maintained effective internal control over financial reporting as of December 31, 2004, is fairly stated, in all material respects, based on the COSO criteria. Also, in our opinion, Pain Therapeutics, Inc. maintained, in all material respects, effective internal control over financial reporting as of December 31, 2004, based on the COSO criteria**.**

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the balance sheets of Pain Therapeutics, Inc. as of December 31, 2004 and 2003, and the related statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2004 and for the period from May 4, 1998 (inception) through December 31, 2004 and our report dated February 9**,** 2005 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Palo Alto, California
February 9, 2005

Report of Independent Registered Public Accounting Firm

The Board of Directors and Stockholders
Pain Therapeutics, Inc.

We have audited the accompanying balance sheets of Pain Therapeutics, Inc. (a development stage enterprise) as of December 31, 2004 and 2003, and the related statements of operations, stockholders' equity (deficit) and cash flows for each of the three years in the period ended December 31, 2004 and for the period from May 4, 1998 (inception) through December 31, 2004. These financial statements are the responsibility of Pain Therapeutics, Inc.'s management. Our responsibility is to express an opinion on these financial statements and schedule based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Pain Therapeutics, Inc. (a development stage enterprise) at December 31, 2004 and 2003, and the results of its operations and its cash flows for each of the three years in the period ended December 31, 2004 and for the period from May 4, 1998 (inception) through December 31, 2004, in conformity with U.S. generally accepted accounting principles.

We also have audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the effectiveness of Pain Therapeutics, Inc.'s internal control over financial reporting as of December 31, 2004, based on criteria established in Internal Control—Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated February 9**,** 2005 expressed an unqualified opinion thereon.

/s/ ERNST & YOUNG LLP

Palo Alto, California
February 9, 2005

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)
BALANCE SHEETS
(in thousands except share and per share data)

	December 31,	
	2004	2003
ASSETS		
Current assets:		
Cash and cash equivalents	$ 1,379	$ 12,027
Marketable securities	98,018	65,402
Prepaid expenses	259	1,321
Total current assets	99,656	78,750
Property and equipment, net	1,461	1,688
Other assets	75	75
Total assets	$ 101,192	$ 80,513
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 877	$ 2,231
Accrued development expense	6,358	1,210
Accrued compensation and benefits	415	369
Other accrued liabilities	146	141
Total current liabilities	7,796	3,951
Commitments and contingencies		
Stockholders' equity:		
Preferred stock; $.001 par value; 10,000,000 shares authorized, none issued and outstanding	—	—
Common stock, $.001 par value; 120,000,000 shares authorized; 43,652,116 and 35,381,309 shares issued and outstanding in 2004 and 2003, respectively	44	35
Additional paid-in-capital	205,920	150,732
Deferred compensation	—	(7)
Accumulated other comprehensive income (loss)	(544)	50
Deficit accumulated during the development stage	(112,024)	(74,248)
Total stockholders' equity	93,396	76,562
Total liabilities and stockholders' equity	$ 101,192	$ 80,513

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)
STATEMENTS OF OPERATIONS
(in thousands except per share data)

	Years ended December 31,			May 4, 1998 (inception) through December 31, 2004
	2004	2003	2002	
Operating expenses:				
Research and development	$ 35,093	$ 18,913	$ 11,396	$ 93,933
General and administrative	3,868	3,338	5,523	26,902
Total operating expenses	38,961	22,251	16,919	120,835
Operating loss	(38,961)	(22,251)	(16,919)	(120,835)
Other income:				
Interest and other income	1,185	634	994	8,811
Net loss	(37,776)	(21,617)	(15,925)	(112,024)
Return to series C preferred stockholders for beneficial conversion feature	—	—	—	(14,231)
Loss available to common stockholders	$(37,776)	$(21,617)	$(15,925)	$ (126,255)
Basic and diluted loss per share	$ (1.01)	$ (0.73)	$ (0.59)	
Weighted-average shares used in computing basic and diluted loss per share	37,267	29,483	27,039	

Included in research and development and general and administrative expenses are stock-based compensation expenses of $401, $139, and $210 for the years ended December 31, 2004, 2003 and 2002, respectively, and $12,330 for the period from May 4, 1998 (inception) through December 31, 2004.

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)

STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
For the period May 4, 1998 (inception) through December 31, 2004
(in thousands except share data)

	Common and Preferred stock		Additional paid-in capital	Deferred compensation	Notes receivable for stock	Accumulated other comprehensive income	Deficit accumulated during development stage	Stockholders' equity (deficit)
	Shares	Par value						
Balance at May 4, 1998 (inception)	—	$ —	$ —	$ —	$ —	$ —	$ —	$ —
Common stock issued in June 1998 at $0.001 per share	8,500,000	9	—	—	—	—	—	9
Series A convertible preferred stock issued between August 1998 and October 1998 at $1.00 per share	2,659,489	3	2,637	—	—	—	—	2,640
Common stock issued in September 1998 at $0.10 per share for notes receivable	350,000	—	35	—	(35)	—	—	—
Common stock issued in September 1998 at $0.10 for cash	150,000	—	15	—	—	—	—	15
Net loss and comprehensive loss	—	—	—	—	—	—	(389)	(389)
Balance at December 31, 1998	11,659,489	12	2,687	—	(35)	—	(389)	2,275
Common stock issued between April and May 1999 at $0.10 per share for notes receivable	444,000	—	44	—	(44)	—	—	—
Issuance of common stock pursuant to exercise of stock options	1,000	—	—	—	—	—	—	—
Issuance of warrants in connection with lease in August 1999	—	—	34	—	—	—	—	34
Deferred compensation for options issued to employees	—	—	2,284	(2,284)	—	—	—	—
Amortization of employee deferred compensation, net of reversals	—	—	—	188	—	—	—	188
Compensation with respect to non-employee option grants	—	—	1,435	—	—	—	—	1,435
Receipt of payment of stockholder notes receivable	—	—	—	—	5	—	—	5
Net loss and comprehensive loss	—	—	—	—	—	—	(4,500)	(4,500)
Balance at December 31, 1999	12,104,489	12	6,484	(2,096)	(74)	—	(4,889)	(563)
Common stock issued pursuant to initial public offering at $12.00 per share, net of issuance costs in July 2000	5,750,000	6	62,933	—	—	—	—	62,939
Common stock issued at $0.20 per share for notes receivable	245,000	—	49	—	(49)	—	—	—
Issuance of common stock pursuant to exercise of stock options	184,740	—	42	—	—	—	—	42
Issuance of warrants in connection with series C preferred stock offering in February 1999	—	—	963	—	—	—	—	963
Deferred compensation for options issued to employees	—	—	4,939	(4,939)	—	—	—	—
Amortization of employee deferred compensation, net of reversals	—	—	—	3,618	—	—	—	3,618
Compensation with respect to non-employee option grants	—	—	2,495	—	—	—	—	2,495
Compensation related to stock purchase rights	—	—	2,646	—	—	—	—	2,646
Issuance of common stock related to employee stock purchase plan	4,664	—	48	—	—	—	—	48
Stockholder notes receivable	—	—	—	—	50	—	—	50
Conversion of 2,659,489 shares of series A convertible preferred stock to common at $1.00 per share in July 2000	(2,659,489)	(3)	—	—	—	—	—	(3)
	2,659,489	3	—	—	—	—	—	3
Conversion of series B redeemable convertible preferred stock to common at $1.85 per share in July 2000	5,405,405	6	9,698	—	—	—	—	9,704
Conversion of series C redeemable convertible preferred stock to common at $5.00 per share in July 2000	3,044,018	3	14,229	—	—	—	—	14,232
Beneficial conversion feature of series C preferred stock	—	—	14,232	—	—	—	—	14,232
Return to series C preferred shareholders for beneficial conversion feature	—	—	(14,232)	—	—	—	—	(14,232)
Net loss and comprehensive loss	—	—	—	—	—	—	(17,480)	(17,480)
Balance at December 31, 2000	26,738,316	27	104,526	(3,417)	(73)	—	(22,369)	78,694

