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As filed with the Securities and Exchange Commission on September 3, 2003

Registration No. 333-108145

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

AMENDMENT NO. 1
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)

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

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

If any of the securities being registered on this Form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933 (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 3, 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 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. 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 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 3, 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 3, 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

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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.

Exhibit 1.1

Pain Therapeutics, Inc.

Shares[1]
Common Stock
($0.001 par value)

Underwriting Agreement

New York, New York
[September], 2003

Citigroup Global Markets Inc.
CIBC World Markets Corp.
Leerink Swann & Company
ThinkEquity Partners LLC
As Representatives of the several Underwriters,
c/o Citigroup Global Markets Inc.
388 Greenwich Street
New York, New York 10013

Ladies and Gentlemen:

Pain Therapeutics, Inc., a corporation organized under the laws of Delaware (the "Company"), proposes to sell to the several underwriters named in Schedule I hereto (the "Underwriters"), for whom you (the "Representatives") are acting as representatives, [ ] shares of Common Stock, $0.001 par value ("Common Stock"), of the Company (said shares to be issued and sold by the Company being hereinafter called the "Underwritten Securities"). The Company also proposes to grant to the Underwriters an option to purchase up to [ ] additional shares of Common Stock to cover over-allotments (the "Option Securities"; the Option Securities, together with the Underwritten Securities, being hereinafter called the "Securities"). To the extent there are no additional Underwriters listed on Schedule I other than you, the term Representatives as used herein shall mean you, as Underwriters, and the terms Representatives and Underwriters shall mean either the singular or plural as the context requires. Any reference herein to the Registration Statement, a Preliminary Prospectus or the Prospectus shall be deemed to refer to and include the documents incorporated by reference therein pursuant to Item 12 of Form S-3 which were filed under the Exchange Act on or before the Effective Date of the Registration Statement or the issue date of such Preliminary Prospectus or the Prospectus, as the case may be; and any reference herein to the terms "amend", "amendment" or "supplement" with respect to the Registration Statement, any Preliminary Prospectus or the Prospectus shall be deemed to refer to and include the filing of any document under the Exchange Act after the Effective Date of the Registration Statement, or the issue date of any Preliminary Prospectus or the Prospectus, as the case may be, deemed to be incorporated therein by reference. Certain terms used herein are defined in Section 17 hereof.

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[1] Plus an option to purchase from Pain Therapeutics, Inc., up to [ ] additional shares to cover over-allotments.

1. Representations and Warranties. The Company represents and warrants to, and agrees with, each Underwriter as set forth below in this Section 1.

(a) The Company meets the requirements for use of Form S-3 under the Act and has prepared and filed with the Commission a registration statement (file number 333-) on Form S-3, including a related preliminary prospectus, for registration under the Act of the offering and sale of the Securities. The Company may have filed one or more amendments thereto, including a related preliminary prospectus, each of which has previously been furnished to you. The Company will next file with the Commission one of the following: either (1) prior to the Effective Date of such registration statement, a further amendment to such registration statement (including the form of final prospectus) or (2) after the Effective Date of such registration statement, a final prospectus in accordance with Rules 430A and 424(b). In the case of clause (2), the Company has included in such registration statement, as amended at the Effective Date, all information (other than Rule 430A Information) required by the Act and the rules thereunder to be included in such registration statement and the Prospectus. As filed, such amendment and form of final prospectus, or such final prospectus, shall contain all Rule 430A Information, together with all other such required information, and, except to the extent the Representatives shall agree in writing to a modification, shall be in all substantive respects in the form furnished to you prior to the Execution Time or, to the extent not completed at the Execution Time, shall contain only such specific additional information and other changes (beyond that contained in the latest Preliminary Prospectus) as the Company has advised you, prior to the Execution Time, will be included or made therein.

(b) On the Effective Date, the Registration Statement did or will, and when the Prospectus is first filed (if required) in accordance with Rule 424(b) and on the Closing Date (as defined herein) and on any date on which Option Securities are purchased, if such date is not the Closing Date (a "settlement date"), the Prospectus (and any supplements thereto) will, comply in all material respects with the applicable requirements of the Act and the Exchange Act and the respective rules thereunder; on the Effective Date and at the Execution Time, the Registration Statement did not or will not contain any untrue statement of a material fact or omit to state any material fact required to be stated therein or necessary in order to make the statements therein not misleading; and, on the Effective Date, the Prospectus, if not filed pursuant to Rule 424(b), will not, and on the date of any filing pursuant to Rule 424(b) and on the Closing Date and any settlement date, the Prospectus (together with any supplement thereto) will not, include any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; provided, however, that the Company makes no representations or warranties as to the information contained in or omitted from the Registration Statement, or the Prospectus (or any supplement thereto) in reliance upon and in conformity with information furnished in writing to the Company by or on behalf of any Underwriter through the Representatives specifically for inclusion in the Registration Statement or the Prospectus (or any supplement thereto).

(c) The Company has been duly incorporated and is validly existing as a corporation in good standing under the laws of the jurisdiction in which it is chartered or organized with full corporate power and authority to own or lease, as the case may be, and to operate its properties and conduct its business as described in the Prospectus, and is duly qualified to do business as a foreign corporation and is in good standing under the laws of each jurisdiction which requires such qualification.

(d) The Company has no subsidiaries and does not own or control, directly or indirectly, any corporation, association or other entity.

(e) The Company's authorized equity capitalization is as set forth in the Prospectus; the capital stock of the Company conforms in all material respects to the description thereof contained in the Prospectus; the outstanding shares of Common Stock have been duly and validly authorized and issued and are fully paid and nonassessable; the Securities have been duly and validly authorized, and, when issued and delivered to and paid for by the Underwriters pursuant to this Agreement, will be fully paid and nonassessable; the certificates for the Securities are in valid and sufficient form; the holders of outstanding shares of capital stock of the Company are not entitled to preemptive or other rights to subscribe for the Securities; and, except as set forth in the Prospectus, no options, warrants or other rights to purchase, agreements or other obligations to issue, or rights to convert any obligations into or exchange any securities for, shares of capital stock of or ownership interests in the Company are outstanding.

(f) There is no franchise, contract or other document of a character required to be described in the Registration Statement or Prospectus, or to be filed as an exhibit thereto, which is not described or filed as required; and the statements in Item 1 of the Company's Annual Report on Form 10-K for the year ended December 31, 2002 (the "2002 Form 10-K") under the captions "Business — Formulation Agreement," "— The Drug Approval Process," "— Other Regulatory Requirements" and the fifth, sixth, seventh and ninth paragraphs under the caption "Technology Overview" incorporated by reference into the Prospectus and the statements in the Prospectus under the captions "Material United States Federal Tax Considerations for Non-U.S. Holders of Common Stock," "Risks Relating to Our Company — Risks Relating to our Intellectual Property" and "— Risks Relating to our Collaboration Agreements" insofar as such statements summarize legal matters, agreements, documents or proceedings discussed therein, are accurate and fair summaries of such legal matters, agreements, documents or proceedings.

(g) This Agreement has been duly authorized, executed and delivered by the Company.

(h) The Company is not and, after giving effect to the offering and sale of the Securities and the application of the proceeds thereof as described in the Prospectus, will not be an "investment company" as defined in the Investment Company Act of 1940, as amended.

(i) No consent, approval, authorization, filing with or order of any court or governmental agency or body is required in connection with the transactions contemplated herein, except such as have been obtained under the Act and such as may be required under the blue sky laws of any jurisdiction in connection with the purchase and distribution of the Securities by the Underwriters in the manner contemplated herein and in the Prospectus.

(j) Neither the issue and sale of the Securities nor the consummation of any other of the transactions herein contemplated nor the fulfillment of the terms hereof will conflict with, result in a breach or violation of, or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to, (i) the charter or by-laws of the Company, (ii) the terms of any indenture, contract, lease, mortgage, deed of trust, note agreement, loan agreement or other agreement, obligation, condition, covenant or instrument to which the Company is a party or bound or to which its property is subject, or (iii) any statute, law, rule, regulation, judgment, order or decree applicable to the Company of any court, regulatory body, administrative agency, governmental body, arbitrator or other authority having jurisdiction over the Company or any of its properties.

(k) Except as set forth in the Registration Statement and Prospectus, no holders of Common Stock or other securities of the Company have registration rights with respect to securities of the Company and, except as set forth in the Registration Statement and Prospectus, all holders of securities of the Company having rights to registration of Common Stock, or other securities pursuant to the Registration Statement, have waived such rights or such rights have expired by reason of lapse of time following notification by the Company of the filing of the Registration Statement [or such Common Stock or other securities have been included in the Registration Statement pursuant to the exercise of and in full satisfaction of such rights].

(l) The historical financial statements and schedules of the Company included in the Prospectus and the Registration Statement present fairly in all material respects the financial condition, results of operations and cash flows of the Company as of the dates and for the periods indicated, comply as to form with the applicable accounting requirements of the Act and have been prepared in conformity with generally accepted accounting principles applied on a consistent basis throughout the periods involved (except as otherwise noted therein). The financial data set forth under the captions “Summary Financial Data” and “Selected Financial Data” in the Prospectus and Registration Statement fairly present, on the basis stated in the Prospectus and the Registration Statement, the information included therein.

(m) No action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or its properties is pending or, to the best knowledge of the Company, threatened that (i) could reasonably be expected to have a material adverse effect on the performance of this Agreement or the consummation of any of the transactions contemplated hereby or (ii) could reasonably be expected to have a material adverse effect on the condition (financial or otherwise), prospects, earnings, business or properties of the Company, whether or not arising from transactions in the ordinary course of business, except as set forth in or contemplated in the Prospectus (exclusive of any supplement thereto).

(n) The Company owns or leases all such properties as are necessary to the conduct of its operations as presently conducted.

(o) The Company is not in violation or default of (i) any provision of its charter or by-laws, (ii) the terms of any indenture, contract, lease, mortgage, deed of trust, note agreement, loan agreement or other agreement, obligation, condition, covenant or instrument to which it is a party or bound or to which its property is subject, or (iii) any statute, law, rule, regulation, judgment, order or decree of any court, regulatory body, administrative agency, governmental body, arbitrator or other authority having jurisdiction over the Company or any of its properties.

(p) Each of Ernst & Young LLP and KPMG LLP, who have certified certain financial statements of the Company and delivered their report with respect to the audited financial statements and schedules included in the Prospectus, are independent public accountants with respect to the Company within the meaning of the Act and the applicable published rules and regulations thereunder.

(q) There are no transfer taxes or other similar fees or charges under Federal law or the laws of any state, or any political subdivision thereof, required to be paid in connection with the execution and delivery of this Agreement or the issuance by the Company or sale by the Company of the Securities.

(r) The Company has filed all foreign, federal, state and local tax returns that are required to be filed or has requested extensions thereof (except in any case in which the failure so to file would not have a material adverse effect on the condition (financial or otherwise), prospects, earnings, business or properties of the Company, whether or not arising from transactions in the ordinary course of business, except as set forth in or contemplated in the Prospectus (exclusive of any supplement thereto)) and has paid all taxes required to be paid by it and any other assessment, fine or penalty levied against it, to the extent that any of the foregoing is due and payable, except for any such assessment, fine or penalty that is currently being contested in good faith or as would not have a material adverse effect on the condition (financial or otherwise), prospects, earnings, business or properties of the Company, whether or not arising from transactions in the ordinary course of business, except as set forth in or contemplated in the Prospectus (exclusive of any supplement thereto).

(s) No labor problem or dispute with the employees of the Company exists or is threatened or imminent, and the Company is not aware of any existing or imminent labor disturbance by the employees of any of its principal suppliers, contractors or customers, that could have a material adverse effect on the condition (financial or otherwise), prospects, earnings, business or properties of the Company, whether or not arising from transactions in the ordinary course of business, except as set forth in or contemplated in the Prospectus (exclusive of any supplement thereto).

(t) The Company is insured by insurers of recognized financial responsibility against such losses and risks and in such amounts as are prudent and customary in the businesses in which they are engaged; all policies of insurance insuring the Company or

its business, assets, employees, officers and directors are in full force and effect; the Company is in compliance with the terms of such policies and instruments in all material respects; and there are no claims by the Company under any such policy or instrument as to which any insurance company is denying liability or defending under a reservation of rights clause; the Company has not been refused any insurance coverage sought or applied for; and the Company does not have any reason to believe that it will not be able to renew its existing insurance coverage as and when such coverage expires or to obtain similar coverage from similar insurers as may be necessary to continue its business at a cost that would not have a material adverse effect on the condition (financial or otherwise), prospects, earnings, business or properties of the Company, whether or not arising from transactions in the ordinary course of business, except as set forth in or contemplated in the Prospectus (exclusive of any supplement thereto).

(u) The Company possesses all licenses, certificates, permits and other authorizations issued by the appropriate federal, state or foreign regulatory authorities necessary to conduct its business, and the Company has not received any notice of proceedings relating to the revocation or modification of any such certificate, authorization or permit which, singly or in the aggregate, if the subject of an unfavorable decision, ruling or finding, would have a material adverse effect on the condition (financial or otherwise), prospects, earnings, business or properties of the Company whether or not arising from transactions in the ordinary course of business, except as set forth in or contemplated in the Prospectus (exclusive of any supplement thereto).

(v) The Company maintains a system of internal accounting controls sufficient to provide reasonable assurance that (i) transactions are executed in accordance with management's general or specific authorizations; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with generally accepted accounting principles and to maintain asset accountability; (iii) access to assets is permitted only in accordance with management's general or specific authorization; and (iv) the recorded accountability for assets is compared with the existing assets at reasonable intervals and appropriate action is taken with respect to any differences.

(w) The Company has not taken, directly or indirectly, any action designed to or that would constitute or that might reasonably be expected to cause or result in, under the Exchange Act or otherwise, stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Securities.

(x) The Company (i) is in compliance with any and all applicable foreign, federal, state and local laws and regulations relating to the protection of human health and safety, the environment or hazardous or toxic substances or wastes, pollutants or contaminants ("Environmental Laws"), (ii) has received and is in compliance with all permits, licenses or other approvals required of it under applicable Environmental Laws to conduct its business and (iii) has not received notice of any actual or potential liability under any environmental law, except where such non-compliance with Environmental Laws, failure to receive required permits, licenses or other approvals, or liability would not, individually or in the aggregate, have a material adverse change in the condition (financial or otherwise), prospects, earnings, business or properties of the Company,

whether or not arising from transactions in the ordinary course of business, except as set forth in or contemplated in the Prospectus (exclusive of any supplement thereto). Except as set forth in the Prospectus, the Company has not been named as a "potentially responsible party" under the Comprehensive Environmental Response, Compensation, and Liability Act of 1980, as amended.

(y) In the ordinary course of its business, the Company periodically reviews the effect of Environmental Laws on the business, operations and properties of the Company, in the course of which it identifies and evaluates associated costs and liabilities (including, without limitation, any capital or operating expenditures required for clean-up, closure of properties or compliance with Environmental Laws, or any permit, license or approval, any related constraints on operating activities and any potential liabilities to third parties). On the basis of such review, the Company has reasonably concluded that such associated costs and liabilities would not, singly or in the aggregate, have a material adverse effect on the condition (financial or otherwise), prospects, earnings, business or properties of the Company, whether or not arising from transactions in the ordinary course of business, except as set forth in or contemplated in the Prospectus (exclusive of any supplement thereto).

(z) The minimum funding standard under Section 302 of the Employee Retirement Income Security Act of 1974, as amended, and the regulations and published interpretations thereunder ("ERISA"), has been satisfied by each "pension plan" (as defined in Section 3(2) of ERISA) which has been established or maintained by the Company, and the trust forming part of each such plan which is intended to be qualified under Section 401 of the Code is so qualified; the Company has fulfilled its obligations, if any, under Section 515 of ERISA; the Company does not maintain or is not required to contribute to a "welfare plan" (as defined in Section 3(1) of ERISA) which provides retiree or other post-employment welfare benefits or insurance coverage (other than "continuation coverage" (as defined in Section 602 of ERISA)); each pension plan and welfare plan established or maintained by the Company is in compliance in all material respects with the currently applicable provisions of ERISA; and the Company has not incurred or could not reasonably be expected to incur any withdrawal liability under Section 4201 of ERISA, any liability under Section 4062, 4063, or 4064 of ERISA, or any other liability under Title IV of ERISA.

