

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM S-1
REGISTRATION STATEMENT
UNDER
THE SECURITIES ACT OF 1933

PAIN THERAPEUTICS, INC.
(EXACT NAME OF REGISTRANT AS SPECIFIED IN ITS CHARTER)

DELAWARE
(STATE OR OTHER JURISDICTION OF
INCORPORATION OR ORGANIZATION)

7841
(PRIMARY STANDARD INDUSTRIAL
CLASSIFICATION CODE NUMBER)

91-1911336
(I.R.S. EMPLOYER
IDENTIFICATION NUMBER)

250 EAST GRAND AVENUE, SUITE 70
SOUTH SAN FRANCISCO, CALIFORNIA 94080
(650) 624-8200
(ADDRESS, INCLUDING ZIP CODE, AND TELEPHONE NUMBER, INCLUDING AREA CODE, OF
REGISTRANT'S PRINCIPAL EXECUTIVE OFFICES)

REMI BARBIER
PRESIDENT AND CHIEF EXECUTIVE OFFICER
250 EAST GRAND AVENUE, SUITE 70
SOUTH SAN FRANCISCO, CALIFORNIA 94080
(650) 624-8200
(NAME, ADDRESS, INCLUDING ZIP CODE, AND TELEPHONE NUMBER, INCLUDING AREA CODE,
OF AGENT FOR SERVICE)

COPIES TO:

MICHAEL J. O'DONNELL, ESQ.
MARTIN J. WATERS III, ESQ.
WILSON SONSINI GOODRICH & ROSATI
PROFESSIONAL CORPORATION
650 PAGE MILL ROAD
PALO ALTO, CA 94304-1050
(650) 493-9300

PETER T. HEALY, ESQ.
O'MELVENY & MYERS LLP
EMBARCADERO CENTER WEST
275 BATTERY STREET, SUITE 2600
SAN FRANCISCO, CA 94111-3305
(415) 984-8833

APPROXIMATE DATE OF COMMENCEMENT OF PROPOSED SALE TO THE PUBLIC:
As soon as practicable after the effective date of this Registration Statement.

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, 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, 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 this Form is a post-effective amendment filed pursuant to Rule 462(d)
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,
check the following box. []

CALCULATION OF REGISTRATION FEE

TITLE OF EACH CLASS OF SECURITIES TO BE REGISTERED	PROPOSED MAXIMUM AGGREGATE OFFERING PRICE (1)	AMOUNT OF REGISTRATION FEE
---	---	-------------------------------

Common Stock, \$0.001 par value..... \$75,000,000 \$19,800

(1) Estimated pursuant to Rule 457(o) of the Securities Act of 1933 solely for the purpose of computing the amount of the registration fee.

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 HEREAFTER 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 SUCH SECTION 8(A), MAY DETERMINE.

EXPLANATORY NOTE

This registration statement contains two forms of prospectus front cover pages: (a) one to be used in connection with an offering in the United States and Canada and (b) one to be used in connection with a concurrent offering outside of the United States and Canada. The U.S. prospectus and the international prospectus are otherwise identical in all respects. The international version of the front cover is included immediately before Part II of this registration statement.

THE INFORMATION IN THIS PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. WE MAY NOT SELL THESE SECURITIES UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THIS PROSPECTUS IS NOT AN OFFER TO SELL THESE SECURITIES AND IT IS NOT SOLICITING AN OFFER TO BUY THESE SECURITIES IN ANY STATE WHERE THE OFFER OR SALE IS NOT PERMITTED.

SUBJECT TO COMPLETION, DATED MARCH 13, 2000

LOGO

SHARES

COMMON STOCK

Pain Therapeutics, Inc. is offering _____ shares of its common stock. This is our initial public offering, and no public market currently exists for our shares. We have applied to have our common stock approved for quotation on the Nasdaq Stock Market's National Market under the symbol "PTIE." We anticipate that the initial public offering price will be between \$ _____ and \$ _____ per share.

 INVESTING IN OUR COMMON STOCK INVOLVES RISKS.
 SEE "RISK FACTORS" BEGINNING ON PAGE 6.

	PER SHARE	TOTAL
	-----	-----
Public Offering Price.....	\$	\$
Underwriting Discounts and Commissions.....	\$	\$
Proceeds to Pain Therapeutics, Inc.....	\$	\$

THE SECURITIES AND EXCHANGE COMMISSION AND STATE SECURITIES REGULATORS HAVE NOT APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

Pain Therapeutics, Inc. has granted the underwriters a 30-day option to purchase up to an additional _____ shares of common stock to cover over-allotments.

ROBERTSON STEPHENS

CIBC WORLD MARKETS

LAZARD FRERES & CO. LLC

THE DATE OF THIS PROSPECTUS IS _____, 2000.