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)

STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)—(Continued)

For the period May 4, 1998 (inception) through December 31, 2004
(in thousands except share data)

	Common and Preferred stock		Additional paid-in capital	Deferred compensation	Notes receivable for stock	Accumulated other comprehensive income	Deficit accumulated during development stage	Stockholders' equity (deficit)
	Shares	Par value						
Balance at December 31, 2000	26,738,316	$ 27	$ 104,526	$ (3,417)	$ (73)	$ —	$ (22,369)	$ 78,694
Issuance of common stock pursuant to exercise of stock options	78,635	—	50	—	—	—	—	50
Amortization of employee deferred compensation, net of reversals	—	—	(347)	2,298	—	—	—	1,951
Compensation with respect to non-employee option grants	—	—	(753)	—	—	—	—	(753)
Issuance of common stock related to employee stock purchase plan	20,374	—	119	—	—	—	—	119
Issuance of notes receivable	—	—	—	—	(108)	—	—	(108)
Net loss and comprehensive loss	—	—	—	—	—	—	(14,337)	(14,337)
Balance at December 31, 2001	26,837,325	27	103,595	(1,119)	(181)	—	(36,706)	65,616
Issuance of common stock pursuant to exercise of stock options	351,278	—	140	—	—	—	—	140
Amortization of employee deferred compensation, net of reversals	—	—	(395)	815	—	—	—	420
Compensation with respect to non-employee option grants	—	—	(210)	—	—	—	—	(210)
Repurchase of restricted stock	(19,480)	—	(3)	—	—	—	—	(3)
Issuance of common stock related to employee stock purchase plan	31,385	—	127	—	—	—	—	127
Receipt of payment of stockholder notes receivable	—	—	—	—	59	—	—	59
Net loss and comprehensive loss	—	—	—	—	—	—	(15,925)	(15,925)
Balance at December 31, 2002	27,200,508	27	103,254	(304)	(122)	—	(52,631)	50,224
Issuance of common stock pursuant to exercise of stock options	272,150	—	227	—	—	—	—	227
Issuance of common stock pursuant to follow-on offering, net of expenses	7,730,500	8	46,650					46,658
Issuance of common stock pursuant to exercise of warrants	120,000	—	600	—	—	—	—	600
Amortization of employee deferred compensation, net of reversals	—	—	(406)	297	—	—	—	(109)
Compensation with respect to non-employee option grants	—	—	248	—	—	—	—	248
Issuance of common stock related to employee stock purchase plan	58,151	—	159	—	—	—	—	159
Receipt of payment of stockholder notes receivable	—	—	—	—	122	—	—	122
Comprehensive loss: Net unrealized gains on investments in marketable securities	—	—	—	—	—	50	—	50
Net loss	—	—	—	—	—	—	(21,617)	(21,617)
Comprehensive loss	—	—	—	—	—	—	—	(21,567)
Balance at December 31, 2003	35,381,309	35	150,732	(7)	—	50	(74,248)	76,562
Issuance of common stock pursuant to exercise of stock options	184,257	1	473		—	—	—	474
Issuance of common stock pursuant to follow-on offering, net of expenses	8,000,000	8	54,074	—	—	—	—	54,082
Amortization of employee deferred compensation, net of reversals	—	—	—	7	—	—	—	7
Compensation with respect to non-employee option grants	—	—	394	—	—	—	—	394
Issuance of common stock related to employee stock purchase plan	86,550	—	247	—	—	—	—	247
Comprehensive loss: Net unrealized losses on investments in marketable securities	—	—	—	—	—	(594)	—	(594)
Net loss	—	—	—	—	—	—	(37,776)	(37,776)
Comprehensive loss	—	—	—	—	—	—	—	(38,370)
Balance at December 31, 2004	43,652,116	$ 44	$ 205,920	$ —	$ —	$ (544)	$ (112,024)	$ 93,396

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC
(A Development Stage Enterprise)
STATEMENTS OF CASH FLOWS
(in thousands)

