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As filed with the Securities and Exchange Commission on September 19, 2003

Registration No. 333-108145

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT NO. 2
TO
FORM S-3
REGISTRATION STATEMENT
Under
The Securities Act of 1933

Pain Therapeutics, Inc.

(Exact Name of Registrant as Specified in its Charter)

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

416 Browning Way
South San Francisco, CA 94080
(Address, including zip code, and telephone number, including area code, of Registrant's principal executive offices)

Remi Barbier
President, Chief Executive Officer
And Director
Pain Therapeutics, Inc.
416 Browning Way
South San Francisco, CA 94080
(650) 624-8200
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Michael O'Donnell, Esq. **Martin Waters, Esq.** **Wilson Sonsini Goodrich & Rosati** **Professional Corporation** **650 Page Mill Road** **Palo Alto, California 94304** **(650) 493-9300**	**David Lopez, Esq.** **Cleary, Gottlieb, Steen & Hamilton** **One Liberty Plaza** **New York, New York 10006** **(212) 225-2000**

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

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

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

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

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

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

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

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The information contained in this preliminary prospectus is not complete and may be changed. These securities may not be sold until the registration statement filed with the Securities and Exchange Commission is effective. This prospectus is not an offer to sell and it is not soliciting an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

SUBJECT TO COMPLETION, DATED SEPTEMBER 19, 2003

PROSPECTUS

7,650,000 Shares

Pain Therapeutics, Inc.

Common Stock

$ per share

We are selling 7,650,000 shares of our common stock. We have granted the underwriters an option to purchase up to 1,147,500 additional shares of common stock to cover over-allotments.

Our common stock is quoted on the Nasdaq National Market under the symbol "PTIE." On September 2, 2003, the last sale price for the common stock as reported on the Nasdaq National Market was $7.97 per share.

Investing in our common stock involves risks. See " Risk Factors" beginning on page 5.

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

	Per Share	Total
Public offering price	$	$
Underwriting discount	$	$
Proceeds to Pain Therapeutics, Inc. (before expenses)	$	$

The underwriters expect to deliver shares to purchasers on or about , 2003.

Sole Book Runner and Joint Lead Manager

Citigroup

Joint Lead Manager

CIBC World Markets

Leerink Swann & Company

ThinkEquity Partners

, 2003.

You should rely only on the information contained in or incorporated by reference in this prospectus. We have not authorized anyone to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information contained in this prospectus is accurate as of any date other than the date on the front of this prospectus.

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Unless specifically stated, information in this prospectus assumes the underwriters will not exercise their over-allotment option and no other person will exercise any other outstanding options or warrants.

SUMMARY

This summary highlights information contained elsewhere or incorporated by reference in this prospectus. This is not intended to be a complete description of the matters covered in this prospectus and is subject to and qualified in its entirety by reference to the more detailed information and financial statements (including the notes thereto) included or incorporated by reference in this prospectus. When we refer to "we," "us," "our" or "the Company," we mean Pain Therapeutics, Inc., unless the context indicates otherwise.

Pain Therapeutics, Inc.

We are a biopharmaceutical company specializing in the clinical development of novel painkillers. We believe our unique insights into the biology and biochemistry of pain will allow us to develop new opioid drugs that address unmet needs in pain management. Total U.S. sales for opioid painkillers exceeded $4.5 billion in 2002, representing a 25% compound annual growth rate since 1998. We own all commercial rights to our drug candidates.

Clinical Pipeline

We intend to have two drug candidates in Phase III clinical trials by the end of 2003. Our clinical results to date show that our drug candidates may provide numerous benefits, including enhanced pain relief with no increase in side effects and prolonged pain relief. Our pre-clinical results also demonstrate a lack of opioid tolerance, physical dependence, withdrawal effects or addiction potential in animals.

Our lead drug candidate is called Oxytrex™. Oxytrex is a small molecule drug to treat severe chronic pain, such as low back, osteoarthritic or cancer pain. On June 30, 2003, we announced the initiation of a Phase III clinical study with Oxytrex. Our Phase II clinical studies indicate that Oxytrex offers more pain relief with no increase in side-effects, compared to opioid painkillers commonly used to treat severe chronic pain, such as oxycodone. We believe these benefits can help alleviate the current tendency of physicians to under-prescribe opioid painkillers. The U.S. market for oxycodone exceeded $1.5 billion in 2002.

Our second drug candidate is called PTI-901. PTI-901 is a small molecule drug to treat irritable bowel syndrome, or IBS, with a novel mechanism of action. There are no drugs approved by the Food and Drug Administration, or FDA, to treat IBS in men; there are only two FDA-approved drugs to treat women with IBS. In contrast, PTI-901 is intended to treat both men and women who suffer from IBS. We plan to announce the initiation of a Phase III clinical study with PTI-901 in the fourth quarter of 2003. If approved by the FDA, we believe PTI-901 will target a $1 billion market in the U.S.

In addition, we plan to announce a new drug candidate in the area of pain management in the fourth quarter of 2003.

Strategy

Our goal is to build a drug franchise in pain management. We intend to develop novel drugs that are more effective or safer than drugs that are widely used in the clinic today. Our strategy to achieve our goal includes:

Focusing on Clinical Development and Late Stage Products. We believe that our clinical development focus will enable us to generate product revenues earlier than if we were conducting research and discovery of new chemical entities.

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

Outsourcing Key Functions. We intend to continue to outsource certain key functions, including pre-clinical studies, clinical trials, formulation and manufacturing. We believe outsourcing permits significant time savings and allows for more efficient deployment of our resources.

Recent Developments

Phase III Study with Oxytrex

On June 30, 2003, we announced the initiation of a Phase III clinical study with Oxytrex, our lead drug candidate to treat severe chronic pain. This study compares the analgesic efficacy of Oxytrex against placebo and oxycodone. The study will enroll up to 700 patients with severe chronic low-back pain over a three-month treatment period. The initiation of this pivotal study followed the successful completion of a large Phase II study in a multi-dose, chronic model of pain. This Phase II study met its clinical efficacy endpoints. In this 350 patient study, Oxytrex showed a statistically significant reduction in severe chronic osteoarthritic pain during a 21-day treatment period against placebo ($p<0.001$) and oxycodone ($p=0.006$).

Phase I/II Study with PTI-901

On May 29, 2003, we announced successful clinical results with PTI-901, a small molecule drug candidate, for patients with IBS. In a 50 patient Phase I/II study, patients of both gender reported a 75% positive response rate to PTI-901. This open-label study also met secondary endpoints, such as improving abdominal pain and bowel habits. No drug-related adverse events were observed in this study. We plan to follow up this Phase I/II study with a 600 patient Phase III trial beginning in the fourth quarter of 2003.

The Offering

Unless specifically stated, information in this prospectus assumes the underwriters will not exercise their over-allotment option and no other person will exercise any other outstanding options or warrants.

Common stock offered by Pain Therapeutics, Inc.	7,650,000 shares
Common stock outstanding after the offering	35,255,811 shares
Use of proceeds	We intend to use the proceeds from this offering for general corporate purposes, including research and development, expansion of our commercial function, acquisition of complimentary technologies or products and working capital.
Nasdaq National Market symbol	PTIE

The number of shares that will be outstanding after the offering is based on the number of shares outstanding as of August 14, 2003 and excludes:

- 6,703,621 shares of common stock authorized for issuance under our stock option plans, under which options to purchase 4,122,901 shares were outstanding and 2,580,720 shares were available for grant as of such date; and
- 220,000 shares of common stock reserved for issuance upon the exercise of warrants outstanding as of such date, at a weighted average exercise price of $1.00 per share.

* * *

We were incorporated in Delaware in May 1998. Our principal executive offices are located at 416 Browning Way, South San Francisco, California 94080.

Summary Financial Data

The tables below set forth summary financial data for the periods indicated. The historical results for the year ended December 31, 1998 reflect the results from the date of our inception (May 4, 1998) through December 31, 1998. The statement of operations data for the year ended December 31, 2002, and the balance sheet data as of December 31, 2002, are derived from our financial statements that have been audited by Ernst & Young LLP, independent auditors, and incorporated by reference into this prospectus. The statement of operations data for the years ended December 31, 1998, 1999, 2000 and 2001, and the balance sheet data as of December 31, 1998, 1999, 2000 and 2001, are derived from our audited financial statements that have been audited by KPMG LLP, independent auditors, and incorporated by reference into this prospectus. The summary statement of operations data for the six months ended June 30, 2002 and 2003, and the summary balance sheet data as of June 30, 2003, are derived from our unaudited financial statements incorporated by reference into this prospectus. In the opinion of management, all adjustments, consisting of normal recurring adjustments, necessary for a fair presentation have been included in preparing the unaudited financial statements. You should read the following selected financial data together with the accompanying "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the accompanying financial statements and related notes that are included in this prospectus. Results for interim periods are not necessarily indicative of results to be expected during the remainder of the fiscal year or for any future period.

