

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**

Washington, DC 20549

FORM 8-K

CURRENT REPORT

**Pursuant to Section 13 or 15(d) of
The Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported)
September 22, 2004**

PAIN THERAPEUTICS, INC.

(Exact name of registrant as specified in its charter)

DELAWARE
(State or other jurisdiction
of incorporation)

000-29959
(Commission File Number)

91-1911336
(IRS Employer
Identification No.)

**416 BROWNING WAY
SOUTH SAN FRANCISCO, CA 94080**
(Address of principal executive offices, including zip code)

650-624-8200
(Registrant's telephone number, including area code)

(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Item 7.01. REGULATION FD DISCLOSURE

On September 22, 2004, Pain Therapeutics, Inc. (the "Company") issued a press release announcing its intention to offer eight million shares of common stock in an underwritten public offering under the Company's previously filed shelf Registration Statement on Form S-3 (File No. 333-115362, the "Registration Statement"), which was declared effective by the Securities and Exchange Commission on June 28, 2004. A copy of the press release is attached to this report as Exhibit 99.1.

Pursuant to General Instruction B.2 of Form 8-K, the press release attached as Exhibit 99.1 is not "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, but is instead furnished for purposes of that instruction.

Item 8.01. OTHER EVENTS

On September 22, 2004, the Company filed a Rule 424(b)(5) preliminary prospectus supplement and accompanying preliminary prospectus with the Securities and Exchange Commission in connection with the Registration Statement containing information attached to this Current Report on Form 8-K as exhibit 99.2.

The Company is also filing as exhibit 5.1 to this Current Report on Form 8-K an opinion of counsel.

This Current Report is being filed for the purpose of incorporating the information from the prospectus supplement and opinion of counsel attached as exhibits hereto by reference into this report and into the Registration Statement.

Item 9.01. FINANCIAL STATEMENTS AND EXHIBITS**(c) Exhibits.**

<u>Exhibit No.</u>	<u>Description</u>
5.1	Legal Opinion of Wilson Sonsini Goodrich & Rosati P.C.
99.1	Press release dated September 22, 2004 announcing the Company's underwritten common stock offering
99.2	Information from Preliminary Prospectus Supplement

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

PAIN THERAPEUTICS, INC.

By: /s/ Peter S. Roddy

Peter S. Roddy
Chief Financial Officer

Date: **September 22, 2004**

EXHIBIT INDEX

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[Letterhead of Wilson Sonsini Goodrich & Rosati PC]

September 21, 2004

Pain Therapeutics, Inc.
416 Browning Way
South San Francisco, California 94080

Re: Registration Statement on Form S-3

Ladies and Gentlemen:

At your request, we have examined the Registration Statement on Form S-3 (File No. 333-115363) (the "Registration Statement"), filed by Pain Therapeutics, Inc., a Delaware corporation (the "Company"), with the Securities and Exchange Commission in connection with the registration pursuant to the Securities Act of 1933, as amended (the "Act"), of up to 9.2 million shares of the Company's Common Stock, \$0.001 par value per share (the "Shares"). The Shares are to be sold in the manner set forth in the Registration Statement, the Prospectus contained therein (the "Prospectus") and the related supplement to the Prospectus (the "Prospectus Supplement").

We have examined the instruments, documents and records that we deemed relevant and necessary for the basis of our opinion hereinafter expressed. In such examination, we have assumed (a) the authenticity of original documents and the genuineness of all signatures, (b) the conformity to the originals of all documents submitted to us as copies and (c) the truth, accuracy and completeness of the information, representations and warranties contained in the records, documents instruments and certificates we have reviewed.

On the basis of the foregoing, and in reliance thereon, we are of the opinion that the Shares, when issued and sold in the manner described in the Registration Statement, the Prospectus and the Prospectus Supplement, will be validly issued, fully paid and nonassessable.

We hereby consent to the filing of this opinion as an exhibit to the above-referenced Registration Statement and to the use of our name wherever it appears in the Registration Statement, the Prospectus, the Prospectus Supplement and in any amendment or supplement thereto. In giving such consent, we do not believe that we are "experts" within the meaning of such term as used in the Act or the rules and regulations of the Securities and Exchange Commission issued thereunder with respect to any part of the Registration Statement, including this opinion as an exhibit or otherwise.

Sincerely,

WILSON SONSINI GOODRICH & ROSATI
Professional Corporation

/s/ Wilson Sonsini Goodrich & Rosati

For More Information Contact:

Christi Waarich
Senior Manager of Investor Relations
Pain Therapeutics, Inc.
cwaarich@paintrials.com
650-825-3324

FOR IMMEDIATE RELEASE

PAIN THERAPEUTICS ANNOUNCES

PROPOSED PUBLIC OFFERING OF COMMON STOCK

SOUTH SAN FRANCISCO, Calif. – September 22, 2004 – Pain Therapeutics, Inc. (Nasdaq: PTIE), a biopharmaceutical company, today announced that it plans to offer approximately 8 million shares of common stock pursuant to its currently effective shelf registration statement. The Company also intends to grant the underwriters of the offering a 30-day option to purchase an additional 1.2 million shares of common stock to cover over-allotments.

Citigroup Global Markets Inc., and UBS Securities LLC are acting as lead underwriters for the proposed offering. CIBC World Markets Corp., and Rodman & Renshaw, LLC will serve as co-managing underwriters.