	Years ended December 31,			May 4, 1998 (inception) through December 31, 2004
	2004	2003	2002	
Cash flows used in operating activities:				
Net loss	$ (37,776)	$(21,617)	$(15,925)	$ (112,024)
Adjustments to reconcile net loss to net cash used in operating activities:				
Depreciation and amortization	383	341	349	1,368
Non-cash net interest income	(484)	(27)	62	(449)
Non-cash stock based compensation	401	139	210	12,330
Non-cash expense for warrants issued	—	—	—	34
Loss on disposal of property and equipment	—	—	2	54
Changes in operating assets and liabilities:			—	
Prepaid expenses	1,062	(220)	(778)	(259)
Other assets	—	—	—	(75)
Accounts payable	(1,354)	960	(899)	877
Accrued development expense	5,148	(167)	1,377	6,358
Accrued compensation and benefits	46	96	(10)	415
Other accrued liabilities	5	(39)	114	146
Net cash used in operating activities	(32,569)	(20,534)	(15,498)	(91,225)
Cash flows used in investing activities:				
Purchase of property and equipment	(156)	(26)	(7)	(2,883)
Purchase of marketable securities	(114,067)	(68,829)	—	(182,896)
Sales and maturities of marketable securities	81,341	3,559	—	84,783
Net cash used in investing activities	(32,882)	(65,296)	(7)	(100,996)
Cash flows from financing activities:				
Proceeds from issuance of preferred stock, net	—	—	—	27,539
Stock subscription note payments received	—	122	59	236
Proceeds from issuance of common stock, net	54,803	47,644	263	165,825
Net cash provided by financing activities	54,803	47,766	322	193,600
Net increase (decrease) in cash and cash equivalents	(10,648)	(38,064)	(15,183)	1,379
Cash and cash equivalents at beginning of period	12,027	50,091	65,274	—
Cash and cash equivalents at end of period	$ 1,379	$ 12,027	$ 50,091	$ 1,379

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)

NOTES TO FINANCIAL STATEMENTS

1. Business

Pain Therapeutics, Inc. is a biopharmaceutical company dedicated to the development of innovative drugs. We specialize in developing safer or more efficacious drugs for use in pain management, particularly in the area of opioid painkillers, which are sometimes referred to as narcotic painkillers.

In the course of our development activities, we have sustained operating losses and expect such losses to continue through the next several years. We expect our current cash, cash equivalents and marketable securities will be sufficient to meet our planned working capital and capital expenditure requirements for at least the next twelve months. There are no assurances that additional financing will be available on favorable terms, or at all.

Our development activities involve inherent risks. These risks include, among others, dependence on key personnel and determination of patentability and protection of our products and processes. In addition, we have drug candidates that have not yet obtained FDA approval. Successful future operations depend on our ability to obtain approval for and commercialize these products.

2. Summary of Significant Accounting Policies

Use of Estimates

The preparation of financial statements in conformity with generally accepted accounting principles requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Cash, Cash Equivalents and Concentration of Cash Risk

We consider all highly liquid financial instruments with original maturities of three months or less to be cash equivalents. Cash and cash equivalents consist of cash maintained at two financial institutions and money market funds.

Marketable Securities

In accordance with Statement of Financial Accounting Standards No. 115, “Accounting for Certain Investments in Debt and Equity Securities,” we consider our investments to be held as “available-for-sale.” We classify these as current assets and carry them at fair value. Unrealized gains and losses are recorded as a separate component of stockholder’s equity as accumulated other comprehensive income (loss). All realized gains and losses on our available-for-sale securities are recognized in results of operations. Our investments are maintained at one financial institution and are governed by our investment policy as approved by our Board of Directors.

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Depreciation is calculated using the straight-line method over the estimated useful lives of the respective assets (generally two to five years). Leasehold improvements are amortized over the shorter of the estimated useful life of the assets or the lease term.

Impairment of Long-Lived Assets

We regularly perform reviews to determine if the carrying value of our long-lived assets is impaired. We look for facts or circumstances, either internal or external that indicate that we may not recover the carrying value of the asset.

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)
NOTES TO FINANCIAL STATEMENTS—(Continued)

We measure impairment loss related to long-lived assets based on the amount by which the carrying amounts of such assets exceed their fair values. Our measurement of fair value is generally based on an analysis of the present value of estimated future discounted cash flows. We use available information and reasonable and supportable assumptions and projections. We consider the likelihood of possible outcomes and our best estimates of projected future cash flows. If necessary, we perform subsequent calculations to measure the amount of the impairment loss based on the excess of the carrying value over the measurement of fair value of the impaired asset. No events or changes in circumstances have occurred with respect to our long-lived assets that would indicate that an impairment analysis should have been performed.

Business Segments

Statement of Financial Accounting Standards No. 131, *Disclosures about Segments of an Enterprise and Related Information,* requires an enterprise to report segment information based on how management internally evaluates the operating performance of its business units (segments). Our operations are confined to one business segment: the clinical development of novel painkillers.

Expenses for clinical trials

Research and development expense includes the cost of clinical trials. Expenses for clinical trials are incurred from planning through patient enrollment to reporting of the underlying data. We estimate expenses incurred for clinical trials that are in process based on patient enrollment and treatment as well as on clinical data collection and management. Costs that are associated with patient enrollment are recognized as each patient in the trial completes enrollment. Costs that are based on clinical data collection and management are recognized based on estimates of unbilled goods and services received. In the event of early termination of a clinical trial, we accrue an amount based on estimates of the remaining non-cancelable obligations associated with winding down the trial.

Stock Based Compensation

We use the intrinsic-value method of accounting for stock based awards granted to employees in accordance with Accounting Principles Board Opinion No. 25 and its related interpretations. Accordingly, we would recognize compensation expense in our financial statements in connection with stock options granted to employees with exercise prices less than fair value at the time the stock option is granted. We record stock based compensation expense for non-employees at the fair value of the options granted in accordance with Statement of Financial Accounting Standards No. 123, or SFAS 123 and Emerging Issues Task Force No. 96-18, or EITF 96-18. The fair value of options granted to non-employees is estimated using a Black-Scholes option valuation model, or Black Scholes. The model considers a number of factors, including the market price and volatility of our common stock at the date of measurement. We periodically re-measure the compensation expense for options granted to non-employees as the underlying options vest. The compensation expense related to all grants is being amortized using the graded vesting method, in accordance with SFAS 123, EITF 96-18 and FASB Interpretation No. 28, over the vesting period of each respective stock option, generally four years. The graded vesting method results in expensing approximately 57% of the total award in year one, 26% in year two, 13% in year three and 4% in year four.