(aa) There is and has been no failure on the part of the Company and any of the Company's directors or officers, in their capacities as such, to comply with any provision of the Sarbanes Oxley Act of 2002 and the rules and regulations promulgated in connection therewith (the "Sarbanes Oxley Act"), including Section 402 related to loans and Sections 302 and 906 related to certifications.

(bb) Neither the Company nor, to the knowledge of the Company, any director, officer, agent, employee or affiliate of the Company is aware of or has taken any action, directly or indirectly, that would result in a violation by such persons of the FCPA, including, without limitation, making use of the mails or any means or instrumentality of interstate commerce corruptly in furtherance of an offer, payment, promise to pay or authorization of the payment of any money, or other property, gift, promise to give, or

authorization of the giving of anything of value to any "foreign official" (as such term is defined in the FCPA) or any foreign political party or official thereof or any candidate for foreign political office, in contravention of the FCPA and the Company and, to the knowledge of the Company, its affiliates have conducted their businesses in compliance with the FCPA and have instituted and maintain policies and procedures designed to ensure, and which are reasonably expected to continue to ensure, continued compliance therewith.

"FCPA" means Foreign Corrupt Practices Act of 1977, as amended, and the rules and regulations thereunder.

(cc) The operations of the Company are and have been conducted at all times in compliance with applicable financial recordkeeping and reporting requirements of the Currency and Foreign Transactions Reporting Act of 1970, as amended, the money laundering statutes of all jurisdictions, the rules and regulations thereunder and any related or similar rules, regulations or guidelines, issued, administered or enforced by any governmental agency (collectively, the "Money Laundering Laws") and no action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company with respect to the Money Laundering Laws is pending or, to the best knowledge of the Company, threatened.

(dd) The Company nor, to the knowledge of the Company, any director, officer, agent, employee or affiliate of the Company is currently subject to any U.S. sanctions administered by the Office of Foreign Assets Control of the U.S. Treasury Department ("OFAC"); and the Company will not directly or indirectly use the proceeds of the offering, or lend, contribute or otherwise make available such proceeds to any joint venture partner or other person or entity, for the purpose of financing the activities of any person currently subject to any U.S. sanctions administered by OFAC.

(ee) The Company owns, possesses, licenses or has other rights to use, on reasonable terms, all patents, patent applications, trade and service marks, trade and service mark registrations, trade names, copyrights, licenses, inventions, trade secrets, technology, know-how and other intellectual property (collectively, the "Intellectual Property") necessary for the conduct of the Company's business as now conducted or as proposed in the Prospectus to be conducted. Except as set forth in the Prospectus, (a) there are no rights of third parties to any such Intellectual Property; (b) there is no material infringement by third parties of any such Intellectual Property; (c) there is no pending or threatened action, suit, proceeding or claim by others challenging the Company's rights in or to any such Intellectual Property, and the Company is unaware of any facts which would form a reasonable basis for any such claim; (d) there is no pending or threatened action, suit, proceeding or claim by others challenging the validity or scope of any such Intellectual Property, and the Company is unaware of any facts which would form a reasonable basis for any such claim; (e) there is no pending or threatened action, suit, proceeding or claim by others that the Company infringes or otherwise violates any patent, trademark, copyright, trade secret or other proprietary rights of others, and the Company is unaware of any other fact which would form a reasonable basis for any such claim; (f) there is no U.S. patent or published U.S. patent application which contains

claims that dominate or may dominate any Intellectual Property described in the Prospectus as being owned by or licensed to the Company or that interferes with the issued or pending claims of any such Intellectual Property; and (g) there is no prior art of which the Company is aware that may render any U.S. patent held by the Company invalid or any U.S. patent application held by the Company unpatentable which has not been disclosed to the U.S. Patent and Trademark Office.

(ff) Each of the License Agreement, dated May 5, 1998 by and between the Company and Albert Einstein College of Medicine, and the First Amendment to the License Agreement, dated December 10, 1999, has been duly authorized by all necessary corporate action on the part of the Company and has been duly executed and delivered by the Company and, assuming due authorization, execution and delivery by Albert Einstein College of Medicine, is a valid and binding agreement of Albert Einstein College of Medicine, enforceable in accordance with its terms.

(gg) There are no business relationships or related-party transactions involving the Company or any other person required to be described in the Prospectus which have not been described as required.

(hh) Neither the Company nor, to the best of the Company's knowledge, any employee or agent of the Company, has made any contribution or other payment to (i) any official of, or candidate for, any federal, state or foreign office in violation of any law or of the character required to be disclosed in the Prospectus or (ii) any clinical researcher in violation of any federal, state or foreign law or any rule or policy of the Food and Drug Administration ("FDA").

Any certificate signed by any officer of the Company and delivered to the Representatives or counsel for the Underwriters in connection with the offering of the Securities shall be deemed a representation and warranty by the Company, as to matters covered thereby, to each Underwriter.

2. Purchase and Sale. (a) Subject to the terms and conditions and in reliance upon the representations and warranties herein set forth, the Company agrees to sell to each Underwriter, and each Underwriter agrees, severally and not jointly, to purchase from the Company, at a purchase price of $ per share, the amount of the Underwritten Securities set forth opposite such Underwriter's name in Schedule I hereto.

(b) Subject to the terms and conditions and in reliance upon the representations and warranties herein set forth, the Company hereby grants an option to the several Underwriters to purchase, severally and not jointly, up to [ ] Option Securities at the same purchase price per share as the Underwriters shall pay for the Underwritten Securities. Said option may be exercised only to cover over-allotments in the sale of the Underwritten Securities by the Underwriters. Said option may be exercised in whole or in part at any time on or before the 30th day after the date of the Prospectus upon written or telegraphic notice by the Representatives to the Company setting forth the number of shares of the Option Securities as to which the several Underwriters are exercising the option and the settlement date. The number of shares of the Option Securities to be purchased by each Underwriter shall be the same percentage of the total number of shares of

the Option Securities to be purchased by the several Underwriters as such Underwriter is purchasing of the Underwritten Securities, subject to such adjustments as you in your absolute discretion shall make to eliminate any fractional shares.

3. Delivery and Payment. Delivery of and payment for the Underwritten Securities and the Option Securities (if the option provided for in Section 2(b) hereof shall have been exercised on or before the third Business Day prior to the Closing Date) shall be made at 10:00 AM, New York City time, on , 2003, or at such time on such later date not more than three Business Days after the foregoing date as the Representatives shall designate, which date and time may be postponed by agreement between the Representatives and the Company or as provided in Section 9 hereof (such date and time of delivery and payment for the Securities being herein called the "Closing Date"). Delivery of the Securities shall be made to the Representatives for the respective accounts of the several Underwriters against payment by the several Underwriters through the Representatives of the purchase price thereof to or upon the order of the Company by wire transfer payable in same-day funds to an account specified by the Company. Delivery of the Underwritten Securities and the Option Securities shall be made through the facilities of The Depository Trust Company unless the Representatives shall otherwise instruct.

If the option provided for in Section 2(b) hereof is exercised after the third Business Day prior to the Closing Date, the Company will deliver the Option Securities (at the expense of the Company) to the Representatives, at 388 Greenwich Street, New York, New York, on the date specified by the Representatives (which shall be within three Business Days after exercise of said option) for the respective accounts of the several Underwriters, against payment by the several Underwriters through the Representatives of the purchase price thereof to or upon the order of the Company by wire transfer payable in same-day funds to an account specified by the Company. If settlement for the Option Securities occurs after the Closing Date, the Company will deliver to the Representatives on the settlement date for the Option Securities, and the obligation of the Underwriters to purchase the Option Securities shall be conditioned upon receipt of, supplemental opinions, certificates and letters confirming as of such date the opinions, certificates and letters delivered on the Closing Date pursuant to Section 6 hereof.

4. Offering by Underwriters. It is understood that the several Underwriters propose to offer the Securities for sale to the public as set forth in the Prospectus.

5. Agreements. The Company agrees with the several Underwriters that:

(a) The Company will use its best efforts to cause the Registration Statement, if not effective at the Execution Time, and any amendment thereof, to become effective. Prior to the termination of the offering of the Securities, the Company will not file any amendment of the Registration Statement or supplement to the Prospectus or any Rule 462(b) Registration Statement unless the Company has furnished you a copy for your review prior to filing and will not file any such proposed amendment or supplement to which you reasonably object. Subject to the foregoing sentence, if the Registration Statement has become or becomes effective pursuant to Rule 430A, or filing of the

Prospectus is otherwise required under Rule 424(b), the Company will cause the Prospectus, properly completed, and any supplement thereto to be filed in a form approved by the Representatives with the Commission pursuant to the applicable paragraph of Rule 424(b) within the time period prescribed and will provide evidence satisfactory to the Representatives of such timely filing. The Company will promptly advise the Representatives (1) when the Registration Statement, if not effective at the Execution Time, shall have become effective, (2) when the Prospectus, and any supplement thereto, shall have been filed (if required) with the Commission pursuant to Rule 424(b) or when any Rule 462(b) Registration Statement shall have been filed with the Commission, (3) when, prior to termination of the offering of the Securities, any amendment to the Registration Statement shall have been filed or become effective, (4) of any request by the Commission or its staff for any amendment of the Registration Statement, or any Rule 462(b) Registration Statement, or for any supplement to the Prospectus or for any additional information, (5) of the issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement or the institution or threatening of any proceeding for that purpose and (6) of the receipt by the Company of any notification with respect to the suspension of the qualification of the Securities for sale in any jurisdiction or the institution or threatening of any proceeding for such purpose. The Company will use its best efforts to prevent the issuance of any such stop order or the suspension of any such qualification and, if issued, to obtain as soon as possible the withdrawal thereof.

(b) If, at any time when a prospectus relating to the Securities is required to be delivered under the Act, any event occurs as a result of which the Prospectus as then supplemented would include any untrue statement of a material fact or omit to state any material fact necessary to make the statements therein in the light of the circumstances under which they were made not misleading, or if it shall be necessary to amend the Registration Statement or supplement the Prospectus to comply with the Act or the Exchange Act or the respective rules thereunder, the Company promptly will (1) notify the Representatives of such event, (2) prepare and file with the Commission, subject to the second sentence of paragraph (a) of this Section 5, an amendment or supplement which will correct such statement or omission or effect such compliance and (3) supply any supplemented Prospectus to you in such quantities as you may reasonably request.

(c) As soon as practicable, the Company will make generally available to its security holders and to the Representatives an earnings statement or statements of the Company which will satisfy the provisions of Section 11(a) of the Act and Rule 158 under the Act.

(d) The Company will furnish to the Representatives and counsel for the Underwriters, without charge, signed copies of the Registration Statement (including exhibits thereto) and to each other Underwriter a copy of the Registration Statement (without exhibits thereto) and, so long as delivery of a prospectus by an Underwriter or dealer may be required by the Act, as many copies of each Preliminary Prospectus and the Prospectus and any supplement thereto as the Representatives may reasonably request. The Company will pay the expenses of printing or other production of all documents relating to the offering.

(e) The Company will arrange, if necessary, for the qualification of the Securities for sale under the laws of such jurisdictions as the Representatives may designate, will maintain such qualifications in effect so long as required for the distribution of the Securities and will pay any fee of the National Association of Securities Dealers, Inc., in connection with its review of the offering; provided that in no event shall the Company be obligated to qualify to do business in any jurisdiction where it is not now so qualified or to take any action that would subject it to service of process in suits, other than those arising out of the offering or sale of the Securities, in any jurisdiction where it is not now so subject.

(f) The Company will not, without the prior written consent of Citigroup Global Markets Inc., offer, sell, contract to sell, pledge, or otherwise dispose of, (or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition (whether by actual disposition or effective economic disposition due to cash settlement or otherwise) by the Company or any affiliate of the Company or any person in privity with the Company or any affiliate of the Company) directly or indirectly, including the filing (or participation in the filing) of a registration statement with the Commission in respect of, or establish or increase a put equivalent position or liquidate or decrease a call equivalent position within the meaning of Section 16 of the Exchange Act, any other shares of Common Stock or any securities convertible into, or exercisable, or exchangeable for, shares of Common Stock; or publicly announce an intention to effect any such transaction, for a period of 90 days after the date of the Underwriting Agreement, provided, however, that the Company may issue and sell Common Stock pursuant to any employee stock option plan, stock ownership plan or dividend reinvestment plan of the Company in effect at the Execution Time and the Company may issue Common Stock issuable upon the conversion of securities or the exercise of warrants outstanding at the Execution Time.

(g) The Company will comply with all applicable securities and other applicable laws, rules and regulations, including, without limitation, the Sarbanes Oxley Act, and to use its best efforts to cause the Company's directors and officers, in their capacities as such, to comply with such laws, rules and regulations, including, without limitation, the provisions of the Sarbanes Oxley Act.

(h) The Company will not take, directly or indirectly, any action designed to or that would constitute or that might reasonably be expected to cause or result in, under the Exchange Act or otherwise, stabilization or manipulation of the price of any security of the Company to facilitate the sale or resale of the Securities.

6. Conditions to the Obligations of the Underwriters. The obligations of the Underwriters to purchase the Underwritten Securities and the Option Securities, as the case may be, shall be subject to the accuracy of the representations and warranties on the part of the Company contained herein as of the Execution Time, the Closing Date and any settlement date pursuant to Section 3 hereof, to the accuracy of the statements of the Company made in any certificates pursuant to the provisions hereof, to the performance by the Company of its obligations hereunder and to the following additional conditions:

(a) If the Registration Statement has not become effective prior to the Execution Time, unless the Representatives agree in writing to a later time, the Registration Statement will become effective not later than (i) 6:00 PM New York City time on the date of determination of the public offering price, if such determination occurred at or prior to 3:00 PM New York City time on such date or (ii) 9:30 AM on the Business Day following the day on which the public offering price was determined, if such determination occurred after 3:00 PM New York City time on such date; if filing of the Prospectus, or any supplement thereto, is required pursuant to Rule 424(b), the Prospectus, and any such supplement, will be filed in the manner and within the time period required by Rule 424(b); and no stop order suspending the effectiveness of the Registration Statement shall have been issued and no proceedings for that purpose shall have been instituted or threatened.