	Years ended December 31,					Six months ended June 30, 2002	Six months ended June 30, 2003
	1998	1999	2000	2001	2002		
	(in thousands, except per share data)						
Statement of operations data:							
Research and development expense	$ 300	$ 3,967	$ 12,596	$ 11,668	$ 11,396	$ 5,490	$ 7,503
General and administrative expense	123	694	7,710	5,647	5,523	2,812	1,720
Total operating expenses	423	4,661	20,306	17,315	16,919	8,302	9,223
Operating loss	(423)	(4,661)	(20,306)	(17,315)	(16,919)	(8,302)	(9,223)
Interest income	34	161	2,826	2,978	994	561	261
Net loss	(389)	(4,500)	(17,480)	(14,337)	(15,925)	(7,741)	(8,962)
Return to series C preferred stockholders for beneficial conversion feature	—	—	(14,231)	—	—	—	—
Loss available to common stockholders	$ (389)	$ (4,500)	$ (31,711)	$ (14,337)	$ (15,925)	$ (7,741)	$ (8,962)
Basic and diluted loss per share	$ (0.39)	$ (1.35)	$ (2.33)	$ (0.57)	$ (0.59)	$ (0.29)	$ (0.33)
Weighted average shares used in computing basic and diluted loss per share	986	3,345	13,635	25,332	27,039	26,973	27,250

	As of December 31,					As of June 30, 2003
	1998	1999	2000	2001	2002	
	(in thousands)					
Balance sheet data:						
Cash and cash equivalents	$ 2,334	$ 9,340	$ 78,927	$ 65,274	$ 50,091	$ 42,546
Working capital	2,264	9,096	77,320	63,195	48,146	40,230
Total assets	2,383	9,441	81,147	68,135	53,325	44,531
Total liabilities	108	301	2,452	2,519	3,101	2,395
Stockholders' equity (deficit)	2,275	(563)	78,695	65,616	50,224	42,136

RISK FACTORS

You should carefully consider the risks described below before making a decision to buy our common stock. The risks and uncertainties described below are not the only ones facing our company. 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, including the financial statements and related notes.

Risks Relating to Our Company

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

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

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

We have incurred net losses each year since our inception. As a result of ongoing operating losses, we had an accumulated deficit of $61.6 million as of June 30, 2003. Even if we succeed in developing and commercializing one or more of our drugs, 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 undertake preclinical and clinical trials for our product candidates, including the Phase III trials of Oxytrex and PTI-901;
- seek regulatory approvals for our product candidates;
- develop, formulate, manufacture and commercialize our drugs;
- implement additional internal systems and develop new infrastructure;
- acquire or in-license additional products or technologies or expand the use of our technology;
- maintain, defend and expand the scope of our intellectual property; and
- hire additional personnel.

We will need to generate significant revenues to achieve and maintain profitability. If we cannot successfully develop and commercialize our products, we will not be able to generate such revenues or achieve

profitability in the future. Our failure to achieve or maintain profitability could negatively impact the market price of our common stock.

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

We have funded all of our operations and capital expenditures with the proceeds from public and private stock offerings. We expect that our current cash and cash equivalents on hand will be sufficient to meet our working capital and capital expenditure needs for at least the next twelve months. However, we may need to raise additional funds sooner and additional financing may not be available on favorable terms, if at all. Even if we succeed in selling additional equity or convertible debt 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 do not succeed in raising additional funds, we may be unable to complete planned clinical trials or obtain FDA approval of our product candidates, and we could be forced to discontinue product development, reduce sales and marketing efforts and forego attractive business opportunities.

Clinical and Regulatory Risks

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

Satisfaction of all regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the product 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 the indicated uses we are studying. The FDA may require us to conduct additional clinical testing, in which case we would have to expend additional time and resources. The approval process may also be delayed by changes in government regulation, future legislation or administrative action or changes in FDA policy that occur prior to or during our regulatory review. Delays in obtaining regulatory approvals will:

- delay commercialization of, and product revenues from, our product 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 product candidates. If we fail to obtain regulatory approval of any of our product candidates we will have fewer saleable products and corresponding lower product revenues. Even if we receive regulatory approval of our products, such approval may involve limitations on the indicated uses or marketing claims we may make for our products. Further, later discovery of previously unknown problems could result in additional regulatory restrictions, including withdrawal of products. The FDA may also require us to commit to perform lengthy post-approval studies, for which we would have to expend additional resources, which could have an adverse effect on our operating results and financial condition.

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

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

In order to obtain FDA approval of any of our product candidates, we must submit to the FDA a New Drug Application, or NDA, which demonstrates that the product 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.

We have several drug candidates in various stages of clinical testing. In June 2003, we announced the results of a 21-day Phase II study of our lead product candidate, Oxytrex, in patients with severe osteoarthritic pain. In June 2003, we announced initiation of a Phase III clinical trial of Oxytrex to demonstrate the safety and efficacy of Oxytrex in patients with documented severe chronic low back pain. In May 2003, we announced the results of a 50 patient pilot study using PTI-901, a proprietary new drug candidate we are developing to treat irritable bowel syndrome. We plan to initiate in the fourth quarter of 2003 a Phase III trial with PTI-901 following discussion with regulatory agencies. These Phase III trials may not demonstrate the safety or efficacy of our drug candidates. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful. Results of later clinical trials may not replicate the results of prior clinical trials and pre-clinical testing. FDA guidelines recommend that the efficacy of new painkillers be demonstrated in more than one clinical model of pain. Even if the results of our Phase III trials are positive, we may have to commit substantial time and additional resources to conducting further preclinical and clinical studies in other types of pain before we can submit NDAs or obtain approvals for our product 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 adverse reactions during the course of such trials, or if we or the FDA believe that participating patients are being exposed to unacceptable health risks, we will have to suspend our clinical trials. Failure can occur at any stage of the trials, and we could encounter problems that cause us to abandon clinical trials or to repeat clinical studies.

Even if our clinical trials are completed as planned, their results may not support our product claims. The clinical trial process may fail to demonstrate that our product candidates are safe and effective for indicated uses. Such failure would cause us to abandon a product candidate and could delay development of other product 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 trial protocols. Over the course of conducting our clinical trials, circumstances may change, such as standards of safety or efficacy or medical practice, that could affect regulatory authorities' perception of the adequacy of any of our trial designs or the data we develop from our studies. 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 products comparing our products 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 to placebo in a particular clinical indication where approved products are available. In that case, both the cost and the amount of time required to conduct a trial could increase.

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

The U.S. Drug Enforcement Agency, or 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 product candidates, such as morphine, hydrocodone and oxycodone, are listed by the DEA as Schedule II or III substances under the Controlled Substances Act of 1970. Consequently, their manufacture, research, shipment, storage, sale and use are subject to a high degree of regulation. For example, all Schedule II drug prescriptions must be signed by a physician, physically presented to a pharmacist and may not be refilled without a new prescription. Furthermore, the amount of Schedule II substances we can obtain for clinical trials and commercial distribution is limited by the DEA and our quota may not be sufficient to complete clinical trials or meet commercial demand. There is a risk that DEA regulations may interfere with the supply of the drugs used in our clinical trials, and in the future, our ability to produce and distribute our products in the volume needed to meet commercial demand.

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

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

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

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

Risks Relating to Commercialization

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

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

- perceptions by members of the healthcare community, including physicians, about the safety and effectiveness of our drugs;
- cost-effectiveness of our drugs relative to competing products;
- availability of reimbursement for our products from government or healthcare payers; 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 product candidates for substantially all of our product revenues for the foreseeable future, the failure of any of these drugs to find market acceptance would harm our business and could require us to seek additional financing.

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

We currently have no sales, marketing or distribution capabilities. In order to commercialize our products, if any are approved by the FDA, we will either have to develop such capabilities internally or collaborate with third

parties who can perform these services for us. If we decide to commercialize any of our drugs ourselves, we may not be able to hire the necessary experienced personnel and build sales, marketing and distribution operations which are capable of successfully launching new drugs and generating sufficient product revenues. In addition, establishing such operations will take time and involve significant expense.

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

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

In addition, any revenues we receive would depend upon our collaborators' efforts which may not be adequate due to lack of attention or resource commitments, management turnover, change of strategic focus, further business combinations or other factors outside of our control. Depending upon the terms of our 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 product candidates is characterized by intense competition and rapid technological advances. If our products 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;
- undertaking preclinical testing and human clinical trials;
- obtaining FDA and other regulatory approvals of drugs;
- formulating and manufacturing drugs; and
- launching, marketing, distributing and selling drugs.

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

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

- government and health administration authorities;
- private health maintenance organizations and health insurers; and
- other healthcare payers.

Significant uncertainty exists as to the reimbursement status of newly approved healthcare products. Healthcare payers, including Medicare, health maintenance organizations and managed care organizations, are challenging the prices charged for medical products and services and/or are seeking pharmacoeconomic data to justify formulary acceptance and reimbursement practices. Government and other healthcare payers increasingly are attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for drugs, and by refusing, in some cases, to provide coverage for uses of approved products for disease indications for which the FDA has or has not granted labeling approval. Third-party insurance coverage may not be available to patients for any products we discover and develop, alone or with collaborators. If government and other healthcare payers do not provide adequate coverage and reimbursement levels for our products, market acceptance of them could be limited.