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)
NOTES TO FINANCIAL STATEMENTS—(Continued)

If we had recorded compensation cost of our stock based plans in a manner consistent with the fair value approach of SFAS 123, our net loss and loss per share would have been increased as follows (in thousands, except per share data):

	Years Ended December 31,		
	2004	2003	2002
Net loss as reported	$(37,776)	$(21,617)	$(15,925)
Deduct: Total stock based employee compensation expense determined under the fair valued based method for all awards	(6,188)	(5,153)	(6,452)
Add (deduct): Total stock based employee compensation included in net loss	7	(109)	420
Adjusted net loss	$(43,957)	$(26,879)	$(21,957)
Net loss per share basic and diluted as reported	$ (1.01)	$ (0.73)	$ (0.59)
Adjusted net loss per share basic and diluted	$ (1.18)	$ (0.90)	$ (0.81)

The weighted average fair value of stock options granted to employees was $6.25 in 2004, $5.48 in 2003, and $5.09 in 2002. The fair value of each option granted to both employees and non-employees was estimated using Black-Scholes with an expected life of options of 5 years for employees, 10 years for non-employee options and no dividend yield. We assumed volatility was between 89% and 95% in 2004, between 91% and 100% in 2003 and 89% in 2002. We used risk-free interest rates of between 3% and 4% in 2004, 2% and 5% in 2003 and 3% and 4% in 2002.

For the 2000 Employee Stock Purchase Plan, the weighted-average fair value of purchase rights granted was $2.85 per share in 2004, $2.74 in 2003 and $3.79 in 2002 calculated using Black-Scholes with an expected life of 2 years and no dividend yield. We assumed volatility was between 89% and 94% in 2004, between 91% and 100% in 2003 and 89% in 2003. We used risk-free interest rates of 3% in 2004, between 1% and 2% in 2003 and 2% in 2002.

Loss per Share

Basic loss per share is computed on the basis of the weighted-average number of shares outstanding for the reporting period. We have computed its weighted-average shares outstanding for all periods presented excluding those common shares issued and outstanding which remain subject to our repurchase rights. Diluted loss per share is computed on the basis of the weighted-average number of common shares plus dilutive potential common shares outstanding using the treasury-stock method. Potential dilutive common shares consist of convertible preferred stock, common shares issued and outstanding subject to our repurchase rights, outstanding stock options and outstanding warrants.

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)
NOTES TO FINANCIAL STATEMENTS—(Continued)

In all years presented we have reported a loss and therefore all potential common shares related to potentially dilutive securities have been excluded from the calculation of diluted loss per share because they are anti-dilutive. The following table sets forth the number of weighted-average potential shares of common stock that are in-the-money for the periods indicated but have not been included in the computation of diluted net loss per share because to do so would be anti-dilutive:

	Years Ended December 31,		
	2004	2003	2002
Options to purchase common shares	3,363,985	1,084,553	767,250
Common stock subject to repurchase	—	—	51,453
Warrants	220,000	220,000	220,000
	3,583,985	1,304,553	1,038,703

Comprehensive Loss

Comprehensive loss is comprised of net loss and unrealized holding gains and losses on available-for-sale securities as follows (in thousands):

	Years Ended December 31,			May 4, 1998 (inception) through September 30, 2004
	2004	2003	2002	
Net loss	$(37,776)	$(21,617)	$(15,925)	$ (112,024)
Other comprehensive income	(594)	50	—	(544)
Comprehensive loss	$(38,370)	$(21,567)	$(15,925)	$ (112,568)

Income Taxes

Income taxes are accounted for under the liability method. Deferred tax assets and liabilities are recognized for the future tax consequences attributable to differences between the financial statement carrying amounts of existing assets and liabilities and their respective tax bases, and operating loss and tax credit carryforwards. Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in income in the period that includes the enactment date. Deferred tax assets are reduced by a valuation allowance when, in the opinion of management, it is more likely than not that some or all of the deferred tax assets may not be realized.

Reclassifications

Certain reclassifications have been made to the prior year financial statements to conform to the presentation in 2004.

Recent Accounting Pronouncements

In December 2004, the Financial Accounting Standards Board, or FASB, issued a revision of Financial Accounting Standards No. 123, or SFAS 123R, which requires all share-based payments to employees, including grants of employee stock options, to be recognized in the income statement based on their values. We expect to

calculate the value of share-based payments under SFAS 123R on a basis substantially consistent with the fair value approach of SFAS 123. We plan to adopt SFAS 123R in our fiscal quarter ending September 30, 2005. We expect the adoption of SFAS 123R will have a material impact on our financial statements in that fiscal quarter, but we cannot reasonable estimate the impact of adoption because we expect certain assumptions that can materially affect the calculation of the value share-based payments to employees to change in 2005.

In March 2004, the FASB issued Emerging Issues Task Force No 93-1, "The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments", or EITF 93-1, which determines the meaning of other-than-temporary impairment and its application to investments classified as either available-for-sale or held-to-maturity under Statement 115 (including individual securities and investments in mutual funds), and investments accounted for under the cost method or the equity method. We adopted EITF 93-1 in our fiscal quarter ended March 31, 2004.

3. Related Party Transactions

We had no outstanding loans to related parties as of December 31, 2004 and 2003. We had full recourse loans aggregating $122,000 to a former officer of the Company at December 31, 2002 that was repaid in 2003. The notes bore interest at rates ranging from 4.5% to 8.0%. In November 2002 a former officer of the Company was retained as a consultant, receiving $28,000 for his services in 2002.

4. Research and Collaboration Agreements

Durect Corporation

In December 2002, we entered into an exclusive, worldwide licensing agreement with Durect Corporation. Under this agreement, Durect will formulate certain oral opioids into long-acting formulations. We have exclusive worldwide rights to develop and commercialize these opioid drugs formulated with Durect's proprietary technology. We paid Durect an undisclosed upfront fee and will make milestone payments based upon achievement of certain technical, clinical or regulatory milestones. We fund certain formulation activities performed by Durect and will pay Durect royalties on sales of products resulting from the agreement.