(b) The Company shall have requested and caused Wilson Sonsini Goodrich & Rosati, Professional Corporation, counsel for the Company, to have furnished to the Representatives their opinion, dated the Closing Date and addressed to the Representatives, to the effect that:

(i) the Company has been duly incorporated and is validly existing as a corporation in good standing under the laws of the jurisdiction in which it is chartered or organized, with full corporate power and authority to own or lease, as the case may be, and to operate its properties and conduct its business as described in the Prospectus, and is duly qualified to do business as a foreign corporation and is in good standing under the laws of each jurisdiction which requires such qualification. To such counsel's knowledge, the Company does not own or control, directly or indirectly, any corporation, association or other entity;

(ii) the Company's authorized equity capitalization is as set forth in the Prospectus; the capital stock of the Company conforms in all material respects to the description thereof contained in the Prospectus; the outstanding shares of Common Stock have been duly and validly authorized and issued and are fully paid and nonassessable; the Securities have been duly and validly authorized, and, when issued and delivered to and paid for by the Underwriters pursuant to this Agreement, will be fully paid and nonassessable; the certificates for the Securities are in valid and sufficient form; the holders of outstanding shares of capital stock of the Company are not entitled to preemptive or other rights to subscribe for the Securities; and, except as set forth in the Prospectus, no options, warrants or other rights to purchase, agreements or other obligations to issue, or rights to convert any obligations into or exchange any securities for, shares of capital stock of or ownership interests in the Company are outstanding;

(iii) to the knowledge of such counsel, there is no pending or threatened action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or its properties of a character required to be disclosed in the Registration Statement which is not adequately disclosed in the Prospectus, and there is no franchise, contract or other document of a character required to be described in the Registration Statement or

Prospectus, or to be filed as an exhibit thereto, which is not described or filed as required; and the statements included or incorporated by reference in the Prospectus under the caption "Material United States Federal Tax Considerations for Non-U.S. Holders of Common Stock," insofar as such statements summarize legal matters, agreements, documents or proceedings discussed therein, are accurate and fair summaries of such legal matters, agreements, documents or proceedings;

(iv) the Registration Statement has become effective under the Act; any required filing of the Prospectus, and any supplements thereto, pursuant to Rule 424(b) has been made in the manner and within the time period required by Rule 424(b); to the knowledge of such counsel, no stop order suspending the effectiveness of the Registration Statement has been issued, no proceedings for that purpose have been instituted or threatened and the Registration Statement and the Prospectus (other than the financial statements and other financial and statistical information contained therein, as to which such counsel need express no opinion) comply as to form in all material respects with the applicable requirements of the Act and the Exchange Act and the respective rules thereunder; and such counsel has no reason to believe that on the Effective Date or the date the Registration Statement was last deemed amended the Registration Statement contained any untrue statement of a material fact or omitted to state any material fact required to be stated therein or necessary to make the statements therein not misleading or that the Prospectus as of its date and on the Closing Date included or includes any untrue statement of a material fact or omitted or omits to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading (in each case, other than the financial statements and other financial and statistical information contained therein, as to which such counsel need express no opinion);

(v) this Agreement has been duly authorized, executed and delivered by the Company;

(vi) the Company is not and, after giving effect to the offering and sale of the Securities and the application of the proceeds thereof as described in the Prospectus, will not be an "investment company" as defined in the Investment Company Act of 1940, as amended;

(vii) no consent, approval, authorization, filing with or order of any court or governmental agency or body is required in connection with the transactions contemplated herein, except such as have been obtained under the Act and such as may be required under the blue sky laws of any jurisdiction in connection with the purchase and distribution of the Securities by the Underwriters in the manner contemplated in this Agreement and in the Prospectus and such other approvals (specified in such opinion) as have been obtained;

(viii) neither the issue and sale of the Securities, nor the consummation of any other of the transactions herein contemplated nor the fulfillment of the

terms hereof will conflict with, result in a breach or violation of, or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to, (i) the charter or by-laws of the Company, (ii) the terms of any indenture, contract, lease, mortgage, deed of trust, note agreement, loan agreement or other agreement, obligation, condition, covenant or instrument to which the Company is a party or bound or to which its property is subject, or (iii) any statute, law, rule, regulation, judgment, order or decree applicable to the Company or of any court, regulatory body, administrative agency, governmental body, arbitrator or other authority having jurisdiction over the Company or any of its properties;

(ix) the Securities to be issued by the Company pursuant to the terms of the Underwriting Agreement have been duly authorized and, upon issuance and delivery against payment therefore in accordance with the terms hereof, will be duly and validly issued and fully paid and nonassessable, and will not have been issued in violation of or subject to any preemptive right arising under the certificate of incorporation or Delaware General Corporation Law, or, any co-sale right, right of first refusal or other similar right;

(x) the description incorporated by reference into the Registration Statement and the Prospectus of the charter and by-laws of the Company, of the capital stock of the Company, and of statutes are accurate and fairly present the information required to be presented by the Act;

(xi) to such counsel's knowledge, the Company is not presently (a) in material violation of its charter or by-laws, or (b) in material breach of any applicable statute, rule or regulation known to such counsel or, to such counsel's knowledge, any order, writ or decree of any court or governmental agency or body having jurisdiction over the Company or over any of its properties or operations;

(xii) to such counsel's knowledge, except as set forth in the Registration Statement and Prospectus, no holders of Common Stock or other securities of the Company have registration rights with respect to securities of the Company and, except as set forth in the Registration Statement and Prospectus, all holders of securities of the Company having rights to registration of Common Stock, or other securities pursuant to the Registration Statement, have waived such rights or such rights have expired by reason of lapse of time following notification by the Company of the filing of the Registration Statement [or such Common Stock or other securities have been included in the Registration Statement pursuant to the exercise of and in full satisfaction of such rights]; and

(xiii) (a) Each of the License Agreement, dated May 5, 1998 by and between the Company and Albert Einstein College of Medicine (the "License Agreement"), and the First Amendment to the License Agreement, dated December 10, 1999 (the "First Amendment"), has been duly authorized by all necessary corporate action on the part of the Company and has been duly

executed and delivered by the Company and, assuming due authorization, execution and delivery by Albert Einstein College of Medicine, is a valid and binding agreement of Albert Einstein College of Medicine, enforceable in accordance with its terms; and (b) the Company is not in material breach or violation of the License Agreement or the First Amendment;

In rendering such opinion, such counsel may rely (A) as to matters involving the application of laws of any jurisdiction other than the State of Delaware, the State of New York, the State of California or the Federal laws of the United States, to the extent they deem proper and specified in such opinion, upon the opinion of other counsel of good standing whom they believe to be reliable and who are satisfactory to counsel for the Underwriters and (B) as to matters of fact, to the extent they deem proper, on certificates of responsible officers of the Company and public officials. References to the Prospectus in this paragraph (b) shall also include any supplements thereto at the Closing Date.

(c) The Company shall have requested and caused McAndrews, Held & Malloy, Ltd., intellectual property counsel for the Company, to have furnished to the Representatives their opinion dated the Closing Date and addressed to the Representatives. Such counsel shall state that they are familiar with the technology used by the Company in its business and the manner of its use thereof and have read the Registration Statement and the Prospectus, including particularly the portions of the Registration Statement and the Prospectus referring to patents, trade secrets, trademarks, service marks or other proprietary information or materials and that in their opinion:

(i) The information in the Prospectus under the caption “Risks Relating to Our Company — Risks Relating to our Intellectual Property” and the information incorporated by reference into the prospectus from the fifth, sixth, seventh and ninth paragraphs of “Business — Technology Overview” in Item I of the 2002 Form 10-K, to the extent that such information constitutes matters of law or legal conclusions, has been reviewed by such counsel and is an accurate and fair summary of such matters and conclusions; and

(ii) Such counsel knows of no material action, suit, claim or proceeding relating to patents, patent rights or licenses, trademarks or trademark rights, copyrights, collaborative research, licenses or royalty arrangements or agreements or trade secrets, know-how or proprietary techniques, including processes and substances, owned by, licensed by or affecting the business or operations of the Company which are pending or threatened against the Company or Albert Einstein College of Medicine or any of their respective officers or directors.

(d) The Company shall have requested and caused Amster, Rothstein & Ebenstein, intellectual property counsel for Albert Einstein College of Medicine, to have furnished to the Representatives their opinion dated the Closing Date and addressed to the Representatives. Such counsel shall state that they are familiar with the technology used by the Company in its business and the manner of its use thereof and have read the Registration Statement and the Prospectus, including particularly the portions of the

Registration Statement and the Prospectus referring to patents, trade secrets, trademarks, service marks or other proprietary information or materials and that in their opinion:

(i) Albert Einstein College of Medicine is listed in the records of the United States Patent and Trademark Office as the sole holder of record of the patents listed on a schedule to such opinion (the "Patents") and each of the applications listed on Schedule 1 to such opinion (the "Applications"). Albert Einstein College of Medicine has granted the Company an exclusive worldwide license to each of the Patents and Applications listed in such schedule. To the knowledge of such counsel, there are no claims of third parties to any ownership interest, license or lien with respect to any of the Patents or Applications, other than the U.S. Government to the extent indicated on such schedule. Such counsel is not aware of any material defect in form in the preparation or filing of the Applications. To the knowledge of such counsel, the Applications are being pursued by the Company or Albert Einstein College of Medicine (as applicable). To the knowledge of such counsel, except as indicated on such schedule, Albert Einstein College of Medicine (apart from the license to the Company) owns as its sole property the Patents and Applications;

(ii) The license agreement between Albert Einstein College of Medicine and Alan E. Kligerman, dated October 1, 1994, as amended, has been validly and effectively terminated and neither Alan E. Kligerman nor his successors or assigns retain any residual interest in any of the Patents or Applications. The license agreement between AECOM and the _____ dated August 30, 1996, as amended, has been validly and effectively terminated and neither the _____ nor its successors or assigns retain any residual interest in any of the Patents or Applications;

(iii) The Company or Albert Einstein College of Medicine, as applicable, is listed in the records of the appropriate foreign offices as the sole holder of record of the foreign patents listed on a schedule to such opinion (the "Foreign Patents") and each of the applications listed on a schedule to such opinion (the "Foreign Applications"). Albert Einstein College of Medicine has granted the Company an exclusive worldwide license to each of the Foreign Patents and Foreign Applications listed in such schedule that are shown as being owned by Albert Einstein College of Medicine. Such counsel knows of no claims of third parties to any ownership interest or lien with respect to the Foreign Patents or Foreign Applications. Such counsel is not aware of any material defect of form in the preparation or filing of the Foreign Applications. To the knowledge of such counsel, the Foreign Applications are being pursued by the Company or Albert Einstein College of Medicine (as applicable). To the knowledge of such counsel, the Company or Albert Einstein College of Medicine (apart from the license to the Company), as applicable, owns as it sole property the Foreign Patents and pending Foreign Applications; and

(iv) Such counsel knows of no reason why the Patents or Foreign Patents are not valid as issued. Such counsel has no knowledge of any reason

why any patent to be issued as a result of any Application or Foreign Application would not be valid or would not afford the Company or Albert Einstein College of Medicine, as applicable, useful patent protection with respect thereto.

In addition, such counsel shall state that they have reviewed the Registration Statement and Prospectus and, although such counsel is not passing upon and does not assume any responsibility for the accuracy, completeness or fairness of any statements contained in the Registration Statement or the Prospectus (other than as specified above), and any supplements or amendments thereto, on the basis of the foregoing, nothing has come to their attention which would lead them to believe that either the Registration Statement or any amendments thereto, at the time the Registration Statement or such amendments became effective, contained an untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary to make the statements therein not misleading or that the Prospectus, as of its date or at the date of such opinion letter, contained an untrue statement of a material fact or omitted to state a material fact regarding the Company's Intellectual Property necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading (it being understood that such counsel need express no belief as to the financial statements or schedules or other financial or statistical data derived therefrom, included or incorporated by reference in the Registration Statement or the Prospectus or any amendments or supplements thereto).

(e) The Company shall have requested and caused Wilson Sonsini Goodrich & Rosati, Professional Corporation, FDA regulatory counsel for the Company, to have furnished to the Representatives their opinion dated the Closing Date and addressed to the Representatives. Such counsel shall state that they act as the Company's FDA counsel and in such capacity are familiar with the Company's submissions to and relations with the FDA. Such counsel shall further state that they have read the Registration Statement and the Prospectus, including particularly those portions of the Registration Statement and the Prospectus describing (a) the Company's FDA applications and the status thereof and (b) the Federal Food, Drug, and Cosmetic Act ("FDC Act"), the Public Health Service Act ("PHS Act") or the FDA regulations (such matters (a) and (b) collectively, the "FDA Regulatory Matters") and that in their opinion:

(i) The information in the Prospectus under the caption "Risks Relating to Our Company — Clinical and Regulatory Risks" and the information incorporated by reference into the Prospectus from Item I of the 2002 Form 10-K under the captions "Business — Government Regulation" and "The Drug Approval Process," insofar as such statements constitute legal conclusions under the FDC Act, the PHS Act or FDA regulations or summaries of FDA Regulatory Matters, has been reviewed by such counsel and is an accurate and fair summary of such matters and conclusions;

(ii) Such counsel knows of no material action, suit, claim or proceeding relating to FDA Regulatory Matters which is pending or threatened against the Company or any of its officers or directors, nor is such counsel aware of any material violations of the FDC Act, the PHS Act or FDA regulations by the Company or any of its officers or directors;

(iii) The Company has filed the Investigational New Drug ("IND") applications to the FDA listed on Schedule 1 to such opinion (collectively, the "US Applications"). The FDA has not denied any of the Company's US Applications, [other than as noted on Schedule 1]. [Apart from such denied US Applications,] such counsel is not aware of any material defect in form in the preparation or filing of the US Applications, other than as noted in Schedule 1. To the knowledge of such counsel, [apart from such denied US Applications,] the US Applications are being diligently pursued by the Company, [other than as noted in Schedule 1]. To the knowledge of such counsel, the Company is the sole owner of the US Applications, [other than as noted in Schedule 1];

(iv) The FDA has issued to the Company the IND approval letters listed on Schedule 2 to such opinion, and none of such approvals has been modified, revoked or rescinded;

(v) The Company has filed the applications with foreign regulators listed on Schedule 3 to such opinion (collectively, the "Foreign Applications"). No foreign authority has denied any of the Company's Foreign Applications, [other than as noted on Schedule 3]. [Apart from such denied Foreign Applications,] such counsel is not aware of any material defect in form in the preparation or filing of the Foreign Applications, [other than as noted in Schedule 3]. To the knowledge of such counsel, [apart from such denied Foreign Applications,] the Applications are being diligently pursued by the Company, [other than as noted in Schedule 3]. To the knowledge of such counsel, the Company is the sole owner of the Foreign Applications, [other than as noted in Schedule 3]; and

(vi) The foreign authorities named in Schedule 4 to such opinion have issued to the Company the approvals listed on Schedule 4, and none of such approvals has been modified, revoked or rescinded.

In addition, such counsel shall state that they have reviewed the Registration Statement and Prospectus (including the documents incorporated therein by reference) and, although such counsel is not passing upon and does not assume any responsibility for the accuracy, completeness or fairness of any statements contained in the Registration Statement or the Prospectus (other than as specified above), and any supplements or amendments thereto, on the basis of the foregoing, nothing has come to their attention which would lead them to believe that either the Registration Statement (including the documents incorporated therein by reference) or any amendments thereto, at the time the Registration Statement or such amendments became effective, contained an untrue statement of a material fact regarding the FDA Regulatory Matters or omitted to state a material fact regarding the FDA Regulatory Matters required to

be stated therein or necessary to make the statements therein not misleading or that the Prospectus (including the documents incorporated therein by reference), as of its date or at the Closing Date contained an untrue statement of a material fact regarding the FDA Regulatory matters or omitted to state a material fact regarding the FDA Regulatory Matters necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading (it being understood that such counsel need express no belief as to the financial statements or schedules or other financial statements or statistical data derived therefrom, included or incorporated by reference in the Registration Statement or the Prospectus or any amendments or supplements thereto).

(f) The Representatives shall have received from Cleary, Gottlieb, Steen & Hamilton, counsel for the Underwriters, such opinion or opinions, dated the Closing Date and addressed to the Representatives, with respect to the issuance and sale of the Securities, the Registration Statement, the Prospectus (together with any supplement thereto) and other related matters as the Representatives may reasonably require, and the Company shall have furnished to such counsel such documents as they request for the purpose of enabling them to pass upon such matters.

(g) The Company shall have furnished to the Representatives a certificate of the Company, signed by the Chairman of the Board or the President and the principal financial or accounting officer of the Company, dated the Closing Date, to the effect that the signers of such certificate have carefully examined the Registration Statement, the Prospectus, any supplements to the Prospectus and this Agreement and that:

(i) the representations and warranties of the Company in this Agreement are true and correct on and as of the Closing Date with the same effect as if made on the Closing Date and the Company has complied with all the agreements and satisfied all the conditions on its part to be performed or satisfied at or prior to the Closing Date;

(ii) no stop order suspending the effectiveness of the Registration Statement has been issued and no proceedings for that purpose have been instituted or, to the Company's knowledge, threatened; and

(iii) since the date of the most recent financial statements included or incorporated by reference in the Prospectus (exclusive of any supplement thereto), there has been no material adverse effect on the condition (financial or otherwise), prospects, earnings, business or properties of the Company, whether or not arising from transactions in the ordinary course of business, except as set forth in or contemplated in the Prospectus (exclusive of any supplement thereto).