Risks Relating to our Intellectual Property

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

Our success, competitive position and potential future revenues will depend in part on our ability to protect our intellectual property. If either 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 and reexaminations are pending in the PTO. In each of the reexaminations, the PTO has issued a first/initial office action and responses to those office actions have been filed. In one of the reexaminations, the PTO has issued a second/final office action in which the PTO affirmed the patentability of certain claims related to uses of the drugs under development and maintained rejections with respect to other claims. We intend to file an appropriate response to that office action. We cannot provide any assurance as to the outcome of any ongoing PTO proceedings. An adverse outcome of the reexamination process could result in loss of claims of these patents that pertain to certain drugs we currently have under development and could have a material adverse impact on our future revenues.

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

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

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

Our technology could infringe upon claims of patents owned by others. If we were found to be infringing on a patent held by another, we might have to seek a license to use the patented technology. In that case, we might

not be able to obtain such a license on terms acceptable to us, or at all. If a legal action were to be brought against us or our licensors, we could incur substantial defense costs, and any such action might not be resolved in our favor. If such a dispute were to be resolved against us, we could have to pay the other party large sums of money and our use of our technology and the testing, manufacture, marketing or sale of one or more of our proposed products could be restricted or prohibited.

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 and the regulatory approval process or in formulating, manufacturing, marketing and selling our potential products.

We will need to hire additional qualified personnel with expertise in clinical research, preclinical testing, government regulation, formulation and manufacturing and sales and marketing. We compete for qualified individuals with numerous biopharmaceutical companies, universities and other research institutions. Competition for such individuals, particularly in the San Francisco Bay area, is intense, and our search for such personnel may not be successful. Attracting and retaining qualified personnel will be critical to our success.

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

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

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

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

Business interruptions could limit our ability to operate our business.

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

Risks Relating to Manufacturing

If third-party manufacturers of our product 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 product 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 product candidates and commercialization of our products, result in higher costs, or deprive us of potential product revenues:

- Contract commercial manufacturers, their sub-contractors or other third parties we rely on, may encounter difficulties in achieving the volume of production needed to satisfy clinical needs or commercial demand, may experience technical issues that impact quality, and may experience shortages of qualified personnel to adequately staff production operations.
- Our contract manufacturers could default on their agreements with us to provide clinical supplies or meet our requirements for commercialization of our products.
- The use of alternate manufacturers may be difficult because the number of potential manufacturers that have the necessary governmental licenses to produce narcotic products is limited. Additionally, the FDA 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.

Risks Relating to our Collaboration Agreements

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

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

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

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

Our strategy to focus on drug discovery of novel drugs discovered by third parties requires us to enter into collaborative agreements from time to time. Collaborative 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. Collaborative agreements often take longer to conclude and may be more expensive to conduct than originally expected. Other factors relating to collaborative agreements may adversely affect the success of our potential products, 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 the Offering and to an Investment in our Common Stock

You will suffer immediate and substantial dilution because the net tangible book value of shares purchased in this offering will be substantially lower than the offering price.

The public offering price of the shares of common stock in this offering will significantly exceed the net tangible book value per share of our common stock. Any shares of common stock that investors purchase in this offering will have a post-closing net tangible book value per common share of $5.15 per share less than the public offering price paid, assuming a public offering price per share of $7.97. Accordingly, if you purchase common stock in this offering, you will incur immediate and substantial dilution of your investment. If outstanding options or warrants are exercised, you will incur additional dilution.

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 market price if trading in our stock is not active or the volume is low. The following factors, in addition to other risk factors described in this section, may have a significant impact on the market price of our common stock:

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

The NASD and the Securities and Exchange Commission have adopted or proposed and are in the process of adopting certain new rules which, if adopted in their current form, may require us to make changes to the

membership of our board of directors and audit, compensation and nominating committees. If we were unable to continue to comply with the new rules within the time frame prescribed by the NASD, we could be delisted from trading on such market, and thereafter trading in our common stock, if any, would be conducted through the over-the-counter market or on the Electronic Bulletin Board of the National Association of Securities Dealers, Inc. As a consequence of such delisting, an investor would likely find it more difficult to dispose of, or to obtain quotations as to the price of, our common stock. Delisting of our common stock could also result in lower prices per share of our common stock than would otherwise prevail.

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

The stock market in general, and the NASDAQ National Market and the market for technology companies in particular, have experienced significant price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of those companies. Further, there has been particular volatility in the market prices of securities of early stage and development stage life sciences companies. These broad market and industry factors may seriously harm the market price of our common stock, regardless of our operating performance. In the past, following periods of volatility in the market price of a company's 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 shareholders (shareholders holding greater than 5% of our common stock) acting collectively may have the ability to exercise significant influence over matters requiring shareholder 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 shareholders.

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 product candidates, our need for clinical supplies and the re-measurement of certain deferred stock compensation. Thus, quarter-to-quarter comparisons of our operating results are not indicative of what we might expect in the future. As a result, in some future quarters our operating results may not meet the expectations of securities analysts and investors which could result in a decline in the price of our stock.

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

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

Our management may not use the proceeds of this offering in ways which increase our operating results.

Our management has broad discretion over the use of proceeds of this offering. In addition, our management has not designated a specific use for a substantial portion of the proceeds of this offering. Accordingly, it is possible that our management may allocate the proceeds differently than investors in this offering would have preferred, or that we fail to maximize our return on the proceeds.

FORWARD-LOOKING STATEMENTS

This prospectus and the documents incorporated by reference into this 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 believe our unique insights into the biology and biochemistry of pain will allow us to develop new opioid drugs to treat painful chronic conditions.
- We intend to have two drug candidates in Phase III clinical trials by the end of 2003.
- We plan to announce the initiation of a Phase III clinical study with PTI-901 in the fourth quarter of 2003.
- We intend to independently develop our drug candidates through late-stage clinical trials.
- We intend to continue to outsource certain key functions, including pre-clinical studies, clinical trials, formulation and manufacturing.
- We believe our drugs will offer enhanced pain relief or reduced tolerance/physical dependence or addiction potential compared to existing opioid painkillers.
- We expect research and develop expenses to increase significantly over the next several years as we expand our development efforts and as our product candidates progress through various stages of clinical trials.
- We expect to incur significant additional operating losses for the next several years.
- We expect general and administrative expense to increase in future periods in support of increased research and development or general corporate activities.
- We intend to file an appropriate response to that office action.

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 the 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 the Company’s intellectual property or trade secrets;
- potential infringement of the intellectual property rights or trade secrets of third parties;
- our ability to obtain additional financing if necessary; and
- those risks and uncertainties relating to the fact that our common stock is thinly traded.

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

USE OF PROCEEDS

We estimate our net proceeds from the sale of the 7,650,000 shares of our common stock offered in this offering will be approximately $56.8 million based on the assumed public offering price of $7.97 per share and after deducting the underwriting discount and estimated offering expenses.

The net proceeds are expected to be used for general corporate purposes, including research and development, expansion of our commercial function, acquisition of complementary technologies or products and working capital. Pending use, we intend to invest the net proceeds in short-term, investment-grade, interest-bearing securities.

CAPITALIZATION

The following table sets forth our unaudited cash and cash equivalents and capitalization as of June 30, 2003:

- on a historical basis; and
- on an as adjusted basis to give effect to this offering at an assumed offering price of $7.97 per share, after deducting the underwriting discount and the expenses related to the offering.

	As of June 30, 2003	
	Historical	As Adjusted
	(in thousands)	
Cash and cash equivalents	$ 42,546	$ 99,395
Total debt	$ —	$ —
Stockholders' equity:		
Convertible preferred stock, $.001 par value; 10,000,000 shares authorized, no shares issued and outstanding	—	—
Common stock, $.001 par value; actual—120,000,000 shares authorized, 27,447,755 shares issued and outstanding; as adjusted—35,097,755 shares issued and outstanding	27	35
Additional paid-in capital	103,770	160,611
Deferred stock compensation	(58)	(58)
Deficit accumulated during the development stage	(61,593)	(61,593)
Notes receivable from stockholders	(10)	(10)
Total stockholders' equity	42,136	98,985
Total capitalization	$ 42,136	$ 98,985

DILUTION

The net tangible book value of our common stock as of June 30, 2003 was approximately $42.1 million, or $1.54 per share. Net tangible book value per share represents the amount of our total assets, excluding net intangible assets, less our total liabilities, divided by the total number of shares of our common stock outstanding.