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)
NOTES TO FINANCIAL STATEMENTS—(Continued)

5. Cash and Cash Equivalents and Marketable Securities

Cash, cash equivalents and marketable securities held as available-for sale consisted of the following (in thousands):

	Cash, Cash Equivalents and Marketable Securities				
(in thousands)	Amortized Cost	Accrued Interest	Unrealized Gains	Unrealized Loss	Estimated Fair Value
December 31, 2004					
Cash and Cash Equivalents:					
Money Market Securities	$ 1,379	$ —	$ —	$ —	$ 1,379
Marketable Securities Available-for-Sale:					
U.S. Government and Agency Obligations	41,676	228	—	(265)	41,639
Corporate Obligations	44,574	648	—	(227)	44,995
Mortgage/Asset-Backed Securities	11,424	12	—	(52)	11,384
	97,674	888	—	(544)	98,018
	$ 99,053	$ 888	$ —	$ (544)	$ 99,397
December 31, 2003					
Cash and Cash Equivalents:					
Money Market Securities	$ 3,724	$ 1	$ —	$ —	$ 3,725
Municipal Securities	3,500	—	—	—	3,500
Corporate Obligations	4,800	2	—	—	4,802
Total	12,024	3	—	—	12,027
Marketable Securities Available-for-Sale:					
Money Market	7,684	4	—	—	7,688
U.S. Government and Agency Obligations	22,791	99	52	—	22,942
Corporate Obligations	22,556	280	10	(6)	22,840
Mortgage/Asset-Backed Securities	11,875	63	—	(6)	11,932
	64,906	446	62	(12)	65,402
	$ 76,930	$ 449	$ 62	$ (12)	$ 77,429

To date we have not recorded any impairment charges on marketable securities related to other-than-temporary declines in market value. We recognize an impairment charge when the decline in the estimated fair value of a marketable security below the amortized cost is determined to be other-than-temporary. We consider various factors in determining whether to recognize an impairment charge, including the duration of time and the severity to which the fair value has been less than our amortized cost, any adverse changes in the investees' financial condition and our intent and ability to hold the marketable security for a period of time sufficient to allow for any anticipated recovery in market value.

The gross realized losses and gains on the sale of available-for-sale securities during the years ended December 31, 2004 and 2003 were not material.

PAIN THERAPEUTICS, INC.
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NOTES TO FINANCIAL STATEMENTS—(Continued)

The contractual maturities of our marketable securities at December 31, 2004, consisted of the following (in thousands):

Less than one year	$39,136
Greater than one year	58,882
	$98,018

6. Property and Equipment

Property and equipment at December 31, consisted of the following (in thousands):

	2004	2003
Furniture and fixtures	$ 630	$ 509
Computers and software	224	239
Leasehold improvements	1,887	1,891
	2,741	2,639
Accumulated depreciation and amortization	(1,280)	(951)
	$ 1,461	$1,688

7. Return to Series C Preferred Stockholders for Beneficial Conversion Feature

In 2000, we issued 3,044,018 shares of series C redeemable convertible preferred stock, or Series C Stock, for $14.2 million, net of issuance costs. We determined that our Series C Stock was issued with a beneficial conversion feature. The value of the beneficial conversion feature was recognized by allocating to additional paid in capital a portion of the preferred stock, limited to the net proceeds received. As our Series C Stock was convertible into common stock at the option of the holder, at the issuance date of the preferred stock the entire $14.2 million was allocated to the intrinsic value of that feature and has been treated as a dividend and recognized as a return to the preferred stockholders for purposes of computing basic and diluted loss per share for the period ended December 31, 2000. Upon the closing of our initial public offering in July 2000, all 3,044,018 shares of our Series C Stock automatically converted into shares of common stock on a one to one basis.

8. Stockholders' Equity (Deficit)

Common Stock and Conversion of Preferred Stock

In 2000, we completed an initial public offering in which we sold 5,750,000 shares of common stock at $12.00 per share. We received net proceeds from the initial public offering of approximately $62.9 million, after deducting underwriting discounts, commissions and other expenses. Upon the closing of the offering, all 11,108,922 shares of our then outstanding preferred stock automatically converted into common stock on a one to one basis.

In 2003, we issued 7,730,500 shares of common stock at $6.50 per share in a follow-on public offering and received approximately $46.7 million, after deducting underwriting discounts and related expenses.

In 2004, we registered with the Securities and Exchange Commission and reserved 15,000,000 shares of common stock to be offered via prospectus in amounts, at prices and at terms determined at the time of an offering and may be sold directly by us to investors, through agents designated from time to time, or to or

through underwriters or dealers. In 2004, we issued 8,000,000 shares of common stock at $7.25 per share in a follow-on public offering pursuant to the Shelf and received approximately $54.5 million after deducting underwriting discounts and related expenses.

Under the terms of the 1998 Stock Plan, in 1998 through 2002, we granted stock purchase rights and subsequently issued shares of common stock to certain employees and non-employees in exchange for full-recourse promissory notes or cash. As of December 31, 2004 all such previously issued shares were vested and all related promissory notes were paid.

Preferred Stock

Our Board of Directors has the authority to issue preferred stock in one or more series and to fix the rights, preferences, privileges, restrictions and the number of shares constituting any series or the designation of the series.

Warrants

We have outstanding warrants to purchase 220,000 shares of common stock at $1.00 per share in connection with corporate activities. The value of these warrants were immaterial. These warrants expire in 2005 and 2010. Some of the shares underlying the warrants are entitled to certain registration rights.

2000 Employee Stock Purchase Plan

Under the 2000 Employee Stock Purchase Plan, or the Purchase Plan, eligible employees may purchase common stock through payroll deductions of up to 15% of the employee's compensation. The purchase price of the stock is generally 85% of the lower of the fair market value of the common stock at the beginning of the offering period or at the end of the purchase period. A total of 500,000 shares of common stock have been reserved for issuance under the Purchase Plan. Shares reserved for issuance under the Purchase Plan may be automatically increased each year by the amount equal to the lesser of (i) 500,000 shares, (ii) 1% of the initially outstanding shares of common stock on such date, or (iii) an amount determined by our Board of Directors. We have issued 201,124 shares of common stock pursuant to the Purchase Plan through December 31, 2004, leaving 298,876 shares reserved for issuance.

1998 Stock Plan

Under the 1998 Stock Plan, our employees, directors and consultants may be granted options that allow for the purchase of shares of our common stock. Incentive stock options may only be granted to employees and directors. At December 31, 2004 a total of 10,100,000 of common stock were authorized for issuance under the 1998 Stock Plan. The 1998 Stock Plan allows for annual increases in the number of common shares authorized for issuance equal to the lesser of (i) 2,000,000 shares, (ii) 5% of the outstanding shares of common stock on the last day of the immediately preceding fiscal year, or (iii) an amount determined by our Board of Directors.