A preliminary prospectus supplement was filed today with the Securities and Exchange Commission (SEC) and is available on the SEC's website at www.sec.gov. Copies of the preliminary prospectus supplement and accompanying preliminary prospectus meeting the requirements of the Securities Act of 1933, as amended, when available, may be obtained upon request in writing to Citigroup Global Markets Inc., 388 Greenwich Street, 32nd Floor, New York, NY 10013 or UBS Securities LLC, 299 Park Avenue, New York, NY 10171.

This news release is neither an offer to sell nor the solicitation of an offer to buy the securities described herein, nor shall there be any sale of these securities in any state or jurisdiction in which such an offer, solicitation or sale would be unlawful prior to registration or qualification under the securities law of any such state or jurisdiction. The offering may be made only by means of a prospectus supplement and the accompanying prospectus.

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RISK FACTORS

You should carefully consider the risks described below before making a decision to buy our common stock. If any of the following risks actually occur, our business could be harmed, the trading price of our common stock could decline and you may lose all or part of your investment. You should also refer to the other information contained in or incorporated by reference into this prospectus supplement and the accompanying prospectus, including the financial statements and related notes.

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 product 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 \$93.5 million as of June 30, 2004. Even if we succeed in developing and commercializing one or more of our drug candidates, we expect to continue to incur substantial losses for the foreseeable future, and we may never become profitable. We anticipate that our expenses will increase substantially in the foreseeable future as we:

- continue to conduct preclinical and clinical trials for our drug candidates, including the Phase III trials of Oxytrex, PTI-901 and the Phase III clinical program and 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 equivalent and marketable securities on hand will be

sufficient to meet our working capital and capital expenditure needs for at least the next 12 months. However, we may need to raise additional funds within such 12-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 drugs, and we will not generate product revenues.

Satisfaction of all regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the drug candidate, and requires the expenditure of substantial resources for research and development and testing. Our research and clinical approaches may not lead to drugs that the FDA considers safe for humans and effective for indicated uses we are studying. The FDA may require us to conduct additional clinical testing, in which case we would have to expend additional time and resources 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.

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

If we are unable to design, conduct and complete clinical trials successfully, we will not be able to obtain regulatory approval for our 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. Two of our drug candidates, Oxytrex and PTI-901,

are in Phase III clinical trials. In September 2004, we received regulatory clearance to initiate clinical studies with Remoxy in the United States and we plan to initiate a Phase III program in December 2004.

Our Phase III trials may not demonstrate the safety or efficacy of our drug candidates. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful. Results of later clinical trials may not replicate the results of prior clinical trials and pre-clinical testing. FDA guidelines recommend that the efficacy of new painkillers be demonstrated in more than one clinical model of pain. This means that even if one of our Phase III 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 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. 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.

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.

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 product 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

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

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

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

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 shareholders to remove or replace management, engage in proxy contests and effect changes in control. These provisions include:

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

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.

FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus contain forward-looking statements. We use words like “anticipates,” “believes,” “plans,” “expects,” “future,” “intends” and similar expressions to identify these forward-looking statements. Examples of such statements include:

- We expect our third drug candidate to enter a Phase III clinical program by the end of 2004.
- We expect to unblind our first Phase III Oxytrex study and to announce clinical results in the first quarter of 2005.
- We plan to enroll over 700 patients with severe osteoarthritic pain in our second Phase III Oxytrex study.
- We expect to complete patient enrollment for our second Phase III Oxytrex study in the first quarter of 2005 and to announce clinical results of this study in the second quarter of 2005.
- If approved by the FDA for this indication, we believe PTI-901 will target a market in excess of \$1 billion per year.
- The first Phase III study for PTI-901 plans to enroll 600 women, while the second Phase III study for PTI-901 study plans to enroll 600 men.
- We expect to complete patient enrollment for the PTI-901 Phase III study in women in the second quarter of 2005 and patient enrollment for the PTI-901 Phase III study in men in the second half of 2005.
- We plan to announce new anti-abuse data in human volunteers with Remoxy in the fourth quarter of 2004.
- We also plan to initiate a Phase III clinical program with Remoxy in the United States in December 2004.
- Using our Remoxy platform technology, we will seek to develop anti-abuse versions of one or more additional opioid painkillers.
- We believe our focus on clinical development and late stage products will enable us to generate product revenues earlier than if we were focused on early-stage research and discovery activities.
- In general, we intend to independently develop our drug candidates through late-stage clinical trials.
- We intend to continue to outsource pre-clinical studies, clinical trials and formulation and manufacturing activities.
- We intend to evaluate promising drug candidates or technologies to further expand our product pipeline.
- We expect to announce initial Phase III clinical results from our Phase III study with Oxytrex in the first quarter of 2005.
- We plan to meet with the FDA and to initiate a Phase III program with Remoxy by the end of 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.
- We expect that our current cash, cash equivalent and marketable securities on hand will be sufficient to meet our working capital and capital expenditure needs for at least the next 12 months.
- We expect to rely on sales generated by our current lead drug candidates for substantially all of our product revenues for the foreseeable future.

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- We intend to file additional patent applications relating to our technology, products and processes.
 - We expect that we will rely upon trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position.

We have based these forward-looking statements on our current expectations and projections about future events. These forward-looking statements involve risks and uncertainties, including, but not limited to, the following:

- those risks and uncertainties relating to difficulties or delays in development, testing, regulatory approval, production and marketing 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; and
- our ability to obtain additional financing if necessary; and those risks and uncertainties relating to an investment in our common stock.

In light of those risks, uncertainties and assumptions, the forward-looking events discussed in this prospectus supplement, the accompanying prospectus and the documents incorporated by reference into this prospectus supplement and the accompanying prospectus might not occur.