Without taking into account any other changes in net tangible book value, other than to give effect to the sale of 7,650,000 shares of common stock offered by us in this prospectus at the assumed public offering price, and after deducting the estimated underwriting discount and estimated offering expenses payable by us, our as adjusted net tangible book value as of June 30, 2003 would have been approximately $99.0 million, or $2.82 per share. This represents an immediate increase in net tangible book value of $1.28 per share to existing stockholders and an immediate dilution of $5.15 per share to investors purchasing shares of common stock in this offering. The following table illustrates this per share dilution:

Assumed public offering price per share		$7.97
Net tangible book value per share as of June 30, 2003	$1.54	
Increase per share attributable to new investors	1.28	
Net tangible book value per share after this offering		2.82
Dilution per share to new investors		$5.15

The calculation of net tangible book value and other computations above assume that no options or warrants were exercised after June 30, 2003. As of June 30, 2003, there were 1,837,844 shares of common stock were issuable upon exercise of outstanding options at a weighted average exercise price of $5.85 and warrants outstanding to purchase a total of 220,000 shares of common stock at a weighted average exercise price of $1.00 per share. If all of these options and warrants had been exercised as of June 30, 2003, our net tangible book value on that date would have been $53.1 million or $1.80 per share, the increase in net tangible book value attributable to new investors would have been $1.16 per share and the dilution in net book value to new investors would have been $5.01 per share.

DIVIDEND POLICY

To date, we have not paid any cash dividends on our common stock. We currently anticipate that we will retain any available funds to finance the growth and operation of our business and we do not anticipate paying any cash dividends in the foreseeable future. Certain present or future agreements may limit or prevent the payment of dividends on our common stock.

PRICE RANGE OF COMMON STOCK

Our common stock has been traded in The Nasdaq Stock Market under the symbol “PTIE” since our initial public offering on July 14, 2000. As of August 20, 2003, we had approximately 81 holders of record of our common stock. 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:

	Sales Price	
	High	Low
2001:		
First Quarter	$15.75	$6.75
Second Quarter	10.94	5.40
Third Quarter	8.24	5.91
Fourth Quarter	9.25	5.30
2002:		
First Quarter	10.61	7.46
Second Quarter	12.12	6.10
Third Quarter	10.00	3.86
Fourth Quarter	4.76	2.00
2003:		
First Quarter	3.90	1.68
Second Quarter	8.11	1.68
Third Quarter (through September 2, 2003)	8.95	6.20

SELECTED FINANCIAL DATA

The table below sets forth selected financial data for the periods indicated. The historical results for the year ended December 31, 1998 reflect the results from the date of our inception (May 4, 1998) through December 31, 1998. The statement of operations data for the year ended December 31, 2002, and the balance sheet data as of December 31, 2002, are derived from our financial statements that have been audited by Ernst & Young LLP, independent auditors, and incorporated by reference into this prospectus. The statement of operations data for the years ended December 31, 1998, 1999, 2000 and 2001, and the balance sheet data as of December 31, 1998, 1999, 2000 and 2001, are derived from our audited financial statements that have been audited by KPMG LLP, independent auditors, and incorporated by reference into this prospectus. The summary statement of operations data for the six months ended June 30, 2002 and 2003, and the period from inception (May 4, 1998) through June 30, 2003, and the summary balance sheet data as of June 30, 2003, are derived from our unaudited financial statements incorporated by reference into this prospectus. In the opinion of management, all adjustments, consisting of normal recurring adjustments, necessary for a fair presentation have been included in preparing the unaudited financial statements. You should read the following selected financial data together with the accompanying "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the accompanying financial statements and related notes that are included in this prospectus. Results for interim periods are not necessarily indicative of results to be expected during the remainder of the fiscal year or for any future period.

	Years ended December 31,					Six months ended June 30, 2002	Six months ended June 30, 2003	Inception (May 4, 1998) through June 30, 2003
	1998	1999	2000	2001	2002			
	(in thousands, except per share data)							
Statement of operations data:								
Research and development expense	$ 300	$ 3,967	$ 12,596	$ 11,668	$ 11,396	$ 5,490	$ 7,503	$ 47,430
General and administrative expense	123	694	7,710	5,647	5,523	2,812	1,720	21,417
Total operating expenses	423	4,661	20,306	17,315	16,919	8,302	9,223	68,847
Operating loss	(423)	(4,661)	(20,306)	(17,315)	(16,919)	(8,302)	(9,223)	(68,847)
Interest income	34	161	2,826	2,978	994	561	261	7,254
Net loss	(389)	(4,500)	(17,480)	(14,337)	(15,925)	(7,741)	(8,962)	(61,593)
Return to series C preferred stockholders for beneficial conversion feature	—	—	(14,231)	—	—	—	—	(14,231)
Loss available to common stockholders	$ (389)	$ (4,500)	$ (31,711)	$ (14,337)	$ (15,925)	$ (7,741)	$ (8,962)	$ (75,824)
Basic and diluted loss per share	$ (0.39)	$ (1.35)	$ (2.33)	$ (0.57)	$ (0.59)	$ (0.29)	$ (0.33)	
Weighted average shares used in computing basic and diluted loss per share	986	3,345	13,635	25,332	27,039	26,973	27,250	

	As of December 31,					As of June 30, 2003
	1998	1999	2000	2001	2002	
	(in thousands)					
Balance sheet data:						
Cash and cash equivalents	$ 2,334	$ 9,340	$ 78,927	$ 65,274	$ 50,091	$ 42,546
Working capital	2,264	9,096	77,320	63,195	48,146	40,230
Total assets	2,383	9,441	81,147	68,135	53,325	44,531
Total liabilities	108	301	2,452	2,519	3,101	2,395
Stockholders' equity (deficit)	2,275	(563)	78,695	65,616	50,224	42,136

MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

Overview

Pain Therapeutics, Inc. is developing a new generation of opioid painkillers with improved clinical benefits. We believe our drugs will offer enhanced pain relief or reduced tolerance/physical dependence or addiction potential compared to existing opioid painkillers. 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.

We have yet to generate any revenues from product sales. We have not been profitable and, since our inception on May 4, 1998 through June 30, 2003, we have incurred an accumulated deficit of approximately $61.6 million. These losses have resulted principally from costs incurred in connection with research and development activities, including costs of preclinical and clinical trials as well as clinical supplies associated with our product candidates, salaries and other personnel related costs, including non-cash stock based compensation associated with options granted to employees and non-employees, and general corporate expenses. Our operating results may fluctuate substantially from period to period as a result of the timing and enrollment rates of clinical trials for our product 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 undertake preclinical and clinical trials for our product candidates, including the Phase III trials of Oxytrex and PTI-901;
- seek regulatory approvals for our product candidates;
- develop, formulate, manufacture and commercialize our drugs;
- implement additional internal systems and develop new infrastructure;
- acquire or in-license additional products or technologies, or expand the use of our technology;
- maintain, defend and expand the scope of our intellectual property; and
- hire additional personnel.

Product revenue will depend on our ability to receive regulatory approvals for, and successfully market, our product candidates. If our development efforts result in regulatory approval and successful commercialization of our product candidates, we will generate revenue from direct sales of our products and/or, if we license our products to future collaborators, from the receipt of license fees and royalties from licensed products.

Recent Developments

We have several drug candidates in various stages of clinical testing. In June 2003, we announced the results of a 21-day Phase II study of our lead product candidate, Oxytrex, in patients with severe osteoarthritic pain. The Phase II study met its primary efficacy endpoint, showing a statistically significant reduction in chronic pain using Oxytrex. In June 2003, we announced initiation of a Phase III clinical trial of Oxytrex to demonstrate its safety and efficacy in patients with documented severe chronic low back pain. In May 2003, we announced the results of a 50 patient pilot study using PTI-901, a proprietary new drug we are developing to treat irritable bowel syndrome. We plan to initiate in the fourth quarter of 2003 a Phase III trial with PTI-901 following discussion with regulatory agencies. We will have to commit substantial time and additional resources to conducting further preclinical or clinical studies in several types of pain before we can submit New Drug Applications, or NDAs, with respect to any of our product candidates.

Results of Operations

Comparison of Six Months Ended June 30, 2003 and 2002

Research and Development

Research and development expense consists primarily of drug development work associated with our product candidates, including costs of preclinical, clinical trials, clinical supplies and other formulation and design costs and salaries and other personnel related expenses, as well as non-cash stock based compensation. Research and development expense increased to $7.5 million from $5.4 million for the six months ended June 30, 2003 and 2002, respectively. The increase in expense was primarily due to expenses incurred in the ongoing clinical development of Oxytrex, for formulation related expense and for development of our other drug candidates. We have several other opioid painkillers in various stages of clinical testing.

We expect research and development expenses to increase significantly over the next several years as we expand our development efforts and as our product candidates progress through various stages of clinical trials, including the Phase III trials of Oxytrex and PTI-901. This increase may fluctuate from quarter to quarter and year to year due to the timing and scope of these activities.

General and Administrative

General and administrative expenses decreased to $1.7 million from $2.8 million for the six months ended June 30, 2003 and 2002, respectively. The decrease was primarily due to a decrease in non-cash stock based compensation expenses as well as a reclassification and decrease in 2003 in certain common occupancy expenses. General and administrative expense consists primarily of compensation and other general corporate expenses as well as non-cash stock based compensation. The decrease in non-cash stock based compensation expense was primarily due to the accelerated amortization methodology utilized in accordance with FASB Interpretation No. 28 (“FIN 28”) as well as the recapture of expenses under FIN 28 related to employees who terminated their employment prior to completion of the vesting period for the underlying stock options. Non-cash stock based compensation expense may fluctuate from period to period due in part to fluctuations in the fair market value of our common stock as well as other factors used to calculate such expenses. We expect general and administrative expense to increase in future periods in support of increased research and development or general corporate activities.