Our Board of Directors or a designated Committee of the Board is responsible for administration of the 1998 Stock Plan and determines the terms and conditions of each option granted, consistent with the terms of the plan. Incentive stock options may be granted under the 1998 Stock Plan at a price not less than 100% of the fair market value of the stock on the date of grant (not less than 110% of the fair market value on the date of grant in the case of holders of more than 10% of our voting stock). Options granted under the 1998 Stock Plan generally expire ten years from the date of grant (five years for incentive stock options granted to holders of more than 10% of our voting stock). Forfeited options become available for reissuance under the 1998 Stock Plan.

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)
NOTES TO FINANCIAL STATEMENTS—(Continued)

The 1998 Stock Plan also provides for the automatic grant of options to purchase shares of common stock to outside directors. On the date of each annual stockholder's meeting, each outside director is automatically granted an option to purchase 25,000 shares of common stock. The term of the option is ten years, the exercise price is 100% of the fair market value of the stock on the date of grant, and the option becomes exercisable as to 25% of the shares on the anniversary of its date of grant provided the optionee continues to serve as a director on such dates.

The following table summarizes option activity under the 1998 Stock Plan:

	Number of options	Weighted-average exercise price
Options outstanding as of December 31, 2001	2,884,716	$ 5.39
Granted	1,692,213	6.38
Exercised	(351,278)	0.40
Forfeited	(232,022)	6.91
Options outstanding as of December 31, 2002	3,993,629	6.15
Granted	1,146,300	6.70
Exercised	(272,150)	0.83
Forfeited	(499,270)	7.00
Options outstanding as of December 31, 2003	4,368,509	6.53
Granted	1,373,100	7.56
Exercised	(184,257)	2.57
Forfeited	(222,618)	6.28
Options outstanding as of December 31, 2004	5,334,734	$ 6.94

Shares available for grant under the 1998 Stock Plan were 2,504,206 as of December 31, 2004.

The following table summarizes information about stock options outstanding as of December 31, 2004:

	Options outstanding			Options exercisable	
Range of exercise prices	Number of options	Weighted average remaining contractual life (years)	Weighted average exercise price	Number of vested options	Weighted average exercise price
$ 0.10—$ 3.19	733,897	6.45	$ 2.07	542,397	$ 1.74
6.06— 6.71	928,413	7.74	6.53	519,054	6.63
6.82— 6.82	116,000	9.62	6.82	9,666	6.82
6.90— 6.90	700,000	7.45	6.90	510,416	6.90
7.93— 7.05	206,800	7.95	7.03	89,599	7.04
7.16— 7.16	611,100	8.53	7.16	211,740	7.16
7.25— 7.75	513,600	8.86	7.59	122,598	7.40
7.78— 7.78	681,000	9.47	7.78	81,893	7.78
8.00— 18.63	843,924	6.72	10.43	653,176	10.94
$ 0.10—$18.63	5,334,734	7.83	$ 6.94	2,740,539	$ 6.86

As of December 31, 2004, a total of 2,740.539 shares were fully vested and exercisable with a weighted average exercise price of $6.86 per share.

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)
NOTES TO FINANCIAL STATEMENTS—(Continued)

As of December 31, 2004, the number of shares available for future grants pursuant to our stock plans consisted of the following:

1998 Stock Plan	2.504,206
Purchase Plan	298,876
Total available for future grants	2,803,082

Stock Based Compensation

We use the intrinsic-value method of accounting for stock based awards granted to employees in accordance with Accounting Principles Board Opinion No. 25 and its related interpretations. Accordingly, we would recognize compensation expense in our financial statements in connection with stock options granted to employees with exercise prices less than fair value at the time the stock option is granted. We record stock based compensation expense for non-employees at the fair value of the options granted in accordance with SFAS 123 and EITF 96-18. The fair value of options granted to non-employees is estimated using a Black-Scholes option valuation model. The model considers a number of factors, including the market price and volatility of our common stock at the date of measurement. We periodically re-measure the compensation expense for options granted to non-employees as the underlying options vest. The compensation expense related to all grants issued prior to 2003 is being recognized using the graded vesting method, in accordance with SFAS 123, EITF 96-18 and FASB Interpretation No. 28, over the vesting period of each respective stock option for employees, generally four years and the service period for non-employees. The graded vesting method results in expensing approximately 57% of the total award in year one, 26% in year two, 13% in year three and 4% in year four.

Amounts recognized in the statement of operations as compensation expense (recovery) for employees were $7,000, ($109,000) and $420,000 for the years ended December 31, 2004, 2003, and 2002, respectively. Amounts amortized in the statement of operations as compensation expense for non-employees were $394,000, $249,000 and ($210,000) for the years ended December 31, 2004, 2003, and 2002, respectively.

9. Employee 401(k) Benefit Plan

We have a defined-contribution savings plan under Section 401(k) of the Internal Revenue Code. The plan covers substantially all employees. Employees are eligible to participate in the plan the first day of the month after hire and may elect to contribute the lesser of 20% of their annual compensation or the current statutory limits under Internal Revenue Service regulations. The 401(k) plan permits us to make additional matching contributions on behalf of all employees. Through December 31, 2004, we have not made any matching contributions.

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)
NOTES TO FINANCIAL STATEMENTS—(Continued)

10. Income Taxes

There is no provision for income taxes because we have incurred losses. Deferred income taxes reflect the tax effects of net operating loss and tax credit carryovers and temporary differences between the carrying amounts of assets and liabilities for financial reporting purposes and the amounts used for income tax purposes. Significant components of our deferred tax assets are as follows (in thousands):

	December 31,		
	2004	2003	2002
Deferred tax assets:			
Net operating loss carryforwards	$ 38,300	$ 25,300	$ 16,000
Research and development credits	7,700	4,800	1,090
Stock related compensation	900	4,700	4,680
Other	3,000	800	1,240
Total deferred tax assets	49,900	35,600	23,010
Valuation allowance	(49,900)	(35,600)	(23,010)
Net deferred tax assets	$ —	$ —	$ —

Realization of deferred tax assets is dependent upon future earnings, if any, the timing and amount of which we are uncertain. Accordingly, the total deferred tax assets have been fully offset by a valuation allowance. The valuation allowance increased by $14,300, $12,590, and $7,283, during 2004, 2003 and 2002, respectively.