(h) The Company shall have requested and caused Ernst & Young LLP to have furnished to the Representatives, at the Execution Time and at the Closing Date, letters, dated respectively as of the Execution Time and as of the Closing Date, in form and substance satisfactory to the Representatives, confirming that they are independent accountants within the meaning of the Act and the Exchange Act and the respective

applicable rules and regulations adopted by the Commission thereunder and that they have performed a review of the unaudited interim financial information of the Company for the six-month period ended June 30, 2003, and as at June 30, 2003 in accordance with Statement on Auditing Standards No. 100, and stating in effect that:

(i) in their opinion the audited financial statements and financial statement schedules included or incorporated by reference in the Registration Statement and the Prospectus and reported on by them comply as to form in all material respects with the applicable accounting requirements of the Act and the Exchange Act and the related rules and regulations adopted by the Commission;

(ii) on the basis of a reading of the latest unaudited financial statements made available by the Company; their limited review, in accordance with standards established under Statement on Auditing Standards No. 100, of the unaudited interim financial information for the six-month period ended June 30, 2003, and as at June 30, 2003 incorporated by reference in the Registration Statement and the Prospectus; carrying out certain specified procedures (but not an examination in accordance with generally accepted auditing standards) which would not necessarily reveal matters of significance with respect to the comments set forth in such letter; a reading of the minutes of the meetings of the stockholders, directors and audit and compensation committees of the Company; and inquiries of certain officials of the Company who have responsibility for financial and accounting matters of the Company as to transactions and events subsequent to December 31, 2002, nothing came to their attention which caused them to believe that:

(1) any unaudited financial statements included or incorporated by reference in the Registration Statement and the Prospectus do not comply as to form in all material respects with applicable accounting requirements of the Act and with the related rules and regulations adopted by the Commission with respect to financial statements included or incorporated by reference in quarterly reports on Form 10-Q under the Exchange Act; and said unaudited financial statements are not in conformity with generally accepted accounting principles applied on a basis substantially consistent with that of the audited financial statements included or incorporated by reference in the Registration Statement and the Prospectus;

(2) with respect to the period subsequent to June 30, 2003, there were any changes, at a specified date not more than five days prior to the date of the letter, in the total liabilities of the Company or capital stock of the Company or decreases in the stockholders' equity, cash and cash equivalents or working capital of the Company as compared with the amounts shown on the June 30, 2003, balance sheet included or incorporated by reference in the Registration Statement and the Prospectus, or for the period from July 1, 2003 to such specified date there were any decreases, as compared with June 30, 2002 in operating loss, net

loss or basic and diluted loss per share, except in all instances for changes or decreases set forth in such letter, in which case the letter shall be accompanied by an explanation by the Company as to the significance thereof unless said explanation is not deemed necessary by the Representatives;

(3) the information included or incorporated by reference in the Registration Statement and Prospectus in response to Regulation S-K, Item 301 (Selected Financial Data), Item 302 (Supplementary Financial Information) and Item 402 (Executive Compensation) is not in conformity with the applicable disclosure requirements of Regulation S-K; and

(iii) they have performed certain other specified procedures as a result of which they determined that certain information of an accounting, financial or statistical nature (which is limited to accounting, financial or statistical information derived from the general accounting records of the Company) set forth in the Registration Statement and the Prospectus and in Exhibit 12 to the Registration Statement, including the information set forth under the captions "Summary Financial Data" and "Selected Financial Data" in the Prospectus, the information included or incorporated by reference in Items 1, 2, 6, 7 and 11 of the Company's Annual Report on Form 10-K, incorporated by reference in the Registration Statement and the Prospectus, and the information included in the "Management's Discussion and Analysis of Financial Condition and Results of Operations" included or incorporated by reference in the Company's Quarterly Reports on Form 10-Q, incorporated by reference in the Registration Statement and the Prospectus, agrees with the accounting records of the Company, excluding any questions of legal interpretation.

References to the Prospectus in this paragraph (g) include any supplement thereto at the date of the letter.

(i) The Company shall have requested and caused KPMG LLP to have furnished to the Representatives, at the Execution Time and at the Closing Date, letters, dated respectively as of the Execution Time and as of the Closing Date, in form and substance satisfactory to the Representatives, confirming that they are independent accountants within the meaning of the Act and the Exchange Act and the respective applicable rules and regulations adopted by the Commission thereunder and stating in effect that:

(i) in their opinion the audited financial statements and financial statement schedules included or incorporated by reference in the Registration Statement and the Prospectus and reported on by them comply as to form in all material respects with the applicable accounting requirements of the Act and the Exchange Act and the related rules and regulations adopted by the Commission;

(ii) on the basis of a reading of the latest audited and unaudited financial statements made available by the Company; carrying out certain

specified procedures (but not an examination in accordance with generally accepted auditing standards) which would not necessarily reveal matters of significance with respect to the comments set forth in such letter; a reading of the minutes of the meetings of the stockholders, directors and audit and compensation committees of the Company; and inquiries of certain officials of the Company who have responsibility for financial and accounting matters of the Company as to transactions and events subsequent to December 31, 2001, nothing came to their attention which caused them to believe that the information included or incorporated by reference in the Registration Statement and Prospectus in response to Regulation S-K, Item 301 (Selected Financial Data), Item 302 (Supplementary Financial Information) and Item 402 (Executive Compensation) is not in conformity with the applicable disclosure requirements of Regulation S-K.

(iii) they have performed certain other specified procedures as a result of which they determined that certain information of an accounting, financial or statistical nature (which is limited to accounting, financial or statistical information derived from the general accounting records of the Company set forth in the Registration Statement and the Prospectus, including the information set forth under the captions “Summary Financial Data” and “Selected Financial Data” in the Prospectus, the information included or incorporated by reference in Items 1, 2, 6, 7 and 11 of the Company’s Annual Report on Form 10-K, incorporated by reference in the Registration Statement and the Prospectus, agrees with the accounting records of the Company, excluding any questions of legal interpretation.

References to the Prospectus in this paragraph (h) include any supplement thereto at the date of the letter.

(j) Subsequent to the Execution Time or, if earlier, the dates as of which information is given in the Registration Statement (exclusive of any amendment thereof) and the Prospectus (exclusive of any supplement thereto), there shall not have been (i) any change or decrease specified in the letter or letters referred to in paragraph (e) of this Section 6 or (ii) any change, or any development involving a prospective change, in or affecting the condition (financial or otherwise), earnings, business or properties of the Company, taken as a whole, whether or not arising from transactions in the ordinary course of business, except as set forth in or contemplated in the Prospectus (exclusive of any supplement thereto) the effect of which, in any case referred to in clause (i) or (ii) above, is, in the sole judgment of the Representatives, so material and adverse as to make it impractical or inadvisable to proceed with the offering or delivery of the Securities as contemplated by the Registration Statement (exclusive of any amendment thereof) and the Prospectus (exclusive of any supplement thereto).

(k) Prior to the Closing Date, the Company shall have furnished to the Representatives such further information, certificates and documents as the Representatives may reasonably request.

(l) Subsequent to the Execution Time, there shall not have been any decrease in the rating of any of the Company's debt securities by any "nationally recognized statistical rating organization" (as defined for purposes of Rule 436(g) under the Act) or any notice given of any intended or potential decrease in any such rating or of a possible change in any such rating that does not indicate the direction of the possible change.

(m) The Securities shall have been listed and admitted and authorized for trading on the Nasdaq National Market, and satisfactory evidence of such actions shall have been provided to the Representatives.

(n) At the Execution Time, the Company shall have furnished to the Representatives a letter substantially in the form of Exhibit A hereto from each officer and director of the Company and WS Investment Company addressed to the Representatives.

If any of the conditions specified in this Section 6 shall not have been fulfilled when and as provided in this Agreement, or if any of the opinions and certificates mentioned above or elsewhere in this Agreement shall not be reasonably satisfactory in form and substance to the Representatives and counsel for the Underwriters, this Agreement and all obligations of the Underwriters hereunder may be canceled at, or at any time prior to, the Closing Date by the Representatives. Notice of such cancelation shall be given to the Company in writing or by telephone or facsimile confirmed in writing.

The documents required to be delivered by this Section 6 shall be delivered at the office of Cleary, Gottlieb, Steen & Hamilton, counsel for the Underwriters, at One Liberty Plaza, New York, New York 10006, on the Closing Date.

7. Reimbursement of Underwriters' Expenses. If the sale of the Securities provided for herein is not consummated because any condition to the obligations of the Underwriters set forth in Section 6 hereof is not satisfied, because of any termination pursuant to Section 10 hereof or because of any refusal, inability or failure on the part of the Company to perform any agreement herein or comply with any provision hereof other than by reason of a default by any of the Underwriters, the Company will reimburse the Underwriters severally through Citigroup Global Markets Inc. on demand for all out-of-pocket expenses (including reasonable fees and disbursements of counsel) that shall have been incurred by them in connection with the proposed purchase and sale of the Securities.

8. Indemnification and Contribution. (a) The Company agrees to indemnify and hold harmless each Underwriter, the directors, officers, employees and agents of each Underwriter and each person who controls any Underwriter within the meaning of either the Act or the Exchange Act against any and all losses, claims, damages or liabilities, joint or several, to which they or any of them may become subject under the Act, the Exchange Act or other Federal or state statutory law or regulation, at common law or otherwise, insofar as such losses, claims, damages or liabilities (or actions in respect thereof) arise out of or are based upon any untrue statement or alleged untrue statement of a material fact contained in the registration statement for the registration of the

Securities as originally filed or in any amendment thereof, or in any Preliminary Prospectus or the Prospectus, or in any amendment thereof or supplement thereto, or arise out of or are based upon the omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, and agrees to reimburse each such indemnified party, as incurred, for any legal or other expenses reasonably incurred by them in connection with investigating or defending any such loss, claim, damage, liability or action; provided, however, that the Company will not be liable in any such case to the extent that any such loss, claim, damage or liability arises out of or is based upon any such untrue statement or alleged untrue statement or omission or alleged omission made therein in reliance upon and in conformity with written information furnished to the Company by or on behalf of any Underwriter through the Representatives specifically for inclusion therein. This indemnity agreement will be in addition to any liability which the Company may otherwise have.

(b) Each Underwriter severally and not jointly agrees to indemnify and hold harmless the Company, each of its directors, each of its officers who signs the Registration Statement, and each person who controls the Company within the meaning of either the Act or the Exchange Act, to the same extent as the foregoing indemnity from the Company to each Underwriter, but only with reference to written information relating to such Underwriter furnished to the Company by or on behalf of such Underwriter through the Representatives specifically for inclusion in the documents referred to in the foregoing indemnity. This indemnity agreement will be in addition to any liability which any Underwriter may otherwise have. The Company acknowledges that the statements set forth in the last paragraph of the cover page regarding delivery of the Securities and, under the caption “Underwriting”, (i) the list of Underwriters and their respective participation in the sale of the Securities, (ii) the sentences related to concessions and reallowances and (iii) the paragraph related to stabilization, syndicate covering transactions and penalty bids in any Preliminary Prospectus and the Prospectus constitute the only information furnished in writing by or on behalf of the several Underwriters for inclusion in any Preliminary Prospectus or the Prospectus.

(c) Promptly after receipt by an indemnified party under this Section 8 of notice of the commencement of any action, such indemnified party will, if a claim in respect thereof is to be made against the indemnifying party under this Section 8, notify the indemnifying party in writing of the commencement thereof; but the failure so to notify the indemnifying party (i) will not relieve it from liability under paragraph (a) or (b) above unless and to the extent it did not otherwise learn of such action and such failure results in the forfeiture by the indemnifying party of substantial rights and defenses and (ii) will not, in any event, relieve the indemnifying party from any obligations to any indemnified party other than the indemnification obligation provided in paragraph (a) or (b) above. The indemnifying party shall be entitled to appoint counsel of the indemnifying party’s choice at the indemnifying party’s expense to represent the indemnified party in any action for which indemnification is sought (in which case the indemnifying party shall not thereafter be responsible for the fees and expenses of any separate counsel retained by the indemnified party or parties except as set forth below); provided, however, that such counsel shall be satisfactory to the indemnified party. Notwithstanding the indemnifying party’s election to appoint counsel to represent the

indemnified party in an action, the indemnified party shall have the right to employ separate counsel (including local counsel), and the indemnifying party shall bear the reasonable fees, costs and expenses of such separate counsel if (i) the use of counsel chosen by the indemnifying party to represent the indemnified party would present such counsel with a conflict of interest, (ii) the actual or potential defendants in, or targets of, any such action include both the indemnified party and the indemnifying party and the indemnified party shall have reasonably concluded that there may be legal defenses available to it and/or other indemnified parties which are different from or additional to those available to the indemnifying party, (iii) the indemnifying party shall not have employed counsel satisfactory to the indemnified party to represent the indemnified party within a reasonable time after notice of the institution of such action or (iv) the indemnifying party shall authorize the indemnified party to employ separate counsel at the expense of the indemnifying party. An indemnifying party will not, without the prior written consent of the indemnified parties, settle or compromise or consent to the entry of any judgment with respect to any pending or threatened claim, action, suit or proceeding in respect of which indemnification or contribution may be sought hereunder (whether or not the indemnified parties are actual or potential parties to such claim or action) unless such settlement, compromise or consent includes an unconditional release of each indemnified party from all liability arising out of such claim, action, suit or proceeding.

(d) In the event that the indemnity provided in paragraph (a) or (b) of this Section 8 is unavailable to or insufficient to hold harmless an indemnified party for any reason, the Company and the Underwriters severally agree to contribute to the aggregate losses, claims, damages and liabilities (including legal or other expenses reasonably incurred in connection with investigating or defending same) (collectively "Losses") to which the Company and one or more of the Underwriters may be subject in such proportion as is appropriate to reflect the relative benefits received by the Company on the one hand and by the Underwriters on the other from the offering of the Securities; provided, however, that in no case shall any Underwriter (except as may be provided in any agreement among underwriters relating to the offering of the Securities) be responsible for any amount in excess of the underwriting discount or commission applicable to the Securities purchased by such Underwriter hereunder. If the allocation provided by the immediately preceding sentence is unavailable for any reason, the Company and the Underwriters severally shall contribute in such proportion as is appropriate to reflect not only such relative benefits but also the relative fault of the Company on the one hand and of the Underwriters on the other in connection with the statements or omissions which resulted in such Losses as well as any other relevant equitable considerations. Benefits received by the Company shall be deemed to be equal to the total net proceeds from the offering (before deducting expenses) received by it, and benefits received by the Underwriters shall be deemed to be equal to the total underwriting discounts and commissions, in each case as set forth on the cover page of the Prospectus. Relative fault shall be determined by reference to, among other things, whether any untrue or any alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information provided by the Company on the one hand or the Underwriters on the other, the intent of the parties and their relative knowledge, access to information and opportunity to correct or prevent such untrue statement or omission. The Company and the Underwriters agree that it would not

be just and equitable if contribution were determined by pro rata allocation or any other method of allocation which does not take account of the equitable considerations referred to above. Notwithstanding the provisions of this paragraph (d), no person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. For purposes of this Section 8, each person who controls an Underwriter within the meaning of either the Act or the Exchange Act and each director, officer, employee and agent of an Underwriter shall have the same rights to contribution as such Underwriter, and each person who controls the Company within the meaning of either the Act or the Exchange Act, each officer of the Company who shall have signed the Registration Statement and each director of the Company shall have the same rights to contribution as the Company, subject in each case to the applicable terms and conditions of this paragraph (d).

9. Default by an Underwriter. If any one or more Underwriters shall fail to purchase and pay for any of the Securities agreed to be purchased by such Underwriter or Underwriters hereunder and such failure to purchase shall constitute a default in the performance of its or their obligations under this Agreement, the remaining Underwriters shall be obligated severally to take up and pay for (in the respective proportions which the amount of Securities set forth opposite their names in Schedule I hereto bears to the aggregate amount of Securities set forth opposite the names of all the remaining Underwriters) the Securities which the defaulting Underwriter or Underwriters agreed but failed to purchase; provided, however, that in the event that the aggregate amount of Securities which the defaulting Underwriter or Underwriters agreed but failed to purchase shall exceed 10% of the aggregate amount of Securities set forth in Schedule I hereto, the remaining Underwriters shall have the right to purchase all, but shall not be under any obligation to purchase any, of the Securities, and if such nondefaulting Underwriters do not purchase all the Securities, this Agreement will terminate without liability to any nondefaulting Underwriter or the Company. In the event of a default by any Underwriter as set forth in this Section 9, the Closing Date shall be postponed for such period, not exceeding five Business Days, as the Representatives shall determine in order that the required changes in the Registration Statement and the Prospectus or in any other documents or arrangements may be effected. Nothing contained in this Agreement shall relieve any defaulting Underwriter of its liability, if any, to the Company and any nondefaulting Underwriter for damages occasioned by its default hereunder.