Interest Income

Interest income decreased to $0.3 million from $0.6 million for the six months ended June 30, 2003 and 2002, respectively. The decrease in interest income is primarily the result of lower average balances of cash and cash equivalents as well as lower returns on the investment of our cash and cash equivalents.

Comparison of Years Ended December 31, 2002 and 2001

Research and Development

Research and development expense consists primarily of drug development work associated with our product candidates, including costs of preclinical, clinical trials, clinical supplies and related formulation and design costs and salaries and other personnel related expenses, as well as non-cash stock based compensation. Research and development expense was $11.4 million for the year ended December 31, 2002 compared to $11.7 million in the year ended December 31, 2001. The $0.3 million decrease from year-to-year was primarily due to a decrease in non-cash stock based compensation. At December 31, 2002, our research and development activities were primarily related to Oxytrex. In the fourth quarter of 2002, we initiated a 21-day, multi-dose safety study for Oxytrex.

General and Administrative

General and administrative expenses were $5.5 million for the year ended December 31, 2002 compared to $5.6 million for the year ended December 31, 2001. General and administrative expense consists primarily of compensation, facilities expenses and other general corporate expenses as well as non-cash stock based compensation. The year-to-year decrease of $0.1 million was primarily due to a decrease in non-cash stock based compensation, partially offset by increases in depreciation and general corporate expenses.

Non-Cash Stock Based Compensation

We recognized non-cash stock based compensation expense for options granted as a component of both research and development expense and general and administrative expense totaling $0.2 million for the year ended December 31, 2002 and $1.2 million for the year ended December 31, 2001. The decrease was principally the result of the lower market price of our common stock during 2002 as compared to 2001, the impact of the reversal of previously expensed options returned to the company due to employee turnover as well as the accelerated amortization methodology utilized in accordance with FIN 28.

Interest Income

Interest income decreased to $1.0 million for the year ended December 31, 2002 from $3.0 million for the year ended December 31, 2001. This decrease resulted from the lower average balances of cash and cash equivalents and to a lesser extent from the decline in interest rates during 2002.

Comparison of Years Ended December 31, 2001 and 2000

Research and Development Expenses

Research and development expense was $11.7 million and $12.6 million for the years ended December 31, 2001 and 2000, respectively. The year-to-year decrease of $0.9 million was primarily due to the decrease in non-cash stock based compensation (as described below) partially offset by increases in preclinical and clinical development activities, clinical supplies and related formulation and design costs, salaries and other personnel related costs associated with increases in staff to support these activities.

General and Administrative Expenses

General and administrative expenses were $5.6 million in the year ended December 31, 2001 compared to $7.7 million in the year ended December 31, 2000. The year-to-year decrease was primarily due to a decrease in non-cash stock based compensation (as described below) partially offset by increases in salaries and other personnel related costs associated with increased staffing, consulting and professional services expenses and other general corporate expenses.

Non-Cash Stock Based Compensation

We recognized non-cash stock based compensation expense for options granted as well as restricted stock purchase agreements as components of both research and development expense and general and administrative expense totaling $1.2 million and $8.7 million for the years ended December 31, 2001 and 2000, respectively.

The decrease was principally the result of the lower market price of our common stock during 2001 as compared to 2000, the accelerated amortization methodology utilized in accordance with FIN 28 and the inclusion of $2.6 million of compensation expense related to restricted stock purchase agreements in the 2000 period.

Interest Income

Interest income increased to $3.0 million for the year ended December 31, 2001 from $2.8 million for the year ended December 31, 2000. The increase resulted from higher average balances of cash and cash equivalents principally as a result of the completion of our initial public offering in July 2000, partially offset by declining interest rates in the 2001 period.

Return to Series C Preferred Stockholders for Beneficial Conversion Feature

In February 2000, we issued 3,044,018 shares of series C redeemable convertible preferred stock for $14.2 million, net of issuance costs. We determined that our series C redeemable convertible preferred 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 redeemable convertible preferred 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 year ended December 31, 2000. Upon the closing of our initial public offering in July 2000, all 3,044,018 shares of our series C redeemable convertible preferred stock automatically converted into shares of common stock on a one to one basis.

Liquidity and Capital Resources

Since inception, we have funded our operations primarily through public and private stock offerings. We intend to continue to use these proceeds to fund research and development activities, working capital requirements, other general corporate purposes and capital expenditures. As of June 30, 2003, cash and cash equivalents were $42.5 million and were invested primarily in money market funds.

Net cash used in operating activities was $8.2 million for the six months ended June 30, 2003. Cash used in operating activities related primarily to the funding of operating losses.

We expect our cash used for capital equipment in 2003 to be approximately $0.1 million. Our requirements for capital equipment may increase in the future.

Our financing activities in the six months ended June 30, 2003 provided cash of $0.7 million, consisting of $0.6 million from the exercise of previously outstanding warrants and $0.1 million in equity from our stock plans.

We lease approximately 10,500 square feet of general office space. We also lease equipment pursuant to operating leases. Our leases expire at various dates through 2010. Under the terms of all of our leases, future minimum lease payments are $0.2 million in each of the years 2003 through 2010.

We have license agreements that require us to make milestone payments upon the successful achievement of milestones, including clinical milestones. These agreements also require us to pay certain royalties to our licensors if we succeed in fully commercializing products under these license agreements.

We expect to incur significant additional operating losses for the next several years. We expect our cash requirements to increase in the foreseeable future as we continue to undertake preclinical and clinical trials for

our product candidates, including the Phase III trials of Oxytrex and PTI-901; seek regulatory approvals for our product candidates; develop, formulate, manufacture and commercialize our drugs; implement additional internal systems and develop new infrastructure; acquire or in-license additional products or technologies, or expand the use of our technology; maintain, defend and expand the scope of our intellectual property; and hire additional personnel. The amount and timing of cash requirements will depend on regulatory and market acceptance of our products 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.

Quantitative and Qualitative Disclosures About Market Risks

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. To minimize this risk in the future, we intend to maintain our portfolio of cash equivalents and short-term investments in a variety of securities, including commercial paper, government and non-government debt securities and/or money market funds that invest in such securities. In general, money market funds are not subject to market risk because the interest paid on such funds fluctuates with the prevailing interest rate. We had no holdings of derivative financial or commodity instruments, and as of June 30, 2003 all of our cash and cash equivalents were in money market accounts and checking funds with variable, market rates of interest.

Recent Accounting Pronouncements

In May 2003, the FASB issued Statement of Financial Accounting Standards No. 150, “Accounting for Certain Financial Instruments with Characteristics of both Liabilities and Equity” (“FAS 150”). FAS 150 establishes standards for how an issuer classifies and measures certain financial instruments with characteristics of both liabilities and equity and it requires that an issuer classify a financial instrument that is within its scope as a liability. We adopted FAS 150 in June 2003 and it had no impact on our financial position and results of operations.

MANAGEMENT

Executive Officers and Directors

Our executive officers and directors, and their ages as of June 30, 2003, are as follows:

Name	Age	Position(s)
Remi Barbier	43	President, Chief Executive Officer, Chairman of the Board of Directors and Class III Director
Nadav Friedmann, Ph.D., M.D.	60	Chief Operating Officer and Class I Director
Peter S. Roddy	43	Chief Financial Officer
Grant L. Schoenhard, Ph.D.	58	Chief Scientific Officer
Robert Z. Gussin, Ph.D.(1)(2)	65	Class II Director
Michael J. O'Donnell, Esq.	45	Class I Director and Secretary
Sanford R. Robertson(1)(2)	72	Class III Director
Richard G. Stevens, CPA(1)	56	Class II Director

(1) Member of Audit Committee.
(2) Member of Compensation Committee.

There is no family relationship between any director or executive officer of the Company.

Remi Barbier, the Company's founder, has served as the Company's President, Chief Executive Officer and Chairman since the Company's inception in May 1998. Prior to that time, Mr. Barbier helped in the growth or founding of: Exelixis Inc., a functional genomics company, ArQule, a chemistry company, and EnzyMed (now owned by Albany Molecular Research), a chemistry company. Mr. Barbier served as Chief Operating Officer of Exelixis from January 1996 to May 1998. Mr. Barbier was Vice President of Corporate Development and Clinical Project Manager of Xoma Corporation, a biotechnology company from October 1993 to December 1995. Mr. Barbier is a director of Mendel Biotechnology, Inc. and Poetic Genetics, Inc. Mr. Barbier received his B.A. from Oberlin College and his M.B.A. from the University of Chicago.