As of December 31, 2004, we had net operating loss carryforwards for federal income tax purposes of approximately $93.5 million, which expire in the years 2018 through 2024 and federal research and developments tax credits of approximately $3.9 million, which expire in the years 2018 through 2024. As of December 31, 2004, we had net operating loss carryforwards for state income tax purposes of approximately $93.5 million, which expire in the years 2009 through 2014 and state research and development tax credits of approximately $3.7 million, which do not expire.

Utilization of our net operating loss and credit carryforwards may be subject to substantial annual limitation due to the ownership change limitations provided by the Internal Revenue Code and similar state provisions. Such an annual limitation could result in the expiration of the net operating loss and credits before utilization.

11. Leases and Commitments

We conduct our product research and development programs through a combination of internal and collaborative programs that include, among others, arrangements with universities, contract research organizations and clinical research sites. We have contractual arrangements with these organizations, however these contracts are cancelable on thirty days notice and are largely based on services performed.

We currently lease office space and equipment pursuant to non-cancelable operating leases that will expire at various dates through 2010. Future minimum lease payments for these leases are as follows for the years ended December 31, (in thousands):

	2005	2006	2007	2008	2009	2010 and Thereafter	Total
Future minimum lease payments	$ 187	$ 191	$ 187	$ 196	$ 206	$ 160	$ 1,127

Rent expense was $178,000, $171,000, and $186,000 for the years ended December 31, 2004, 2003, and 2002 respectively.

PAIN THERAPEUTICS, INC.
(A Development Stage Enterprise)
NOTES TO FINANCIAL STATEMENTS—(Continued)

12. Selected Quarterly Financial Data (Unaudited) (in thousands except per share data)

	Quarters Ended			
	March 31	June 30	September 30	December 31
2004				
Net loss	$(10,163)	$(9,066)	$ (9,231)	$ (9,316)
Basic and diluted loss per common share	$ (0.29)	$ (0.26)	$ (0.26)	$ (0.22)
2003				
Net loss	$ (4,617)	$(4,346)	$ (5,969)	$ (6,685)
Basic and diluted loss per common share	$ (0.17)	$ (0.16)	$ (0.21)	$ (0.19)

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

Not applicable.

Item 9A. ***Controls and Procedures***

Evaluation of disclosure controls and procedures. Our management evaluated, with the participation of our Chief Executive Officer and our Chief Financial Officer, the effectiveness of our disclosure controls and procedures as of the end of the period covered by this Annual Report on Form 10-K. Based on this evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that our disclosure controls and procedures are effective to ensure that information we are required to disclose in reports that we file or submit under the Securities Exchange Act of 1934 is recorded, processed, summarized and reported within the time periods specified in Securities and Exchange Commission rules and forms.

Management's annual report on internal control over financial reporting. We are responsible for establishing and maintaining an adequate internal control structure and procedures our financial reporting. We have assessed the effectiveness of internal control over financial reporting as of December 31, 2004. Our assessment was based on criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission, or COSO, Internal Control-Integrated Framework.

Our internal control over financial reporting is a process designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. Our internal control over financial reporting includes those policies and procedures that:

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

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

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

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness to future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

Based on using the COSO criteria, we believe our internal control over financial reporting as of December 31, 2004 was effective.

Our independent registered public accounting firm, Ernst & Young LLP has audited the financial statements included in this Annual Report on Form 10-K and has issued a report on management's assessment of our internal control over financial reporting as well as on the effectiveness of our internal control over financial reporting. The attestation report of Ernst & Young, the registered public accounting firm, on management's assessment of internal control over financial reporting and on the audit of the financial statements is incorporated by reference from Item 8 of this Annual Report on Form 10-K.

Changes in internal control over financial reporting. There was no change in our internal control over financial reporting that occurred during the period covered by this Annual Report on Form 10-K that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. ***Other Information***

Not applicable.

PART III

Item 10. ***Directors and Officers of the Registrant***

The information regarding our directors, executive officers and the audit committee of our board of directors is incorporated by reference from "Directors and Executive Officers" in our Proxy Statement for our 2004 Annual Meeting of Stockholders.

Section 16(a) Beneficial Ownership Reporting Compliance

Section 16(a) of the Securities Exchange Act of 1934, as amended requires our executive officers and directors and persons who own more than ten percent (10%) of a registered class of our equity securities to file reports of ownership and changes in ownership with the Securities and Exchange Commission, or SEC, and the National Association of Securities Dealers, Inc. Executive officers, directors and greater than ten percent (10%) stockholders are required by Commission regulation to furnish us with copies of all Section 16(a) forms they file. We believe all of our executive officers and directors complied with all applicable filing requirements during the fiscal year ended December 31, 2004.

Code of Ethics

We have adopted a Code of Ethics that applies to all of our directors, officers and employees. We publicize the Code of Ethics through posting the policy on our website, http://www.paintrials.com. We will disclose on our website any waivers of, or amendments to, our Code of Ethics.

Item 11. ***Executive Compensation***

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Executive Compensation and Other Matters."

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

The information required by this Item regarding security ownership of certain beneficial owners and management is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Security Ownership of Certain Beneficial Owners and Management." The table required by this Item regarding equity compensation plans is incorporated by reference from Item 5 above of this Annual Report on Form 10-K.

Item 13. ***Certain Relationships and Related Transactions***

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading "Certain Relationships and Related Transactions."

Item 14. ***Principal Accountant Fees and Services***

The information required by this Item is incorporated by reference from our definitive Proxy Statement referred to in Item 10 above where it appears under the heading **"**Principal Accounting Fees and Services."

PART IV

Item 15. ***Exhibits and Financial Statement Schedules***

(a) The following documents are filed as part of this Form 10-K:

(1) *Financial Statements (included in Part II of this report):*

Reports of Independent Registered Public Accounting Firm

Balance Sheets

Statements of Operations

Statement of Stockholders' Equity (Deficit)

Statements of Cash Flows

Notes to Financial Statements

(2) *Financial Statement Schedules:*

All financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements.