10. Termination. This Agreement shall be subject to termination in the absolute discretion of the Representatives, by notice given to the Company prior to delivery of and payment for the Securities, if at any time prior to such time (i) trading in the Company's Common Stock shall have been suspended by the Commission or the Nasdaq National Market or trading in securities generally on the New York Stock Exchange or the Nasdaq National Market shall have been suspended or limited or minimum prices shall have been established on such Exchange or the Nasdaq National Market, (ii) a banking moratorium shall have been declared either by Federal or New York State authorities or (iii) there shall have occurred any outbreak or escalation of hostilities, declaration by the United States of a national emergency or war, or other calamity or crisis the effect of which on financial markets is such as to make it, in the sole judgment of the Representatives, impractical or inadvisable to proceed with the offering or delivery of the Securities as contemplated by the Prospectus (exclusive of any supplement thereto).

11. Representations and Indemnities to Survive. The respective agreements, representations, warranties, indemnities and other statements of the Company or its officers and of the Underwriters set forth in or made pursuant to this Agreement will remain in full force and effect, regardless of any investigation made by or on behalf of any Underwriter or the Company or any of the officers, directors, employees, agents or controlling persons referred to in Section 8 hereof, and will survive delivery of and payment for the Securities. The provisions of Sections 7 and 8 hereof shall survive the termination or cancelation of this Agreement.

12. Notices. All communications hereunder will be in writing and effective only on receipt, and, if sent to the Representatives, will be mailed, delivered or telefaxed to the Citigroup Global Markets Inc. General Counsel (fax no.: (212) 816-7912) and confirmed to the General Counsel, Citigroup Global Markets Inc., at 388 Greenwich Street, New York, New York, 10013, Attention: General Counsel; or, if sent to the Company, will be mailed, delivered or telefaxed to **[facsimile number]** and confirmed to it at , attention of the Legal Department.

13. Successors. This Agreement will inure to the benefit of and be binding upon the parties hereto and their respective successors and the officers, directors, employees, agents and controlling persons referred to in Section 8 hereof, and no other person will have any right or obligation hereunder.

14. Applicable Law. This Agreement will be governed by and construed in accordance with the laws of the State of New York applicable to contracts made and to be performed within the State of New York.

15. Counterparts. This Agreement may be signed in one or more counterparts, each of which shall constitute an original and all of which together shall constitute one and the same agreement.

16. Headings. The section headings used herein are for convenience only and shall not affect the construction hereof.

17. Definitions. The terms which follow, when used in this Agreement, shall have the meanings indicated.

"Act" shall mean the Securities Act of 1933, as amended, and the rules and regulations of the Commission promulgated thereunder.

"Business Day" shall mean any day other than a Saturday, a Sunday or a legal holiday or a day on which banking institutions or trust companies are authorized or obligated by law to close in New York City.

"Commission" shall mean the Securities and Exchange Commission.

"Effective Date" shall mean each date and time that the Registration Statement, any post-effective amendment or amendments thereto and any Rule 462(b) Registration Statement became or become effective.

"Exchange Act" shall mean the Securities Exchange Act of 1934, as amended, and the rules and regulations of the Commission promulgated thereunder.

"Execution Time" shall mean the date and time that this Agreement is executed and delivered by the parties hereto.

"Preliminary Prospectus" shall mean any preliminary prospectus referred to in paragraph 1(a) above and any preliminary prospectus included in the Registration Statement at the Effective Date that omits Rule 430A Information.

"Prospectus" shall mean the prospectus relating to the Securities that is first filed pursuant to Rule 424(b) after the Execution Time or, if no filing pursuant to Rule 424(b) is required, shall mean the form of final prospectus relating to the Securities included in the Registration Statement at the Effective Date.

"Registration Statement" shall mean the registration statement referred to in paragraph 1(a) above, including exhibits and financial statements, as amended at the Execution Time (or, if not effective at the Execution Time, in the form in which it shall become effective) and, in the event any post-effective amendment thereto or any Rule 462(b) Registration Statement becomes effective prior to the Closing Date, shall also mean such registration statement as so amended or such Rule 462(b) Registration Statement, as the case may be. Such term shall include any Rule 430A Information deemed to be included therein at the Effective Date as provided by Rule 430A.

"Rule 424", "Rule 430A" and "Rule 462" refer to such rules under the Act.

"Rule 430A Information" shall mean information with respect to the Securities and the offering thereof permitted to be omitted from the Registration Statement when it becomes effective pursuant to Rule 430A.

"Rule 462(b) Registration Statement" shall mean a registration statement and any amendments thereto filed pursuant to Rule 462(b) relating to the offering covered by the registration statement referred to in Section 1(a) hereof.

If the foregoing is in accordance with your understanding of our agreement, please sign and return to us the enclosed duplicate hereof, whereupon this letter and your acceptance shall represent a binding agreement among the Company and the several Underwriters.

Very truly yours,

Pain Therapeutics, Inc.

By: _____

Name:
Title:

The foregoing Agreement is hereby confirmed and accepted as of the date first above written.

Citigroup Global Markets Inc.
CIBC World Markets Corp.
Leerink Swann & Company
ThinkEquity Partners LLC

By: Citigroup Global Markets Inc.

By: _____

Name:
Title:

For themselves and the other several Underwriters named in Schedule I to the foregoing Agreement.

[Form of Lock-Up Agreement] **EXHIBIT A**

[Letterhead of officer, director or affiliate of Pain Therapeutics, Inc.]

Pain Therapeutics, Inc.
Public Offering of Common Stock

[September], 2003

Citigroup Global Markets Inc.
CIBC World Markets Corp.
Leerink Swann & Company
ThinkEquity Partners LLC
As Representatives of the several Underwriters,
c/o Citigroup Global Markets Inc.
388 Greenwich Street
New York, New York 10013

Ladies and Gentlemen:

This letter is being delivered to you in connection with the proposed Underwriting Agreement (the "Underwriting Agreement"), between Pain Therapeutics, Inc., a Delaware corporation (the "Company"), and each of you as representatives of a group of Underwriters named therein, relating to an underwritten public offering of Common Stock, $0.001 par value (the "Common Stock"), of the Company.

In order to induce you and the other Underwriters to enter into the Underwriting Agreement, the undersigned will not, without the prior written consent of Citigroup Global Markets Inc., offer, sell, contract to sell, pledge or otherwise dispose of, (or enter into any transaction which is designed to, or might reasonably be expected to, result in the disposition (whether by actual disposition or effective economic disposition due to cash settlement or otherwise) by the undersigned or any affiliate of the undersigned or any person in privity with the undersigned or any affiliate of the undersigned), directly or indirectly, including the filing (or participation in the filing) of a registration statement with the Securities and Exchange Commission in respect of, or establish or increase a put equivalent position or liquidate or decrease a call equivalent position within the meaning of Section 16 of the Securities Exchange Act of 1934, as amended, and the rules and regulations of the Securities and Exchange Commission promulgated thereunder with respect to, any shares of capital stock of the Company or any securities convertible into or exercisable or exchangeable for such capital stock, or publicly announce an intention to effect any such transaction, for a period of 90 days after the date of the Underwriting Agreement, other than shares of Common Stock disposed of as bona fide gifts approved by Citigroup Global Markets Inc.

If for any reason the Underwriting Agreement shall be terminated prior to the Closing Date (as defined in the Underwriting Agreement), the agreement set forth above shall likewise be terminated.

Yours very truly,

[Signature of officer, director or affiliate]

[Name and address of officer, director or affiliate]

SCHEDULE I

Underwriters	Number of Underwritten Securities to be Purchased
Citigroup Global Markets Inc.	
CIBC World Markets Corp.	
Leerink Swann & Company	
ThinkEquity Partners LLC	
Total	

EXHIBIT 10.2

LICENSE AGREEMENT BETWEEN
ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY
AND
PAIN THERAPEUTICS, INC.

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LICENSE AGREEMENT

THIS AGREEMENT, effective as of the date of last signature by a party hereto (the "Effective Date"), is entered into by and between Albert Einstein College of Medicine of Yeshiva University, a division of Yeshiva University, a corporation existing under the laws of the State of New York, having an office and place of business at 1300 Morris Park Avenue, Bronx, New York 10461 ("UNIVERSITY") and Pain Therapeutics, Inc., a corporation organized and existing under the laws of Delaware and having its principal office at 1345 Douglas Street, San Francisco, CA 94131 ("LICENSEE").

WITNESSETH

WHEREAS, in the course of research conducted under UNIVERSITY auspices by Dr. Stanley M. Crain and Dr. Ke-Fei Shen in the Department of Neuroscience of UNIVERSITY certain Know-How and Patent Rights have been developed;

WHEREAS, pursuant to assignments by Dr. Crain and Dr. Shen to UNIVERSITY, which assignments have been recorded in the U.S. Patent and Trademark Office, UNIVERSITY is the owner of the Know-How and Patent Rights, and has the right to grant licenses under the Know-How and Patent Rights;

WHEREAS, UNIVERSITY desires to have the Patent Rights utilized in the public interest and is willing to grant a license to its interest thereunder,

WHEREAS, LICENSEE desires to obtain a license under the Patent Rights and Know-How in accordance with the terms and conditions set forth herein, to commercially develop and exploit the Patent Rights and Know-How;

NOW, THEREFORE, in consideration of the mutual covenants and agreements of the parties herein contained, the parties hereto, intending to be legally bound, do hereby agree as follows.

ARTICLE I
DEFINITIONS

The terms in this Agreement with initial letters capitalized, whether used in the singular or plural, shall have the meaning designated below or, if not designated below, the meaning as designated in places throughout this Agreement.

1.1 "AFFILIATE" means any corporation or other entity which controls, is controlled by, or is under common control with a party to this Agreement. A corporation or other entity shall be regarded as in control of another corporation or entity if it owns or directly or indirectly controls more than fifty percent (50%) of the voting stock or other ownership interest of the other corporation or entity, or if it possesses, directly or indirectly, the power to direct or cause the direction of the management and policies of the corporation or other entity or the power to elect or appoint more than fifty percent (50%) of the members of the governing body of the corporation or other entity.

1.2 "AGENCY" means any governmental regulatory authority responsible for granting health or pricing approvals, registrations, import permits, and other approvals required before Licensed Product may be tested or marketed in any country.

1.3 "CALENDAR QUARTER" means the respective periods of three (3) consecutive calendar months ending on March 31, June 30, September 30 and December 31.

1.4 "CALENDAR YEAR" means each successive period of twelve (12) months commencing on January 1 and ending on December 31.

1.5 "CONFIDENTIAL INFORMATION" means and includes, without limitation, information and data of one party supplied to the other, know-how, and all other scientific, clinical, regulatory, marketing, financial and commercial information or data, whether communicated in writing or orally or by other means, which is provided by one party to the other party in connection with this Agreement, and which is designated confidential by the disclosing party.

1.6 "DEVELOPMENT SCHEDULE" shall have the meaning set forth in Section 5.2 hereof.

1.7 "FIRST COMMERCIAL SALE" means, with respect to a Licensed Product, the first sale for use or consumption by the public of such Licensed Product in a country after all required approvals, including marketing and pricing approvals, have been granted by the governing health authority of such country.

1.8 "IND" means Investigational New Drug application, or the like, as defined in the applicable laws and regulations of the governmental drug regulatory agencies in each country.

1.9 "KNOW-HOW" means all information and materials, including but not limited to, technology, experience, discoveries, improvements, processes, formulae, data (including but not limited to all preclinical, clinical, toxicological, and pharmacological data) and inventions, trade secrets, patentable or otherwise, developed by UNIVERSITY through Drs. Crain and Shen, which on the Effective Date of this Agreement are in UNIVERSITY's possession and control, are not generally known and are necessary or useful for LICENSEE in the research,

development, manufacture, marketing, use or sale of compositions or methods for the attenuation of opioid tolerance and dependence and the enhancement of opioid analgesic potency. Know-How shall also include any Know-How and improvements or modifications to the Know-How which are developed by UNIVERSITY through Drs. Crain, Shen and their staff after the Effective Date of this Agreement as a result of any research funding provided by LICENSEE to UNIVERSITY pursuant to this Agreement.

1.10 "LICENSED PRODUCT" means any and all formulations for human pharmaceutical or animal health use, the manufacture, importation use or sale of which would (a) infringe a Valid Patent Claim but for the license provided under Article II hereof or (b) involve the use of Know-How.

1.11 "MAJOR COUNTRIES" means the following countries: United States, Canada, Japan and collectively the European Community.

1.12 "NDA" means a New Drug Application in the U.S. or the corresponding application for authorization for marketing of Licensed Product in any other country, as defined in the applicable laws and regulations and filed with the Agency of a given country.

1.13 "NET SALES" means the aggregate gross invoice price of Licensed Product sold by LICENSEE, its Affiliates and Sublicensees to an independent third party, including without limitation distributors, after deducting (to the extent not already deducted in the amount invoiced):

(i) trade and quantity discounts given;

(ii) returns and allowances;

(iii) rebates, chargebacks and other amounts paid, credited or accrued;

(iv) retroactive price reductions;

(v) sales commissions paid to distributors and/or selling agents;

(vi) a fixed amount equal to five percent (5%) for U.S. sales and ten percent (10%) for sales outside the U.S., of the amount invoiced to cover bad debt, custom duties, surcharges, sales or excise taxes, cash discounts, transportation and insurance charges; and

(vii) as agreed by the parties, any other specifically identifiable amounts included in gross sales that were or ultimately will be credited and that are substantially similar to those listed above.

1.14 "NET PROCEEDS" shall mean the total consideration. in any form (including, but not limited to, license signing and maintenance fees, minimum payments, research and development funds, and payments for equity of Licensee in excess of fair market value. etc.), received by LICENSEE from any third party or parties in connection with the grant to said third party or parties of a sublicense to make and sell (or otherwise dispose of) Licensed Products. Net Proceeds do not include royalties based on Net Sales of a sublicensee, nor payments made to Licensee that are specifically earmarked for and actually used to conduct clinical trials for Licensed Products.

1.15 "PATENT RIGHTS" means the patents and patent applications listed on Attachment A and any and all divisions, continuations, continuations-in-part, reissues, renewals, extensions or the like of any such patents and patent applications and all foreign equivalents thereof and any and all patents and patent applications owned by UNIVERSITY which contain one or more claims directed to compositions or methods for the attenuation of opioid tolerance and dependence and the enhancement of opioid analgesic potency and which result from the research funding provided by LICENSEE to UNIVERSITY pursuant to this Agreement, and any and all divisions, continuations, continuations-in-part,

reissues, renewals, extensions or the like of any such patents and patent applications and all foreign equivalents thereof.

1.16 “SUBLICENSEE” means a business entity which is sublicensed by LICENSEE under this Agreement.

1.17 “TERRITORY” means the entire world.

1.18 “VALID PATENT CLAIM”‘ means a claim of an issued and unexpired patent included within the Patent Rights which has not been revoked or held unenforceable or invalid by a decision of a court or other governmental agency of competent jurisdiction, unappealable or unappealed within the time allowed for appeal, or which has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue or disclaimer or otherwise.