Nadav Friedmann, Ph.D., M.D. has served as director of Pain Therapeutics, Inc. since September 1998 and in October 2001 Dr. Friedmann joined the Company as Chief Operating Officer. Dr. Friedmann is the owner and President of EMET Research Inc., a consulting firm in the pharmaceutical industry. Dr. Friedmann was President and Chief Executive Officer of Daiichi Pharmaceutical Corporation, a pharmaceutical company, from 1997 to April 2000, and was a Consultant to the Board of Directors of Daiichi Pharmaceutical Co., Ltd. in Tokyo from 1995 to 1997. From 1992 to 1995, Dr. Friedmann served as Vice President, Clinical Research at Xoma Corporation. From 1980 to 1991, Dr. Friedmann held various leadership positions with Johnson and Johnson, a healthcare company, including the position of Vice President and Head of Research of the J&J Biotechnology Center. Prior to that, Dr. Friedmann was Medical Director of Abbott Laboratories. Dr. Friedmann is a graduate of Albert Einstein College of Medicine, where he received an M.D., and of the University of California, San Diego, where he received a Ph.D. degree in Biochemistry.

Peter S. Roddy has served as Chief Financial Officer of Pain Therapeutics, Inc. since November 2002. From 1990 to 2002, Mr. Roddy held a variety of senior management positions at COR Therapeutics, Inc. (now Millenium Pharmaceuticals, Inc.) a biopharmaceutical company, including Senior Vice President, Finance and Chief Financial Officer between 2000 and 2002. Prior to 1990, Mr. Roddy held a variety of positions at Price Waterhouse & Company, Hewlett Packard Company and MCM Laboratories, Inc. Mr. Roddy received his B.S. in Business Administration from the University of California, Berkeley.

Grant L. Schoenhard, Ph.D., joined Pain Therapeutics, Inc. in September 2000 as Vice President of Preclinical Development. In September 2001 Dr. Schoenhard was promoted to Chief Scientific Officer. From February 2000 to September 2000, Dr. Schoenhard was a consultant and provided pharmacodynamic research and development services to various organizations. From September 1998 to February 2000, Dr. Schoenhard was Senior Director of Pharmacokinetics, Drug Metabolism and Pharmacology at Genentech, Inc. From 1974 to July 1998, Dr. Schoenhard held various management positions, including Executive Director of Pharmacokinetics, Drug Metabolism and Radiochemistry at Searle, a pharmaceutical company owned by Monsanto Corporation. Dr. Schoenhard was a member of the Board of Directors of LC Resources, Inc. from December 1998 through January 2002. Dr. Schoenhard was also Adjunct Professor of Pharmacology, School of Medicine, University of Pennsylvania for a number of years. Dr. Schoenhard received his B.S. from Michigan State University and his M.S. and Ph.D. from Oregon State University.

Robert Z. Gussin, Ph.D., has served as a director since March 2003. Dr. Gussin worked at Johnson & Johnson (J&J) for 26 years, most recently as Chief Scientific Officer and Corporate Vice President, Science and Technology from 1986 through his retirement in 2000. Prior to assuming this role, Dr. Gussin worked at J&J's McNeil division for 12 years, most recently as Vice President, Research and Development and Vice President, Scientific Affairs. From 1967 to 1974, Dr. Gussin held various research positions with Lederle Laboratories, a pharmaceutical company. Dr. Gussin sits on the advisory boards of the Duquesne University Pharmacy School, The Graduate School of the University of Notre Dame, The Harvard University School of Public Health and the University of Michigan Medical School Department of Pharmacology. Dr. Gussin received his B.S. and M.S. degrees from Duquesne University and his Ph.D. in Pharmacology from the University of Michigan, Ann Arbor.

Michael J. O'Donnell, Esq. has served as a director since June 1998. Mr. O'Donnell has been a member of the law firm of Wilson Sonsini Goodrich & Rosati, Professional Corporation, the Company's corporate counsel, since 1993. Mr. O'Donnell serves as corporate counsel to numerous public and private biopharmaceutical and life sciences companies. Mr. O'Donnell received a J.D. degree, cum laude, from Harvard University and a B.A. degree from Bucknell University, summa cum laude.

Sanford R. Robertson has served as a director since September 1998. Mr. Robertson is a principal of Francisco Partners, the world's largest technology buyout fund. With a focus on structured investments in technology and technology-related businesses, Francisco Partners is a pioneer in the emerging private equity category of Technology Buyouts. Prior to founding Francisco Partners in January 2000, Mr. Robertson was the founder and chairman of Robertson, Stephens & Company, a leading technology investment bank formed in 1978 and sold to BankBoston in 1998. Since the sale, Mr. Robertson has been an active technology investor and advisor to several technology companies. Mr. Robertson was also the founder of Robertson, Colman, Siebel & Weisel, later renamed Montgomery Securities, another prominent technology investment bank. Mr. Robertson was one of the pioneers in the creation of West Coast technology banking as an industry in the late 1960s, and has remained one of the industry's most renowned participants to this date. He has had significant financing involvement in over 500 growth companies throughout his career, including 3Com Corporation, America Online, Inc., Applied Materials, Inc., Ascend Communications Inc., Dell Computer Corporation, E*Trade Securities, Inc., Siebel Systems, Inc. and Sun Microsystems, Inc. Mr. Robertson is also a director of the Schwab Fund for Charitable Giving and Netro Corporation. Mr. Robertson received his B.B.A. and M.B.A. degrees with distinction from the University of Michigan.

Richard G. Stevens, CPA has served as director since February 2002. Mr. Stevens is currently the founder and managing director of Hunter Stevens LLC, a professional services firm. Prior to forming Hunter Stevens in 1995, Mr. Stevens served as a partner with both Ernst & Young and Coopers & Lybrand. During his tenure with Coopers & Lybrand, Mr. Stevens provided advice and technical support to the firm's approximate 100 domestic practice offices concerning accounting, auditing and SEC matters. Mr. Stevens received his undergraduate B.S. degree with honors from the University of San Francisco.

MATERIAL UNITED STATES FEDERAL TAX CONSIDERATIONS FOR NON-U.S. HOLDERS OF COMMON STOCK

This section summarizes certain material U.S. federal income and estate tax considerations relating to the ownership and disposition of common stock. This summary does not provide a complete analysis of all potential tax considerations. The information provided below is based on existing authorities. These authorities may change, or the IRS might interpret the existing authorities differently. In either case, the tax considerations of owning or disposing of common stock could differ from those described below. For purposes of this summary, a "non-U.S. holder" is any holder other than a citizen or resident of the United States, a corporation organized under the laws of the United States or any state, a trust that is (i) subject to the primary supervision of a U.S. court and the control of one of more U.S. persons or (ii) has a valid election in effect under applicable U.S. Treasury regulations to be treated as a U.S. person or an estate whose income is subject to U.S. income tax regardless of source. If a partnership or other flow-through entity is a beneficial owner of common stock, the tax treatment of a partner in the partnership or an owner of the entity will depend upon the status of the partner or other owner and the activities of the partnership or other entity. This summary generally does not address tax considerations that may be relevant to particular investors because of their specific circumstances, or because they are subject to special rules. Finally, this summary does not describe the effects of any applicable foreign, state, or local laws.

INVESTORS CONSIDERING THE PURCHASE OF COMMON STOCK SHOULD CONSULT THEIR OWN TAX ADVISORS REGARDING THE APPLICATION OF THE U.S. FEDERAL INCOME AND ESTATE TAX LAWS TO THEIR PARTICULAR SITUATIONS AND THE CONSEQUENCES OF FOREIGN, STATE, OR LOCAL LAWS, AND TAX TREATIES.

Dividends

Any dividends paid to a non-U.S. holder on common stock will generally be subject to U.S. withholding tax at a 30 percent rate. The withholding tax might not apply, however, or might apply at a reduced rate, under the terms of an applicable income tax treaty between the United States and the non-U.S. holder's country of residence. A non-U.S. holder must demonstrate its entitlement to treaty benefits by certifying its nonresident status. A non-U.S. holder can meet this certification requirement by providing a Form W-8BEN or appropriate substitute form to us or our paying agent. If the holder holds the note through a financial institution or other agent acting on the holder's behalf, the holder will be required to provide appropriate documentation to the agent. The holder's agent will then be required to provide certification to us or our paying agent, either directly or through other intermediaries. For payments made to a foreign partnership or other flow-through entity, the certification requirements generally apply to the partners or other owners rather than to the partnership or other entity, and the partnership or other entity must provide the partners' or other owners' documentation to us or our paying agent. Special rules, described below, apply if such dividends are effectively connected with a U.S. trade or business conducted by the non-U.S. holder.

Sale of Common Stock

Non-U.S. holders will generally not be subject to U.S. federal income tax on any gains realized on the sale, exchange, or other disposition of common stock. This general rule, however, is subject to several exceptions. For example, the gain would be subject to U.S. federal income tax if:

- the gain is effectively connected with the conduct by the non-U.S. holder of a U.S. trade or business (in which case the special rules described below apply);
- the non-U.S. holder was a citizen or resident of the United States and thus is subject to special rules that apply to expatriates; or
- the rules of the Foreign Investment in Real Property Tax Act (or FIRPTA) (described below) treat the gain as effectively connected with a U.S. trade or business.