(3) *Exhibits:*

Exhibit Number	Description of Document
3.1(1)	Amended and Restated Certificate of Incorporation.
3.2(1)	Amended and Restated Bylaws.
4.1(1)	Specimen Common Stock Certificate.
10.1(1)	Form of Indemnification Agreement between Registrant and each of its directors and officers.
10.2(1)	1998 Stock Plan and form of agreements thereunder.
10.3(1)	2000 Employee Stock Purchase Plan and form of agreements thereunder.
10.4(3)	Employment Agreement dated August 29, 2000, between Registrant and Grant L. Schoenhard, Ph.D.
10.5(3)	Employment Agreement dated October 23, 2001, between Registrant and Nadav Friedmann, M.D., Ph.D.
10.6(1)	Second Amended and Restated Investors' Rights Agreement dated as of February 1, 2000 between Registrant and the holders of its series B and series C redeemable convertible preferred stock.
10.7(2)	Lease Agreement dated July 21, 2000 between Registrant and Goss-Jewett Company of Northern California.
23.1	Consent of Independent Registered Public Accounting Firm.
24.1	Power of Attorney (see page F-24).
31.1	Certification of Chief Executive Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certifications of the Chief Executive Officer and the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

(1) Incorporated by reference from our registration statement on Form S-1, registration number 333-32370, declared effective by the Securities and Exchange Commission on July 13, 2000.

(2) Incorporated by reference from Exhibit 10.1 to our Quarterly Report on Form 10-Q for the fiscal quarter ended September 30, 2000.
(3) Incorporated by reference from exhibits to our report on Form 10-K for the period ending December 31, 2001.

(b) *Exhibits*

The exhibits listed under Item 14(a)(3) hereof are filed as part of this Form 10-K other than Exhibit 32.1, which shall be deemed, furnished.

(c) *Financial Statement Schedules*

All financial statement schedules are omitted because the information is inapplicable or presented in the notes to the financial statements.

SIGNATURES

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

PAIN THERAPEUTICS, INC.

By: /s/ REMI BARBIER

Remi Barbier
President, Chief Executive Officer and
Chairman of the Board of Directors

Dated: February 15, 2005

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, and each of them, his true and lawful attorneys-in-fact, each with full power of substitution, for him in any and all capacities, to sign any amendments to this Annual Report on Form 10-K and to file the same, with exhibits thereto and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that each of said attorneys-in-fact or their substitute or substitutes may do or cause to be done by virtue hereof.

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

Signature	Title	Date
/s/ REMI BARBIER **Remi Barbier**	President, Chief Executive Officer and Chairman of the Board of Directors (Principal Executive Officer)	February 15, 2005
/s/ PETER S. RODDY **Peter S. Roddy**	Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)	February 15, 2005
/s/ NADAV FRIEDMANN, PH.D., M.D., **Nadav Friedmann, PH.D., M.D.,**	Chief Operating and Medical Officer and Director	February 15, 2005
/s/ ROBERT Z. GUSSIN, PH.D. **Robert Z. Gussin, Ph.D.**	Director	February 15, 2005
/s/ VERNON R. LOUCKS, JR **Vernon R. Loucks, Jr.**	Director	February 15, 2005
/s/ MICHAEL J. O'DONNELL, ESQ. **Michael J. O'Donnell, Esq.**	Director and Secretary	February 15, 2005
/s/ SANFORD R. ROBERTSON **Sanford R. Robertson**	Director	February 15, 2005

EXHIBIT INDEX

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31.2	Certification of Chief Financial Officer pursuant to Section 302 of the Sarbanes-Oxley Act of 2002.
32.1	Certifications of the Chief Executive Officer and the Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

(1) Incorporated by reference from our registration statement on Form S-1, registration number 333-32370, declared effective by the Securities and Exchange Commission on July 13, 2000.
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(3) Incorporated by reference from exhibits to our report on Form 10-K for the period ending December 31, 2001.

EXHIBIT 23.1

CONSENT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

We consent to the incorporation by reference in the Registration Statement (Form S-3 No. 333-115362) of Pain Therapeutics, Inc. and in the related Prospectus, and in the Registration Statements (Form S-8 Nos. 333-115361, 333-105138, and 333-68118) pertaining to the 1998 Stock Plan of Pain Therapeutics, Inc. of our reports dated February 9**,** 2005, with respect to the financial statements of Pain Therapeutics, Inc., Pain Therapeutics, Inc.'s management's assessment of the effectiveness of internal control over financial reporting, and the effectiveness of internal control over financial reporting of Pain Therapeutics, Inc. included in the Annual Report (Form 10-K) for the year ended December 31, 2004.

/s/ Ernst & Young LLP

Palo Alto, California
February 15, 2005

Exhibit 31.1

CEO CERTIFICATION PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Remi Barbier, certify that:

1. I have reviewed this Report on Form 10-K of Pain Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ REMI BARBIER

Remi Barbier,
Chairman of the Board of Directors,
President and Chief Executive Officer

Date: February 15, 2005

Exhibit 31.2

CFO CERTIFICATION PURSUANT TO
SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Peter S. Roddy, certify that:

1. I have reviewed this Report on Form 10-K of Pain Therapeutics, Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
   a. Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
   b. Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
   c. Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
   d. Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
   a. All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
   b. Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

/s/ PETER S. RODDY

Peter S. Roddy,
Vice President and Chief Financial Officer

Date: February 15, 2005

Exhibit 32.1

CERTIFICATIONS OF THE CHIEF EXECUTIVE OFFICER AND THE CHIEF FINANCIAL OFFICER PURSUANT TO 18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

Pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, Remi Barbier, Chairman of the Board of Directors, President and Chief Executive Officer and Peter S. Roddy, Vice President and Chief Financial Officer of Pain Therapeutics, Inc. (the "Company"), hereby certify that to the best of our knowledge:

1. The Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2004, and to which this certification is attached as Exhibit 32.1 (the "Periodic Report"), fully complies with the requirements of Section 13 (a) or 15 (d) of the Securities Exchange Act of 1934, and
2. The information contained in this Periodic Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: February 15, 2005

/s/ REMI BARBIER

Remi Barbier,
Chairman of the Board of Directors,
President and Chief Executive Officer

/s/ PETER S. RODDY

Peter S. Roddy,
Vice President and Chief Financial Officer