ARTICLE II

PATENT RIGHTS AND KNOW-HOW

2.1 Subject to paragraph 2.4, UNIVERSITY hereby grants to LICENSEE an exclusive license, with right to grant sublicenses, under the Patent Rights and Know-How to make, have made, use, sell, offer for sale and import Licensed Products in the Territory. LICENSEE shall require all of its sublicensees to expressly agree to indemnify UNIVERSITY in the same manner as LICENSEE is required to indemnify UNIVERSITY pursuant to this Agreement. For each sublicense agreement into which LICENSEE proposes to enter, LICENSEE shall notify UNIVERSITY of the name and address of the sublicensee and provide to UNIVERSITY a copy of the proposed agreement with such sublicensee. Within thirty days of receipt of the proposed agreement and name and address,

UNIVERSITY shall have the right to reject a proposed Sublicensee if such sublicensee:

1. Has, within the past 2 years, engaged in illegal activities;

2. Has an unusually high debt burden or liability (as compared with similar businesses in the same country); and

3. Has, within the past 2 years, been censured by the U.S. Securities and Exchange Commission or, if not a U.S. company, by the securities regulators of its country.

4. Has, within the past 2 years, engaged in a boycott or Israel.

A true and complete copy of all sublicense agreements shall be promptly provided to UNIVERSITY.

2.2 Within thirty (30) days following the Effective Date of this License Agreement, UNIVERSITY shall provide to LICENSEE Know-How not already provided to LICENSEE. Throughout the term of this Agreement, UNIVERSITY will provide additional Know-How to LICENSEE promptly as it is developed.

2.3 LICENSEE's Right of Negotiation. It is recognized that during the term of this Agreement discoveries and inventions may be made as a result of the research funding provided by LICENSEE to UNIVERSITY pursuant to this Agreement that have utility in the pharmaceutical or animal fields which are outside the scope of the license granted under Section 2.1 hereof. Such discoveries and inventions may be made solely by UNIVERSITY or jointly by UNIVERSITY and LICENSEE (said discoveries and inventions referred to herein collectively as "Subject Inventions"). In consideration of this Agreement, UNIVERSITY hereby grants to LICENSEE the fight to require, at LICENSEE's election, that UNIVERSITY negotiate in good faith with LICENSEE with respect to the grant to LICENSEE of an exclusive world-wide license, with right to grant sublicenses, to make, have

made, use, sell, offer for sale and import under UNIVERSITY's rights in any and all Subject Inventions and any patent or patent application claiming such Subject Inventions. The terms and Conditions of such license will be determined giving consideration to product sales, the license scope and rates conventionally granted for inventions with reasonably similar commercial potential and the relative contributions of the parties to the invention, the relative contribution of such invention to the product commercialized, and the cost of subsequent research and development needed to bring the product into the marketplace.

2.4 UNIVERSITY has and will perform research sponsored in part by the United States Government and related to Licensed Products. As a result of this government sponsorship of the aforementioned research, the United States Government retains certain rights in such research as set forth in 35 U.S.C. Section 200 et. seq. and applicable regulations. The continuation of such government sponsored research by UNIVERSITY during the term of this Agreement will not constitute a breach of this Agreement. All rights reserved to the U.S. Government under 35 U.S.C. Section 200 et. seq. and applicable regulations shall remain so reserved and shall in no way be affected by this Agreement. UNIVERSITY is not obligated under this Agreement to take any action which would conflict in any respect with their past, current or future obligations to the U.S. Government as to work already performed and to be performed in the future.

ARTICLE III
PAYMENTS

3.1 LICENSE FEE. In consideration for the rights and licenses granted hereunder, LICENSEE shall pay to UNIVERSITY a one time license fee payment of one hundred thousand dollars ($100,000) which shall be due within thirty (30) days of

the Effective Date. This payment is non-returnable and not creditable against any other payment due under this Agreement.

3.2 RESEARCH FUNDING. In consideration of the license grant and with the understanding that the following payments will be used to fund research at UNIVERSITY in the laboratory of Drs. Crain and Shen, LICENSEE shall pay UNIVERSITY a total of six hundred thousand dollars ($600,000) as follows:

(a) FIRST PAYMENT: one hundred thousand dollars ($100,000) paid in the first year of this Agreement, which shall be due within thirty (30) days of the Effective Date;

(b) SECOND PAYMENT: one hundred thousand dollars ($100,000) paid in the first year of this Agreement, which shall be due within thirty (30) days of the sixth (6) month anniversary of the Effective Date;

(c) THIRD PAYMENT: two hundred thousand dollars ($200,000), paid in the second year of this Agreement, which shall be due within thirty (30) days of the one year anniversary of the Effective Date; and

(d) FOURTH PAYMENT: two hundred thousand dollars ($200,000), paid in the third year of this Agreement, which shall be due within thirty (30) days of the two year anniversary of the Effective Date.

The parties acknowledge and agree that in the event LICENSEE terminates this Agreement as provided under Article VIII hereinbelow, then LICENSEE shall not be obligated to make any payment under this Section 3.2 that, becomes due after such termination. Thus, e.g., if LICENSEE terminates this Agreement on the six month anniversary of the Effective Date, then LICENSEE shall not be obligated to make the payments of Sections 3.2(a) and (b).

3.3 MILESTONES: MILESTONE PAYMENTS. In further consideration of the rights and licenses granted to LICENSEE hereunder, LICENSEE shall make lump sum milestone payments to UNIVERSITY upon the first achievement of the Milestone Events, as set forth in Table I hereinbelow, with respect to Licensed Product.

MILESTONE EVENT	MILESTONE PAYMENT	MILESTONE DATE
Initiation of first Phase III Effective studies in the U.S.	$200,000	4 years from Date
First NDA filing in the U.S. Effective	$300,000	8 years from Date
First NDA approval in the U.S. Effective	$3,000,000	10 Years from Date
First approval to market in each Major Country, other than the U.S.	$500,000	

LICENSEE shall notify UNIVERSITY in writing within thirty (30) days upon the achievement of each Milestone Event and such Milestone Payment shall be paid no later than thirty (30) days following achievement of the Milestone Event. All Milestone Payments under this Agreement shall be made in United States dollars.

Notwithstanding anything to the contrary, LICENSEE shall be deemed to have met a Milestone obligation upon timely payment of the Milestone Payment, regardless of whether the Milestone Event has actually been achieved. Moreover, in the event LICENSEE meets a Milestone by timely payment of the Milestone Payment, and then achieves the Milestone Event some time after the Milestone Date, then the remaining Milestone Dates shall be adjusted into the future by the same amount of time, up to one year, that it took to achieve the Milestone Event. For example, if LICENSEE tendered the Milestone Payment associated with the initiation of first Phase III Studies in the U.S. on the Milestone Date, and achieved this Milestone Event 4.5 years from the Effective Date, then remaining Milestone Dates would be adjusted forward as follows: First NDA filing in the U.S., 8.5 years from Effective Date; First NDA approval in the U.S., 10.5 years. However, if LICENSEE tendered the Milestone Payment associated with the initiation of first Phase III Studies in the U.S. on the Milestone Date, and

achieved this Milestone Event 5.5 years from the Effective Date, then remaining Milestone Dates would be adjusted forward as follows: First NDA filing in the U.S., 9 years from Effective Date; First NDA approval in the U.S., 11 years.

ARTICLE IV
ROYALTIES AND REPORTS

4.1 In consideration of the license rights granted to LICENSEE by UNIVERSITY hereunder, LICENSEE shall pay to UNIVERSITY annual royalties for each Calendar Year on Net Sales of Licensed Product(s) by LICENSEE, its Affiliates and Sublicensees in the Territory. Such royalty shall be payable based upon the

worldwide annual aggregate Net Sales in a Calendar Year of Licensed Product(s) at the rates and in the amounts set forth below:

(a) four percent (4%) of the total aggregate Net Sales of Licensed Product(s) in all countries in the Territory in which the sale of the Licensed Product is covered in whole or in part by a Valid Patent Claim; or, in the event that the Licensed Product is not covered by a Valid Patent Claim,

(b) a royalty of two percent (2%) as a Know-How royalty, for each country in the Territory in which the sale of the Licensed product is not covered in whole or in part by a Valid Patent Claim but involves the use of Know-How.

For each country, royalties on Licensed Product(s) at the rate set forth above shall be payable to UNIVERSITY effective as of the date of First Commercial Sale in the country. The royalty payable under Section 4.1(a) shall be payable until the date of expiration of the last applicable Patent Right containing a Valid Patent Claim in each such country. The royalty payable under Section 4.1(b) shall be payable for a period of ten (10) years from the date of First Commercial Sale.

The royalties payable hereunder shall be subject to the following conditions:

(i) that only one royalty shall be due with respect to the same unit of Licensed Product;

(ii) that no royalties shall be due upon the sale or other transfer between LICENSEE and its Affiliates;

(iii) no royalties shall accrue on the disposition of Licensed Product in reasonable quantities by LICENSEE, Affiliates or its Sublicensees as bona fide samples or as donations to nonprofit institutions or government agencies for non-commercial purposes; and

(iv) notwithstanding the above royalty rates, upon LICENSEE's request. the parties agree to discuss in good faith a reduction of such royalty rate in any given country in the event the level of development, patent protection or general commercial environment affects the commercial viability of the Licensed Product under such royalty rate.

4.2 If LICENSEE grants a sublicense under Patent Rights and/or Know-How prior to the completion of a Phase 11 clinical trial in support of approval to sell the first Licensed Product in the U.S.A., then LICENSEE shall pay to UNIVERSITY fifty percent (50%) of Net Proceeds in addition to payments due to UNIVERSITY pursuant to Paragraph 4.1 with respect to Net Sales of such Sublicensee. If LICENSEE grants a sublicense under Patent Rights and/or Know-How after the completion of a Phase II clinical trial in support of approval to sell the first Licensed Product in the U.S.A., then LICENSEE shall be obligated to make payments to UNIVERSITY pursuant to Paragraph 4.1 with respect to Net Sales of such Sublicensee, but will not be obligated to make additional payments to UNIVERSITY based on Net Proceeds.

4.3 COMPULSORY LICENSES. If a compulsory license is granted with respect to Licensed Product in any country in the Territory with a royalty rate lower than the

royalty rate provided by Section 4.1., then the royalty rate to be paid by LICENSEE on Net Sales in that country under Section 4.1 shall be reduced to be equal to the rate paid by the compulsory licensee.

4.4 THIRD PARTY PATENTS. If LICENSEE, in its reasonable judgment, is required to obtain a license from any third party under any patent in order to import, manufacture, use or sell the Licensed Product, and to pay a royalty under such license, and the infringement of such patent cannot reasonably be avoided by LICENSEE, LICENSEE's obligation to pay royalties under Section 4.1 hereof shall be reduced by one-half of the amount of the royalty paid to such third party, provided, however, that the royalties payable under Section 4.1 hereof shall not be reduced in any such event below one-half (1/2) of the amounts set forth in Sections 4.1(a)-(b) above.

In addition, if LICENSEE is required to pay up-front payments or milestone payments to such third party in consideration for such license, then the milestone payments under Section 3.3 shall be reduced by one-half of the amount of such up-front payments or milestone payments paid to such third party, provided, however, that the milestone payments payable under Section 3.3 hereof shall not be reduced in any such event below one-half (1/2) of the amounts set forth in Section 3.3.

4.5 ROYALTY DURING INFRINGEMENT. If there is substantial infringement of the Patent Rights by a third party or parties and LICENSEE has commenced litigation to abate such infringement, LICENSEE may discontinue payment of up to one half of the royalty with respect to sales in the country where the infringement occurs, until the infringement ends, after which the royalty rate will return to its previous level. Upon successful completion of the litigation and receipt by LICENSEE of a monetary award therefor, LICENSEE shall reimburse UNIVERSITY those royalties withheld under this paragraph 4.5. For the purpose of this paragraph 4.5 "substantial infringement" means unit sales which equal at least 10% of

LICENSEE's unit sales in the country over any three (3) month period, as reported by IMS America Ltd. or another reputable, independent market research firm reasonably acceptable to both parties.

4.6 PAID-UP LICENSE. For each country, upon expiration of LICENSEE's obligation to pay royalties pursuant to Section 4.1, LICENSEE shall have a fully paid-up, non-exclusive license under any Know-How, to make, have made, use and sell Licensed Product in that country.

4.7 REPORTS: PAYMENT OF ROYALTY. During the term of the Agreement following the First Commercial Sale of a Licensed Product, LICENSEE shall furnish to UNIVERSITY a quarterly written report for the Calendar Quarter showing the sales of all Licensed Product(s) subject to royalty payments sold by LICENSEE, its Affiliates and its Sublicensees in the Territory during the reporting period and the royalties payable under this Agreement. Reports shall be due on the ninetieth (90) day following the close of each Calendar Quarter. Royalties shown to have accrued by each royalty report shall be due and payable on the date such royalty report is due. LICENSEE shall keep complete and accurate records in sufficient detail to enable the royalties payable hereunder to be determined.

4.8 AUDITS.

(a) Upon the written request of UNIVERSITY and not more than once in each Calendar Year, LICENSEE shall permit an independent certified public accounting firm of nationally recognized standing selected by UNIVERSITY and reasonably acceptable to LICENSEE, at UNIVERSITY's expense, to have access during normal business hours to such records of LICENSEE as may be reasonably necessary to verify the accuracy of the royalty reports hereunder for any Calendar Year ending not more than twenty-four (24) months prior to the date of such request.

These rights with respect to any Calendar Year shall terminate two (2) years after the end of any such Calendar Year.

(b) If such accounting firm correctly concludes that additional royalties were owed during such period, LICENSEE shall pay the additional royalties within thirty (30) days of the date UNIVERSITY delivers to LICENSEE such accounting firm's written report so correctly concluding. The fees charged by such accounting firm shall be paid by UNIVERSITY unless the audit discloses that the payments payable by LICENSEE for the audited period are more than one hundred ten percent (110%) of the payments actually made for such period, in which case LICENSEE shall pay the reasonable fees and expenses charged by the accounting firm.

(c) LICENSEE shall include in each sublicense granted by it pursuant to this Agreement a provision requiring the Sublicensee to make reports to LICENSEE, to keep and maintain records of sales made pursuant to such sublicense and to grant access to such records by UNIVERSITY's independent accountant to the same extent required of LICENSEE under this Agreement.

(d) UNIVERSITY shall treat all financial information and other LICENSEE information subject to review under this Section 4.8 or under any sublicense agreement in accordance with the confidentiality provisions of this Agreement, and shall cause its accounting firm to enter into a confidentiality agreement with LICENSEE obligating it to retain all such financial information in confidence pursuant to such confidentiality agreement.

4.9 PAYMENT AND EXCHANGE RATE. All payments to be made by LICENSEE to UNIVERSITY under this Agreement shall be made in United States dollars and shall be paid by bank wire transfer in immediately available funds to such bank account in the United States designated in writing by UNIVERSITY from time to time. In the case of sales outside the United States by LICENSEE, the rate of exchange to be used in computing the amount of currency equivalent in United States dollars due UNIVERSITY shall be the month-end exchange rate applicable for the month in which the sales are recorded. Such month-end exchange rate is the exchange rate utilized by LICENSEE in its worldwide accounting system and reflects the average exchange rate for each month.

4.10 INTEREST ON LATE PAYMENTS. UNIVERSITY reserves the right to charge and LICENSEE hereby agrees to pay interest on any overdue amounts owing from LICENSEE which are overdue through the fault of LICENSEE, at the rate of one-half percent (0.5%) per month calculated from the date any payment was due and payable.

ARTICLE V

DEVELOPMENT AND COMMERCIALIZATION

5.1 LICENSEE shall use its good faith efforts, to safely and appropriately manage at its own cost all scientific, medical and business activities that lead to regulatory approval, manufacturing, marketing and sale of Licensed Products worldwide.

5.2 Within ninety (90) days of the Effective Date of this Agreement, LICENSEE shall provide to UNIVERSITY a proposed schedule for the development of the Licensed Product (the “Development Schedule”). LICENSEE shall provide to UNIVERSITY an updated Development Schedule on an annual basis during the development of Licensed Product.