The FIRPTA rules may apply to a sale, exchange or other disposition of common stock if we are, or were within five years before the transaction, a "U.S. real property holding corporation" (or USRPHC). In general, we

would be a USRPHC if interests in U.S. real estate comprised most of our assets. We do not believe that we are a USRPHC or that we will become one in the future.

Dividends or Gain Effectively Connected With a U.S. Trade or Business

If any dividends on common stock, or gain from the sale, exchange or other disposition of common stock is effectively connected with a U.S. trade or business conducted by the non-U.S. holder, then the dividends or gain will be subject to U.S. federal income tax at the regular graduated rates. If the non-U.S. holder is eligible for the benefits of a tax treaty between the United States and the holder's country of residence, any "effectively connected" dividends or gain would probably be subject to U.S. federal income tax only if it is also attributable to a permanent establishment or fixed base maintained by the holder in the United States. Payments of dividends that are effectively connected with a U.S. trade or business, and therefore included in the gross income of a non-U.S. holder, will not be subject to the 30 percent withholding tax. To claim exemption from withholding, the holder must certify its qualification, which can be done by filing a Form W-8ECI. If the non-U.S. holder is a corporation, that portion of its earnings and profits that is effectively connected with its U.S. trade or business would generally be subject to a "branch profits tax." The branch profits tax rate is generally 30 percent, although an applicable income tax treaty might provide for a lower rate.

U.S. Federal Estate Tax

The estates of nonresident alien individuals are generally subject to U.S. federal estate tax on property with a U.S. situs. Because we are a U.S. corporation, our common stock will be U.S. situs property and therefore will be included in the taxable estate of a nonresident alien decedent. The U.S. federal estate tax liability of the estate of a nonresident alien may be affected by a tax treaty between the United States and the decedent's country of residence.

Backup Withholding and Information Reporting

The Code and the Treasury regulations require those who make specified payments to report the payments to the IRS. Among the specified payments are dividends and proceeds paid by brokers to their customers. The required information returns enable the IRS to determine whether the recipient properly included the payments in income. This reporting regime is reinforced by "backup withholding" rules. These rules require the payors to withhold tax from payments subject to information reporting if the recipient fails to cooperate with the reporting regime by failing to provide his taxpayer identification number to the payor, furnishing an incorrect identification number, or repeatedly failing to report interest or dividends on his returns. The withholding tax rate is currently 28 percent. The backup withholding rules do not apply to payments to corporations, whether domestic or foreign.

Payments to non-U.S. holders of dividends on common stock will generally not be subject to backup withholding, and payments of proceeds made to non-U.S. holders by a broker upon a sale of common stock will not be subject to information reporting or backup withholding, in each case so long as the non-U.S. holder certifies its nonresident status. Some of the common means of certifying nonresident status are described under "—Dividends." We must report annually to the IRS any dividends paid to each non-U.S. holder and the tax withheld, if any, with respect to such dividends. Copies of these reports may be made available to tax authorities in the country where the non-U.S. holder resides.

Any amounts withheld from a payment to a holder of common stock under the backup withholding rules can be credited against any U.S. federal income tax liability of the holder.

THE PRECEDING DISCUSSION OF U.S. FEDERAL INCOME TAX CONSIDERATIONS IS FOR GENERAL INFORMATION ONLY. IT IS NOT TAX ADVICE. EACH PROSPECTIVE INVESTOR SHOULD CONSULT ITS OWN TAX ADVISOR REGARDING THE PARTICULAR U.S. FEDERAL, STATE, LOCAL, AND FOREIGN TAX CONSEQUENCES OF PURCHASING, HOLDING, AND DISPOSING OF OUR COMMON STOCK, INCLUDING THE CONSEQUENCES OF ANY PROPOSED CHANGE IN APPLICABLE LAWS.

UNDERWRITING

Citigroup Global Markets Inc. is acting as sole bookrunning manager of the offering, and, Citigroup Global Markets Inc., CIBC World Markets Corp., Leerink Swann & Company, and ThinkEquity Partners LLC are acting as representatives of the underwriters named below. Subject to the terms and conditions stated in the underwriting agreement dated the date of this prospectus, each underwriter named below has agreed to purchase, and we have agreed to sell to that underwriter, the number of shares set forth opposite the underwriter's name.

Underwriter	Number of shares
Citigroup Global Markets Inc.	
CIBC World Markets Corp.	
Leerink Swann & Company	
ThinkEquity Partners LLC	
Total	7,650,000

The underwriting agreement provides that the obligations of the underwriters to purchase the shares included in this offering are subject to approval of legal matters by counsel and to other conditions. The underwriters are obligated to purchase all the shares (other than those covered by the over-allotment option described below) if they purchase any of the shares.

The underwriters propose to offer some of the shares directly to the public at the public offering price set forth on the cover page of this prospectus and some of the shares to dealers at the public offering price less a concession not to exceed $ per share. The underwriters may allow, and dealers may re-allow, a concession not to exceed $ per share on sales to other dealers. If all of the shares are not sold at the initial offering price, the representatives may change the public offering price and the other selling terms.

We have granted to the underwriters an option, exercisable for 30 days from the date of this prospectus, to purchase up to 1,147,500 additional shares of common stock at the public offering price less the underwriting discount. The underwriters may exercise the option solely for the purpose of covering over-allotments, if any, in connection with this offering. To the extent the option is exercised, each underwriter must purchase a number of additional shares approximately proportionate to that underwriter's initial purchase commitment.

We, our officers and directors and our affiliate have agreed that, for a period of 90 days from the date of this prospectus, we and they will not, without the prior written consent of Citigroup, dispose of or hedge any shares of our common stock or any securities convertible into or exchangeable for our common stock subject to certain exceptions. The exceptions permit our officers and directors, subject to certain conditions, to transfer common stock for estate planning purposes or for the purpose of making a charitable contribution to a not-for-profit- organization. The exceptions also permit us, beginning on the date that is 30 days after the date of this prospectus, to issue an aggregate of up to 1 million shares of common stock in connection with any corporate development transaction or any merger or acquisition transaction, provided that the recipients of those shares agree in writing to be bound by the foregoing transfer restrictions for the remainder of the 90-day period. Citigroup in its sole discretion may release any of the securities subject to these lock-up agreements at any time without notice.

Each underwriter has represented, warranted and agreed that:

- it has not offered or sold and, prior to the expiry of a period of six months from the closing date, will not offer or sell any shares included in this offering to persons in the United Kingdom except to persons whose ordinary activities involve them in acquiring, holding, managing or disposing of investments (as principal or agent) for the purposes of their businesses or otherwise in circumstances which have not resulted and will not result in an offer to the public in the United Kingdom within the meaning of the Public Offers of Securities Regulations 1995;

- it has only communicated and caused to be communicated and will only communicate or cause to be communicated any invitation or inducement to engage in investment activity (within the meaning of section 21 of the Financial Services and Markets Act 2000 ("FSMA")) received by it in connection with the issue or sale of any shares included in this offering in circumstances in which section 21(1) of the FSMA does not apply to us;
- it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares included in this offering in, from or otherwise involving the United Kingdom; and
- the offer in the Netherlands of the shares included in this offering is exclusively limited to persons who trade or invest in securities in the conduct of a profession or business (which include banks, stockbrokers, insurance companies, pension funds, other institutional investors and finance companies and treasury departments of large enterprises).

The common stock is quoted on the Nasdaq National Market under the symbol "PTIE."

The following table shows the underwriting discounts and commissions that we are to pay to the underwriters in connection with this offering. These amounts are shown assuming both no exercise and full exercise of the underwriters' option to purchase additional shares of common stock.

	Paid by Pain Therapeutics, Inc.	
	No Exercise	Full Exercise
Per share	$	$
Total	$	$

In connection with the offering, Citigroup on behalf of the underwriters, may purchase and sell shares of common stock in the open market. These transactions may include short sales, syndicate covering transactions and stabilizing transaction. Short sales involve syndicate sales of common stock in excess of the number of shares to be purchased by the underwriters in the offering, which creates a syndicate short position. "Covered" short sales are sales of shares made in an amount up to the number of shares represented by the underwriters' over-allotment option. In determining the source of shares to close out the covered syndicate short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option. Transactions to close out the covered syndicate short involve either purchases of the common stock in the open market after the distribution has been completed or the exercise of the over-allotment option. The underwriters may also make "naked" short sales of shares in excess of the over-allotment option. The underwriters must close out any naked short position by purchasing shares of common stock in the open market. A naked short position is more likely to be created if the underwriters are concerned that there may be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering. Stabilizing transactions consist of bids for or purchases of shares in the open market while the offering is in progress.

The underwriters also may impose a penalty bid. Penalty bids permit the underwriters to reclaim a selling concession from a syndicate member when Citigroup repurchases shares originally sold by that syndicate member in order to cover syndicate short positions or make stabilizing purchases.