ARTICLE VI

CONFIDENTIALITY AND PUBLICATION

6.1 The parties hereby agree to not disclose and to use all reasonable efforts to maintain the secrecy of any and all Confidential Information disclosed by one party to the other under the terms of this Agreement without the express, written consent of the disclosing party, with the exception of the following:

(a) information which, at the time of disclosure, is available to the public;

(b) information which, after disclosure, becomes available to the public by publication or otherwise, other than by breach of this Agreement by the receiving party;

(c) information that the receiving party can establish by prior record was already known to it or was in its possession or in the possession of an Affiliate (as such term is defined below) at the time of disclosure and was not acquired, directly or indirectly, from the disclosing party;

(d) information that the receiving party obtains from a third party; provided however, that such information was not obtained by said third party, directly or indirectly, from the disclosing party under an obligation of confidentiality toward the disclosing party;

(e) information that the receiving party can establish was independently developed by persons in its employ or otherwise who had no contact with and were not aware of the content of the Confidential Information; and

(f) information that the receiving party is compelled to disclose by a court or other tribunal of competent jurisdiction, provided however, that in such case the receiving party shall immediately give notice to the providing party so that the providing party may seek a protective order or other remedy from said court or tribunal. In any event, the receiving party shall

disclose only that portion of the Confidential Information that, in the opinion of its legal counsel, is legally required to be disclosed and will exercise reasonable efforts to ensure that any such information so disclosed will be accorded confidential treatment by said court or tribunal.

6.2 The receiving party will not disclose any such Confidential Information to any person other than to Rs directors, officers or employees, or to, directors, officers or employees of an Affiliate and sublicensees, and only then if they have a clear need to know such Confidential Information in connection with the performance of their professional responsibilities.

6.3 The receiving party shall take all reasonable steps, including, but not limited to, those steps taken to protect its own information, data or other tangible or intangible property that it regards as proprietary or confidential, to insure that the Confidential Information is not disclosed or duplicated for the use of any third party, and shall take all reasonable steps to prevent its officers and employees, or any others having access to the Confidential Information, from disclosing or making unauthorized use of any Confidential Information, or from committing any acts or omissions that may result in a violation of this Agreement.

6.4 Title to, and all rights emanating from the ownership of, all Confidential Information disclosed under this Agreement shall remain vested in the disclosing party. Nothing herein shall be construed as granting any license or other right to use the Confidential Information other than as specifically agreed upon by the parties.

6.5 Upon written request of the disclosing party, the receiving party shall return promptly to the disclosing party all written materials and documents, as well as any computer software or other media, made available or supplied by the

disclosing party to the receiving party that contains Confidential Information, together with any copies thereof, except that the receiving party may retain one copy of each such document or other media for archival purposes, subject to protection and non-disclosure in accordance with the terms of this Agreement

6.6 The receiving party agrees that the disclosure of Confidential Information without the express written consent of the disclosing party will cause irreparable harm to the disclosing party, and that any breach or threatened breach of this Agreement by the receiving party will entitle the disclosing party to injunctive relieve, in addition to any other legal remedies available to it, in any court of competent jurisdiction.

6.7 USE OF CONFIDENTIAL IN INFORMATION. Both parties agree that the Confidential Information shall only be used in connection with the parties' respective rights and obligations under this Agreement.

6.8 PUBLICATION. During the term of this Agreement, LICENSEE and UNIVERSITY each acknowledge the other party's interest in publishing its results to obtain recognition within the scientific community and to advance the state of scientific knowledge. Each party also recognizes the mutual interest in obtaining valid patent protection and in protecting business interests and trade secret information. Consequently, either party, its employees or consultants wishing to make a publication of the research funded by LICENSEE pursuant to this Agreement shall deliver to the other party a copy of the proposed written publication or an outline of an oral disclosure at least thirty (30) days prior to submission for publication or presentation. The reviewing party shall have the right (i) to propose modifications to the publication for patent reasons, trade secret reasons or business reasons or (ii) to request a reasonable delay in publication or presentation in order to protect patentable information. If the

reviewing party requests a delay, the publishing party shall delay submission or presentation for a period of sixty (60) days to enable patent applications protecting each party's rights in such information to be filed. Upon expiration of such sixty (60) days, the publishing party shall be free to proceed with the publication or presentation. If the reviewing party requests modifications to the publication, the publishing party shall edit such publication to prevent disclosure or trade secret or proprietary business information prior to submission of the publication or presentation. In addition, the contributions of the parties to the research shall be expressly noted in such publications or other public disclosures by acknowledgment or co-authorship, whichever is appropriate.

ARTICLE VII

PATENTS

7.1 FILING, PROSECUTION AND MAINTENANCE OF PATENTS. The parties shall diligently take all commercially reasonable steps required to maintain the Patent Rights in full force and effect, UNIVERSITY shall be responsible for the day-to-day activities associated with filing, prosecuting and maintaining the Patent Rights. UNIVERSITY agrees to consult with and cooperate with LICENSEE to promptly file, prosecute and maintain the Patent Rights in the Territory. All filing, prosecution, and maintenance decisions with respect to the Patent Rights, including without limitation decisions about reexaminations and reissue proceedings, shall be made by LICENSEE with the approval of UNIVERSITY, such approval not to be unreasonably withheld. All such filing, prosecution, and maintenance of the Patent Rights shall be carried out by outside patent counsel selected by LICENSEE with the approval of UNIVERSITY, such approval not to be unreasonably withheld. Such outside patent counsel shall at all times during the term of this Agreement keep LICENSEE and UNIVERSITY advised of the status of patent filings and upon request of either party shall provide copies of

any papers relating to the filing, prosecution or maintenance of such Patent Rights. During the term of this Agreement the parties shall cooperate in providing information to assist the outside counsel with the patent prosecution of the Patent Rights.

7.2 PATENT COSTS. In consideration of this Agreement, during the term of this Agreement LICENSEE shall reimburse UNIVERSITY for the documented filing, prosecution, and maintaining costs with respect to the Patent Rights which are invoiced by such outside patent counsel (the "Patent Costs"). Outside patent counsel shall provide LICENSEE with detailed invoices, reasonably satisfactory to LICENSEE, for the Patent Costs. LICENSEE shall pay outside patent counsel within thirty (30) days of receipt of such invoices. UNIVERSITY shall promptly give notice to LICENSEE of the grant, lapse, revocation, surrender, invalidation, or abandonment of any Patent Rights licensed to LICENSEE for which UNIVERSITY is responsible for the filing, prosecution and maintenance. In the event that UNIVERSITY desires to discontinue maintenance or prosecution of the Patent Rights, UNIVERSITY shall first agree to assign such Patent Rights to LICENSEE at no cost.

7.3 PATENT TERM RESTORATION. The parties hereto shall cooperate with each other in obtaining patent term restoration or supplemental protection certificates or their equivalents in any country in the Territory where applicable to Patent Rights. In the event that elections with respect to obtaining such patent term restoration, supplemental protection certificates or their equivalents are to be made, LICENSEE shall have the right to make the election and UNIVERSITY agrees to abide by such election.

7.4 INFRINGEMENT.

(a) UNIVERSITY and LICENSEE each shall immediately give notice to the other of any potential infringement or infringement by a third party of any Patent Rights of which they become aware or of any certification of which they become aware filed under the United States "Drug Price Competition and Patent Term Restoration Act of 1984" claiming that Patent Rights covering the Licensed Product are invalid or unenforceable or that infringement will not arise from the manufacture, use or sale of Licensed Product by a third party.

(b) LICENSEE as exclusive licensee will have the right to settle with the infringer or to bring suit or other proceeding at its expense against the infringer in its own name or in the name of UNIVERSITY where necessary, after consultation with UNIVERSITY. UNIVERSITY shall be kept advised at all times of such suit or proceedings brought by LICENSEE. UNIVERSITY may, in its discretion, join LICENSEE as party to the suit or other proceeding, provided that LICENSEE shall retain control of the prosecution of such suit or proceedings in such event. UNIVERSITY agrees to cooperate with LICENSEE in its efforts to protect Patent Rights, including joining as a party where necessary.

(c) If LICENSEE does not settle with the infringer or bring suit or other proceeding against the infringer, UNIVERSITY may in its discretion, bring suit or other proceeding at its expense against the infringer, provided however, that UNIVERSITY shall first consult with LICENSEE as to whether such act(s) by a third party reasonably constitute infringement and whether it is commercially advisable to bring such suit or proceeding, as reasonably determined by LICENSEE. LICENSEE shall be kept

advised at all times of such suit or proceedings brought by UNIVERSITY. LICENSEE may, in its discretion, join LICENSEE as party to the suit or other proceeding, provided that UNIVERSITY shall retain control of the prosecution of such suit or proceedings in such event. LICENSEE agrees to cooperate with UNIVERSITY in its efforts to protect Patent Rights, including joining as a party where necessary.

(d) Each party will bear its own expenses with respect to any suit or other proceeding against an infringer. Any recovery in connection with such suit or proceeding will first be applied to reimburse UNIVERSITY and LICENSEE for their out-of-pocket expenses, including attorney's fees. The party controlling the suit will retain the balance of any recovery. However, if the damages awarded LICENSEE include an amount based on lost sales or profit, then LICENSEE shall pay to UNIVERSITY four percent (4%) of the award after first subtracting from the award those amounts not based on lost sales or profit (such as punitive damages including treble damages, e.g.). If the damages awarded LICENSEE include an amount based on a reasonable royalty then, LICENSEE shall pay to UNIVERSITY twenty percent (20%) of the award after first subtracting from the award those amounts not based on a reasonable royalty (such as punitive damages including treble damages, e.g.).

ARTICLE VIII

TERM AND TERMINATION

8.1 TERM AND EXPIRATION. This Agreement shall be effective as of the Effective Date and unless terminated earlier pursuant to Section 8.2, 8.3 or 8.4 below, the terms of this Agreement shall continue in effect on a country-by-country basis until expiration date of the last obligation of LICENSEE to pay royalty to

UNIVERSITY for the sale of a Licensed Product in that country. Upon expiration of this Agreement as to any country due to the expiration of the obligation of LICENSEE to pay royalty to UNIVERSITY for the sale of a Licensed Product in that country, the licenses hereunder with respect to Licensed Product shall become fully paid-up, perpetual licenses.

8.2 TERMINATION FOR CAUSE. This Agreement may be terminated by notice by either party at any time during the term of this Agreement:

(a) if it is shown by credible evidence that the other party is in breach of its material obligations hereunder (including all obligations of Licensee to make payments to UNIVERSITY hereunder) by causes and reasons within its control and has not cured such breach within ninety (90) days after written notice requesting cure of the breach; or

(b) upon the filing or institution of bankruptcy, liquidation or receivership proceedings, or upon an assignment of a substantial portion of the assets for the benefit of creditors by the other party; provided, however, in the case of any involuntary bankruptcy proceeding such right to terminate shall only become effective if the party consents to the involuntary bankruptcy or such proceeding is not dismissed within ninety (90) days after the filing thereof.

8.3 TERMINATION WITHOUT CAUSE. This Agreement may be terminated by LICENSEE at any time on fifteen (15) days written notice. Upon such termination all right, title and interest in the Patent Rights, Know-How and all preclinical and clinical data shall revert to UNIVERSITY and LICENSEE shall have no further obligations under this Agreement.

8.4 TERMINATION by UNIVERSITY. If LICENSEE has not initiated a Phase III clinical trial in the U.S.A. for a Licensed Product before the fourth anniversary of the Effective Date, then UNIVERSITY may terminate and the licenses granted hereunder by giving notice to LICENSEE FIFTEEN (15) days prior to such termination. Upon such termination all right, title and interest in the Patent Rights, Know-how and all preclinical data shall revert to UNIVERSITY and LICENSEE shall have no further obligations under this Agreement.

8.5 EFFECT OF TERMINATION. Expiration or termination of the Agreement shall not relieve the parties of any obligation accruing prior to such expiration or termination. Any expiration or early termination of this Agreement shall be without prejudice to the rights of either party against the other accrued or accruing under this Agreement prior to termination, including the obligation to pay royalties for Licensed Product sold prior to such termination.

ARTICLE IX

INDEMNIFICATION

9.1 INDEMNIFICATION BY LICENSEE. LICENSEE shall at all times during the term of this Agreement and thereafter, indemnify, defend and hold harmless UNIVERSITY, its trustees, officers, employees and affiliates, from and against any and all claim, loss, damage, liability, injury, cost or expense, including without limitation expenses of litigation and reasonable attorneys' fees, in connection with any claims made or suits brought against LICENSEE relating to this Agreement: (i) arising from the negligence, willful misconduct, or material breach of this Agreement by LICENSEE, its Affiliates, subcontractors, sublicensees, or agents or (ii)

arising out of the death of or injury to any person or persons or out of any damage to property and resulting from the production, manufacture, sale, use, lease, consumption or advertisement of Licensed Product; provided however that LICENSEE shall not be obligated to provide indemnification hereunder to the extent that any such claim, loss, damage, liability, injury, cost or expense results form the gross negligence, willful misconduct, or material breach of this Agreement by UNIVERSITY.

9.2 INSURANCE. LICENSEE represents and warrants that prior to any clinical trials of Licensed Product, LICENSEE shall have liability protection, the nature and extent of which is commensurate with usual and customary industry practices.

9.3 PROCEDURE. Should UNIVERSITY or any of its officers, agents, parent companies, affiliates, or employees (the "Indemnitee") intend to claim indemnification under this Article 9, such Indemnitee shall promptly notify LICENSEE (the "Indemnitor") in writing of any loss, claim, damage, liability or action in respect of which the Indemnitee intends to claim such indemnification, and the Indemnitor shall be entitled to assume the defense thereof with counsel selected by the Indemnitor and approved by the Indemnitee, such approval not to be unreasonably withheld; provided, however, that if representation of Indemnitee by such counsel first selected by the Indemnitor would be inappropriate due to a conflict of interest between such Indemnitee and any other party represented by such counsel, then Indemnitor shall select other counsel for the defense of Indemnitee, with the fees and expenses to be paid by the Indemnitor, such other counsel to be approved by Indemnitee and such approval not to be

unreasonably withheld. The indemnity agreement in this Article 9 shall not apply to amounts paid in settlement of any loss, claim, damage, liability or action if such settlement is effected without the consent of the Indemnitor, which consent shall not be withheld unreasonably. The failure to deliver notice to the Indemnitor within a reasonable time after the commencement of any such action, prejudicial to its ability to defend such action, shall relieve such Indemnitor of any liability to the Indemnitee under this Article 9, but the omission so to deliver notice to the Indemnitor will not relieve it of any liability that it may have to any Indemnitee otherwise than under this Article 9. The Indemnities under this Article 9, its employees and agents, shall cooperate fully with the Indemnitor and its legal representatives in the investigation of any action, claim or liability covered by this indemnification.

9.4 Except as otherwise expressly set forth in this Agreement, UNIVERSITY MAKES NO REPRESENTATIONS AND EXTENDS NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING BUT NOT LIMITED TO WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE NON-INFRINGEMENT OF THIRD PARTY RIGHTS, AND VALIDITY OF PATENT RIGHTS CLAIMS, ISSUED OR PENDING.

ARTICLE X

MISCELLANEOUS

10.1 FORCE MAJEURE. Neither party shall be held liable or responsible to the other party nor be deemed to have defaulted under or breached the Agreement for failure or delay in fulfilling or performing any term of the

Agreement when such failure or delay is caused by or results from causes beyond the reasonable control of the affected party including, but not limited to, fire, floods, embargoes, war, acts of war (whether war be declared or not), insurrections, riots, civil commotions, strikes, lockouts of other labor disturbances, acts of God or acts, omissions or delays in acting by any governmental authority or the other party.

10.2 ASSIGNMENT. This Agreement may not be assigned or otherwise transferred by either party without the consent of the other party; provided, however, that LICENSEE may, without such consent, assign this Agreement and its rights and obligations hereunder to its Affiliates or in connection with the transfer or sale of all or substantially all of its business, or in the event of its merger or consolidation or change in control or similar transaction. Any purported assignment in violation of the preceding sentences shall be void. Any permitted assignee shall assume all obligations of its assignor under this Agreement.

10.3 SEVERABILITY. In the event any one or more of the provisions contained in this Agreement should be held invalid, illegal or unenforceable in any respect, the validity, legality and enforceability of the remaining provisions contained herein shall not in any way be affected or impaired thereby, unless the absence of the invalidated provision(s) adversely affect the substantive rights of the parties. The parties shall in such an instance use their best efforts to replace the invalid, illegal or unenforceable provision(s) with valid, legal and enforceable provision(s) which, insofar as practical, implement the purposes of this Agreement.

10.4 NOTICES. Any payment, notice or other communication pursuant to this Agreement shall be sufficiently made or given on the date of mailing if sent to such party by facsimile on such date, with paper copy being sent by certified first class mail, postage prepaid, or by next day express delivery service, addressed to it at is address below (or such address as it shall designate by written notice given to the other party).

In the case of LICENSEE:

Pain Therapeutics, Inc.
1345 Douglas Street
San Francisco, CA 94131
Attn: Mr. Remi Barbier

In the case of UNIVERSITY:

Office of Industrial Liaison
Albert Einstein College of Medicine of Yeshiva University
Jack and Pearl Resnick Campus
1300 Morris Park Avenue
Bronx, NY 10461
Telephone No. (718) 430-3357
Fax No. (718) 430-8822

With copy to:

Kenneth P. George, Esq.
AMSTER, ROTHSTEIN & EBENSTEIN
90 Park Avenue
New York, NY 10016
Telephone No. (212) 697-5995
Fax No. (212) 286-0854

10.5 APPLICABLE LAW/JURISDICTION. This Agreement is acknowledged to have been made in and shall be construed, governed, interpreted and applied in accordance with the laws of the State of New York, without giving effect to

its conflict of laws provisions. The parties shall attempt in good faith to amicably resolve any disputes under this Agreement. LICENSEE and UNIVERSITY agree to negotiate in good faith a resolution of any dispute between them regarding this Agreement. In this regard, the President and CEO of LICENSEE and the Director of the Office of Industrial Liaison of UNIVERSITY shall meet in person for at least two continuous hours to attempt in good faith to resolve the dispute. With respect to such disputes, any litigation instituted by LICENSEE shall be brought in a state or federal court located in New York, and any litigation instituted by UNIVERSITY shall be brought in a state or federal court located in New York. Each party hereby irrevocably consents to the personal and exclusive jurisdiction and venue of such courts.

10.6 ENTIRE AGREEMENT. This Agreement sets forth the entire agreement and understanding of the parties as to the subject matter hereof. This Agreement may be amended only by a written instrument duly executed by both parties hereto.

10.7 HEADINGS. The captions to the Articles and Sections hereof are not a part of the Agreement, but are merely guides or labels to assist in locating and reading the Articles and Sections hereof.

10.8 INDEPENDENT CONTRACTORS. It is expressly agreed that UNIVERSITY and LICENSEE shall be independent contractors with respect to this Agreement and that the relationship between the two parties created by this Agreement shall not constitute a partnership, joint venture or agency. Neither UNIVERSITY nor LICENSEE shall have the authority to make any

statements, representations or commitments of any kind, or to take any action, which shall be binding on the other, without the prior consent of the party to do so.

10.9 WAIVER. The waiver by either party hereto of any right hereunder or the failure to perform or of a breach by the other party shall not be deemed a waiver of any other right hereunder or of any other breach or failure by said other party whether of a similar nature or otherwise.

10.10 COUNTERPARTS. The Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

10.11 REPRESENTATIONS AND WARRANTIES. UNIVERSITY hereby represents and warrants that: (1) it has the right to enter into this Agreement and to grant the licenses contained herein and owns the Patent Rights and Know-How licensed hereunder by virtue of assignments from Drs. Crain and Shen and (2) no other person or organization presently has any effective option or license from UNIVERSITY to manufacture, use, sell or import Licensed Product or is presently authorized by UNIVERSITY to use the Know-How. Each party warrants and represents to the other that it has the full eight and authority to enter into this Agreement, and that it is not aware of any impediment, including any charge of infringement of patents, which would inhibit its ability to perform the terms and conditions imposed on it by such Agreement.

10.12 Nothing in this Agreement is or shall be construed as:

(a) A warranty or representation by UNIVERSITY that anything made or used by LICENSEE under any license granted in this Agreement is or will be free from infringement of patents, copyrights, and other rights of third parties; or

(b) Granting by implication, estoppel, or otherwise any license, right or interest other than as expressly set forth herein.

10.13 As of the Effective Date, to the best of UNIVERSITY's knowledge and belief, it has advised Licensee in writing of any conditions that may:

(a) materially affect pre-clinical/clinical development, regulatory approval or commercialization of Licensed Products, or

(b) raise reasonable doubts about the safety or utility of Licensed Products, including serious or unexpected side effects, toxicity or sensitivity reactions related to the clinical use or administration of the Licensed Products.

10.14 PUBLICITY. Each party agrees not to issue any press release or other public statement, whether oral or written, disclosing the existence of this Agreement or any information relating to this Agreement without the prior written consent of the other party, provided however, that neither party will be prevented from complying with any duty of disclosure it may have pursuant to law or government regulation.

10.15 USE OF NAMES. Neither party will, without prior written consent of the other party, use the name or any trademark or trade name owned by the other party, or, owned by an affiliate or parent corporation of the other party, in any publication, publicity, advertising, or otherwise.

10.16 NON-SOLICITATION. Except in the event of an initial public offering, LICENSEE will not directly or indirectly solicit the general public, or UNIVERSITY, its employees, directors, affiliates and all other parties related to UNIVERSITY, for any fund raising purposes whatsoever.

IN WITNESS WHEREOF, the parties intending to be bound have caused this Agreement to be executed by their duly authorized representatives, Effective as of the Effective Date.

ALBERT EINSTEIN COLLEGE OF MEDICINE
OF YESHIVA UNIVERSITY

BY: /s/ EMANUAL GENN

EMANUEL GENN
ASSOCIATE DEAN FOR BUSINESS
AFFAIRS

DATE: 5/5/98

PAIN THERAPEUTICS, INC.

BY: /s/ REMI BARBIER

TITLE: President & CEO

DATE:

APPENDIX A

[*]

[*] Confidential Treatment Requested

FIRST AMENDMENT TO THE LICENSE AGREEMENT
between
ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY
and
PAIN THERAPEUTICS, INC.

This First Amendment, effective December 10, 1999, is made and entered into by and between Albert Einstein College of Medicine of Yeshiva University, a division of Yeshiva University ("UNIVERSITY"), a New York corporation, having an office at 1300 Morris Park Avenue, Bronx, NY 10461 and Pain Therapeutics, Inc., a Delaware corporation, having an office at 250 East Grand Avenue, Suite 70, South San Francisco, California 94080 ("LICENSEE").

WHEREAS, UNIVERSITY and LICENSEE entered into a License Agreement effective May 5, 1998 ("the Agreement"); and,

WHEREAS, the parties wish to make changes to the Agreement;

NOW, THEREFORE, in consideration of the mutual covenants contained in the Agreement and in this First Amendment and other good and valuable consideration the receipt and sufficiency of which is hereby acknowledged, the parties agree as follows:

1. The definition of "Know-How" (Paragraph 1.9 of the Agreement) is hereby expanded to include the following:

"Know-How" also means all information and materials, including but not limited to technology, experience, discoveries, improvements, processes, formulae, data (including but not limited to all preclinical, clinical, toxicological, and pharmacological data) and inventions, trade secrets, patentable or otherwise, developed by UNIVERSITY through

Drs. Crain and Shen and also Dr. Gerald M. Fleischner, which on the Effective Date of this Agreement are in UNIVERSITY's possession and control, are not generally known and are necessary or useful for LICENSEE in the research, development, manufacture, marketing, use or sale of compositions or methods for the treatment of Irritable Bowel Syndrome. Know-How shall also include any Know-How and improvements or modifications to the Know-How which are developed by UNIVERSITY through Drs. Crain, Shen, Fleischner and their staff after the Effective Date of this Agreement as a result of any research funding provided by LICENSEE to UNIVERSITY pursuant to this Agreement.

2. The definition of "Patent Rights" (Paragraph 1.15 of the Agreement) is hereby expanded to include the following:

"Patent Rights" also means the patents and patent applications listed on Attachment A and any and all divisions, continuations, continuations-in-part, reissues, renewals, extensions or the like of any such patents and patent applications and all foreign equivalents thereof and any and all patents and patent applications owned by UNIVERSITY which contain one or more claims directed to compositions or methods for the treatment of Irritable Bowel Syndrome and which result from the research funding provided by LICENSEE to UNIVERSITY pursuant to this Agreement, and any and all divisions, continuations, continuations-in-part, reissues, renewals, extensions or the like of any such patents and patent applications and all foreign equivalents thereof.

3. The Agreement shall include an updated Attachment A which is attached hereto.

4. UNIVERSITY acknowledges receipt of Ten Thousand Dollars (US$10,000) from LICENSEE in partial consideration for this First Amendment.

5. The following sentence shall be added to the end of paragraph 9.1:

For the purpose of this paragraph 9.1, Dr. Gerald M. Fleischner shall be deemed to be an affiliate of UNIVERSITY.

6. This First Amendment shall be deemed to be incorporated into the Agreement in full and to be an integral part thereof as though fully set forth therein. With the exception of the above amendment, all other provisions of the Agreement shall remain in full force and effect.

IN WITNESS WHEREOF, the parties hereto have entered into and executed this First Amendment on the date first above written.

ALBERT EINSTEIN COLLEGE OF MEDICINE OF YESHIVA UNIVERSITY	**PAIN THERAPEUTICS, INC.**
By: /s/ EMANUEL GENN	By: /s/ REMI BARBIER
Name: Emanuel Genn	Name: Remi Barbier
Title: Associate Dean for Business Affairs	Title: President & CEO

Attachment A

1. U.S. Patent No. 5,472,943, issued December 5, 1995, entitled “Method of Simultaneously Enhancing Analgesic Potency and Attenuating Dependence Liability Caused by Morphine and Other Opioid Agonists” (ARE File No. 96700/242).

2. Australian Patent No. 691515, entitled “Methods of Enhancing Opiate Analgesic Potency or Detoxifying an Opiate Addict” (based on PCT/US94/08288 and claiming priority to No. 1 above) (ARE File No. 96700/504).

3. Canadian Patent Application No. 2168262, entitled “Methods of Enhancing Opiate Analgesic Potency or Detoxifying an Opiate Addict” (based on PCT/US94/08288 and claiming priority to No. 1 above) (ARE File No. 96700/503).

4. EPC Patent Application No. 94924485.9, entitled “Methods of Enhancing Opiate Analgesic Potency or Detoxifying an Opiate Addict” (based on PCT/US94/08288 and claiming priority to No. 1 above) (ARE File No. 96700/502).

5. Japanese Patent Application No. 505899/1995, entitled “Methods of Enhancing Opiate Analgesic Potency or Detoxifying an Opiate Addict” (based on PCT/US94/08288 and claiming priority to No. 1 above) (ARE File No. 96700/501).

6. U.S. Patent No. 5,512,578, issued April 30, 1996, entitled “Method of Simultaneously Enhancing Analgesic Potency and Attenuating Dependence Liability Caused by Exogenous and Endogenous Opioid Agonists” (continuation-in-part of No. 1 above) (ARE File No. 96700/297).

7. U.S. Reissue Patent Application No. 08/782,452, filed January 13, 1997 (reissue of No. 6 above) (ARE File No. 96700/510) (Status—allowed).

8. Australian Patent Application No. 47399/99, entitled “Methods of Enhancing Opiate Analgesic Potency and Attenuating Dependence Liability Caused by Exogenous and Endogenous Opioid Agonists” (divisional of Australian Patent Application No. 32769/95, now abandoned, which is based on PCT/US95/09974 and claims priority to No. 6 above) (ARE File No. 96700/432).

9. Australian Patent Application No. 41135/99, entitled “Methods of Enhancing Opiate Analgesic Potency and Attenuating Dependence Liability Caused by Exogenous and Endogenous Opioid Agonists” (divisional of Australian Patent Application No. 32769/95, now abandoned, which is based on PCT/US95/09974 and claims priority to No. 6 above) (ARE File No. 96700/597).

10. Canadian Patent Application No. 2,195,122, entitled “Methods of Enhancing Opiate Analgesic Potency and Attenuating Dependence Liability Caused by Exogenous and Endogenous Opioid Agonists” (based on PCT/US95/09974 and claiming priority to No. 6 above) (ARE File No. 96700/433).

11. EPC Patent Application No. 95929400.0, entitled “Methods of Enhancing Opiate Analgesic Potency and Attenuating Dependence Liability Caused By Exogenous and Endogenous Opioid Agonists” (based on PCT/US95/09974 and claiming priority to No. 6 above) (ARE File No. 96700/434).

12. Japanese Patent Application No. 08-505298, entitled “Methods of Enhancing Opiate Analgesic Potency and Attenuating Dependence Liability Caused by Exogenous and Endogenous Opioid Agonists” (based on PCT/US95/09974 and claiming priority to No. 6 above) (ARE File No. 96700/435).

13. U.S. Patent No. 5,580,876, issued December 3, 1996, entitled “Method of Simultaneously Enhancing Analgesic Potency and Attenuating Dependence Liability Caused by Morphine and Other Biomodally-Acting Opioid Agonists” (continuation-in-part of No. 6 above) (ARE File No. 96700/389).

14. U.S. Patent No. 5,765,125, issued June 16, 1998, entitled “Method of Simultaneously Enhancing Analgesic Potency and Attenuating Dependence Liability Caused by Morphine and Other Biomodally-Acting Opioid Agonists” (continuation of No. 12 above) (ARE File No. 96700/509).

15. U.S. Patent Application No. 09/094,977, filed June 16, 1998, entitled “Method of Simultaneously Enhancing Analgesic Potency and Attenuating Dependence Liability Caused by Morphine and Other Biomodally-Acting Opioid Agonists” (continuation of No. 13 above) (ARE File No. 96700/542).

16. U.S. Patent Application No. 09/306,164, filed May 6, 1999, entitled “Method of Simultaneously Enhancing Analgesic Potency and Attenuating Adverse Side Effects Caused by Tramadol and Other Biomodally-Acting Opioid Agonists” (continuation-in-part of No. 14 above) (ARE File No. 96700/561).

17. U.S. Patent Application No. 09/261,361, filed March 3, 1999, entitled “Method and Composition for Treating Irritable Bowel Syndrome Using Low Doses of Opioid Receptor Antagonists” (ARE File No. 96700/453).

18. PCT Patent Application No. PCT/US00/05473, filed March 2, 2000, entitled “Method and Composition for Treating Irritable Bowel Syndrome Using Low Doses of Opioid Receptor Antagonists” (based on No. 17 above) (ARE File No. 96700/617).

19. U.S. Patent No. 5,585,348, issued December 17, 1996, entitled “Use Of Excitatory Opioid Receptor Antagonists To Prevent Growth Factor-Induced Hyperalgesia” (AR&E File No. 96700/241).

Exhibit 23.2

CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the references to our firm under the captions “Summary Financial Data”, “Selected Financial Data” and “Experts” in Amendment No. 1 to the Registration Statement (Form S-3 No. 333-108145) and related Prospectus of Pain Therapeutics, Inc. for the registration of 8,797,500 shares of its common stock and to the incorporation by reference therein of our report dated February 18, 2003, with respect to the 2002 financial statements of Pain Therapeutics, Inc. included in its Annual Report (Form 10-K) for the year ended December 31, 2002, filed with the Securities and Exchange Commission.

/s/ ERNST & YOUNG LLP

Palo Alto, California
September 2, 2003

EXHIBIT 23.3

Consent of KPMG LLP, Independent Auditors

The Board of Directors
Pain Therapeutics, Inc.:

We consent to the use of our report dated March 1, 2002, with respect to the balance sheet of Pain Therapeutics, Inc. as of December 31, 2001, and the related statements of operations, stockholders' equity (deficit), and cash flows, for each of the years in the two-year period ended December 31, 2001, incorporated herein by reference and to the references to our firm under the headings "Summary Financial Data", "Selected Financial Data" and "Experts" in the prospectus.

/s/ KPMG LLP

KPMG LLP

San Francisco, California
September 3, 2003