Any of these activities may have the effect of preventing or retarding a decline in the market price of the common stock. They may also cause the price of the common stock to be higher than the price that would otherwise exist in the open market in the absence of these transactions. The underwriters may conduct these transactions on the Nasdaq National Market or in the over-the-counter market, or otherwise. If the underwriters commence any of these transactions, they may discontinue them at any time.

In addition, in connection with this offering, some of the underwriters (and selling group members) may engage in passive market making transactions in the common stock on the Nasdaq National Market, prior to the pricing and completion of the offering. Passive market making consists of displaying bids on the Nasdaq National Market no higher than the bid prices of independent market makers and making purchases at prices no higher than those independent bids and effected in response to order flow. Net purchases by a passive market maker on each day are limited to a specified percentage of the passive market maker's average daily trading volume in the common stock during a specified period and must be discontinued when that limit is reached. Passive market making may cause the price of the common stock to be higher than the price that otherwise would exist in the open market in the absence of those transactions. If the underwriters commence passive market making transactions, they may discontinue them at any time.

We estimate that our portion of the total expenses of this offering will be approximately $450,000.

The underwriters have performed investment banking and advisory services for us from time to time for which they have received customary fees and expenses. The underwriters may, from time to time, engage in transactions with and perform services for us in the ordinary course of their business.

A prospectus in electronic format may be made available on the websites maintained by one or more of the underwriters. The representatives may agree to allocate a number of shares to underwriters for sale to their online brokerage account holders. The representatives will allocate shares to underwriters that may make Internet distributions on the same basis as other allocations. In addition, shares may be sold by the underwriters to securities dealers who resell shares to online brokerage account holders.

We have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933, or to contribute to payments the underwriters may be required to make because of any of those liabilities.

LEGAL MATTERS

Certain legal matters relating to the validity of the securities offered hereby will be passed upon by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Wilson Sonsini Goodrich & Rosati is corporate counsel to Pain Therapeutics, Inc. Michael J. O'Donnell, a member of Wilson Sonsini Goodrich & Rosati is a Director and a Secretary of Pain Therapeutics, Inc. In addition, certain individual attorneys employed by Wilson Sonsini Goodrich & Rosati beneficially own shares of Pain Therapeutics, Inc. common stock. As of August 20, 2003, such individuals beneficially owned an aggregate of approximately 112,388 shares of Pain Therapeutics, Inc. common stock. The validity of the common stock offered by this prospectus will be passed upon for the underwriters by Cleary, Gottlieb, Steen & Hamilton, New York, New York.

EXPERTS

The 2002 financial statements of Pain Therapeutics, Inc. appearing in Pain Therapeutics, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2002 have been audited by Ernst & Young LLP, independent auditors, as set forth in their report included therein and incorporated herein by reference. Such financial statements are incorporated herein by reference in reliance upon such report given on the authority of such firm as experts in accounting and auditing.

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

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the Securities and Exchange Commission. You may read and copy any document we file at the SEC's Public Reference Rooms in Washington, D.C., New York, New York and Chicago, Illinois. The Public Reference Room in Washington, D.C. is located at 450 Fifth Street, N.W. Please call the SEC at 1-800-SEC-0330 for further information on the public conference rooms. Our SEC filings are also available to the public from the SEC's web site at http://www.sec.gov.

The SEC allows us to "incorporate by reference" the information we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and later information filed with the SEC will update and supersede this information. We incorporate by reference the documents listed below and any future filings made by us with the SEC under Section 13(a), 13(c), 14 or 15(d) of the Securities Exchange Act of 1934 until our offering is completed.

(1) Our Annual Report on Form 10-K for the year ended December 31, 2002.

(2) Our Quarterly Report on Form 10-Q for the quarter ended March 31, 2003.

(3) Our Quarterly Report on Form 10-Q for the quarter ended June 30, 2003.

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

You may request a copy of any or all of the information that has been incorporated in this prospectus but that has not been delivered, at no cost, by writing or telephoning us at the following address or phone number:

Pain Therapeutics, Inc.
416 Browning Way
South San Francisco, California 94080
(650) 624-8200

You should rely only on the information incorporated by reference or provided in this prospectus. We have authorized no one to provide you with different information. We are not making an offer of these securities in any state where the offer is not permitted. You should not assume that the information in this prospectus is accurate as of any date other than the date on the front of the document.

7,650,000 Shares

Pain Therapeutics, Inc.

Common Stock

PROSPECTUS

, 2003

Sole Book Runner and Joint Lead Manager

Citigroup

Joint Lead Manager

CIBC World Markets

Leerink Swann & Company
ThinkEquity Partners

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

Item 14. ***Other Expenses of Issuance and Distribution***

The following table sets forth the costs and expenses, other than underwriting discounts and commissions, payable in connection with the sale and distribution of the securities being registered. All amounts are estimates except the Securities and Exchange Commission registration fee, the NASD filing fee and the Nasdaq National Market listing fee.

	Amount To Be Paid
Securities and Exchange Commission registration fee	$ 4,882
NASD filing fee	6,535
Printing and engraving expenses	40,000
Legal fees and expenses	125,000
Accounting fees and expenses	50,000
Blue sky fees and expenses	—
Transfer agent and registrar fees and expenses	20,000
Miscellaneous	203,583
Total	$ 450,000

Item 15. ***Indemnification of Directors and Officers***

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

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

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

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

directors' and officers' liability insurance, which insures against liabilities that our directors or officers may incur in such capacities.

The underwriting agreement, a form of which will be filed as Exhibit 1.1 to this registration statement, provides for indemnification by the underwriters of us and our officers and directors, and by us of the underwriters, for certain liabilities arising under the Securities Act or otherwise.

Item 16. ***Exhibits***

Exhibits	
1.1**	Form of Underwriting Agreement.
3.1*	Amended and Restated Certificate of Incorporation of Pain Therapeutics, Inc.
3.2*	Amended and Restated Bylaws of Pain Therapeutics, Inc.
4.1*	Specimen Common Stock Certificate.
4.2*	Second Amended and Restated Investors' Rights Agreement dated as of February 1, 2000.
5.1**	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation.
10.2**	License Agreement, dated May 5, 1998, between the Registrant and Albert Einstein College of Medicine, as amended on December 10, 1999.
23.1**	Consent of Wilson Sonsini Goodrich & Rosati, Professional Corporation (included in Exhibit 5.1).
23.2**	Consent of Ernst & Young LLP, independent auditors.
23.3**	Consent of KPMG LLP, independent auditors.
24.1**	Power of Attorney (included on p. II-4 of the original filing).

* Incorporated by reference from the Registrant's registration statement on Form S-1, registration number 333-32370, declared effective by the SEC on July 13, 2000.

** Previously filed.

Item 17. ***Undertakings***

(a) The undersigned Registrant hereby undertakes to deliver or cause to be delivered with the prospectus, to each person to whom the prospectus is sent or given, the latest annual report, to security holders that is incorporated by reference in the prospectus and furnished pursuant to and meeting the requirements of Rule 14a-3 or Rule 14c-3 under the Securities Exchange Act of 1934; and, where interim financial information required to be presented by Article 3 of Regulation S-X is not set forth in the prospectus, to deliver, or cause to be delivered to each person to whom the prospectus is sent or given, the latest quarterly report that is specifically incorporated by reference in the prospectus to provide such interim financial information.

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

(c) The undersigned Registrant hereby undertakes that:

(1) for purposes of determining any liability under the Securities Act, the information omitted from the form of prospectus filed as part of this registration statement in reliance upon Rule 430A and contained in a form of prospectus filed by the Registrant pursuant to Rule 424(b)(1) or (4) or 497(h) under the Securities Act shall be deemed to be part of this Registration Statement as of the time it was declared effective.

(2) for the purpose of determining liability under the Securities Act, each post-effective amendment that contains a form of prospectus shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the Registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of South San Francisco, State of California, on September 19, 2003.

PAIN THERAPEUTICS, INC.

By: /s/ REMI BARBIER

Remi Barbier
Chief Executive Officer and President

POWER OF ATTORNEY

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed below by the following persons in the capacities indicated on behalf of the Registrant on September 19, 2003.

Signature	Title
/s/ REMI BARBIER **Remi Barbier**	Chief Executive Officer, President (Principal Executive Officer) and Director
/s/ PETER S. RODDY* **Peter S. Roddy**	Chief Financial Officer (Principal Financial and Accounting Officer)
/s/ NADAV FRIEDMANN, PH.D., M.D.* **Nadav Friedmann, Ph.D., M.D.**	Director
/s/ ROBERT Z. GUSSIN, PH.D.* **Robert Z. Gussin, Ph.D.**	Director
/s/ MICHAEL J. O'DONNELL, ESQ.* **Michael J. O'Donnell, Esq.**	Director
/s/ SANFORD R. ROBERTSON* **Sanford R. Robertson**	Director
/s/ RICHARD G. STEVENS, CPA* **Richard G. Stevens, CPA**	Director

*By: /S/ REMI BARBIER

Remi Barbier, Attorney-in-fact

EXHIBIT INDEX

Exhibits	
1.1**	Form of Underwriting Agreement.
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