YOU SHOULD RELY ONLY ON THE INFORMATION CONTAINED IN THIS PROSPECTUS. YOU SHOULD NOT RELY ON PRESS RELEASES, NEWS ARTICLES OR OTHER INFORMATION NOT CONTAINED IN THIS PROSPECTUS. WE HAVE NOT AUTHORIZED ANYONE TO PROVIDE YOU WITH INFORMATION DIFFERENT FROM THAT CONTAINED IN THIS PROSPECTUS. WE ARE OFFERING TO SELL AND SEEKING OFFERS TO BUY SHARES OF COMMON STOCK ONLY IN JURISDICTIONS WHERE OFFERS AND SALES ARE PERMITTED. THE INFORMATION CONTAINED IN THIS PROSPECTUS IS ACCURATE ONLY AS OF THE DATE OF THIS PROSPECTUS, REGARDLESS OF THE TIME OF DELIVERY OF THIS PROSPECTUS OR OF ANY SALE OF THE COMMON STOCK.

 TABLE OF CONTENTS

	PAGE

Summary.....	1
Risk Factors.....	6
Forward-Looking Statements.....	18
Use of Proceeds.....	19
Dividend Policy.....	19
Capitalization.....	20
Dilution.....	22
Selected Financial Data.....	23
Management's Discussion and Analysis of Financial Condition and Results of Operations.....	24
Business.....	29
Management.....	42
Certain Relationships and Related Transactions.....	50
Principal Stockholders.....	51
Description of Capital Stock.....	54
Shares Eligible for Future Sale.....	57
Underwriting.....	60
Legal Matters.....	63
Experts.....	63
Where You Can Find More Information.....	63
Index to Financial Statements.....	F-1

 Pain Therapeutics and our logo are trademarks of Pain Therapeutics, Inc. This prospectus also contains trademarks and tradenames of other parties.

In this prospectus, "Pain Therapeutics," the "Company," "we," "us" and "our" refer to Pain Therapeutics, Inc., which is a Delaware corporation.

SUMMARY

Because this is only a summary, it does not contain all the information that may be important to you. You should read the following summary together with the more detailed information in this prospectus, including risk factors, before making a decision to invest in our company and the common stock being sold in this offering.

PAIN THERAPEUTICS, INC.

Pain Therapeutics is developing a new generation of opioid painkillers. Opioids are drugs derived from the poppy plant. We use our proprietary technology, to reformulate opioid drugs, such as morphine, into branded painkillers with improved clinical benefits. We currently have four opioid painkillers in Phase II clinical trials. We believe our drugs offer enhanced pain relief, fewer adverse side effects and attenuated tolerance and addiction compared to existing opioid painkillers. If approved by the Food and Drug Administration, or FDA, we believe our proprietary drugs could replace many commonly used opioid painkillers. Our product candidates consist of component drugs, which individually, are FDA approved. For this reason, we believe we will encounter fewer clinical and regulatory hurdles than if we were developing new chemical entities.

OPIOID PAINKILLERS

The clinical use of opioid painkillers is widely accepted throughout the world. Despite their widespread clinical use, opioid painkillers have significant adverse side effects including respiratory depression, nausea, vomiting, dizziness, sedation, mental clouding, constipation, urinary retention and severe itching. Chronic use leads to tolerance and, potentially, addiction. Adverse side effects limit the usefulness of opioid painkillers. In many cases, patients voluntarily take less than the prescribed dosage to avoid adverse side effects. Some patients even prefer to endure pain rather than to suffer from adverse side effects. As a result, many patients are seriously under-treated and may be suffering from pain unnecessarily.

To date, innovations in the field of opioid painkillers have largely focused on increasing the convenience of opioid drugs. In contrast, we are focusing on improving clinical benefits. Based on clinical and pre-clinical data, we believe our painkillers address the shortcomings of existing opioids.

OUR MARKET

Medical economists estimate the direct and indirect costs associated with pain to be \$100 billion annually in the United States. Drugs are the key element in the treatment of pain. In the United States and Western Europe, the market for pain drugs totaled nearly \$12 billion in 1997. This market has grown by approximately 15% annually over the past five years. In 1998, U.S. opioid painkiller sales exceeded \$1.7 billion.

OUR PRODUCTS

Each of our product candidates consists of two components: an opioid agonist, such as morphine, and an opioid antagonist, such as naltrexone or naloxone. An opioid agonist is a drug that blocks pain, and an opioid antagonist is a compound that inhibits pain relief. Normally, combining an antagonist with an agonist cancels out the effects of the agonist. Studies indicate, however, that with opioids, combining a low-dose antagonist with an agonist actually improves the performance of the agonist. By combining low-dose opioid antagonists,

such as naltrexone or naloxone, with opioid agonists such as morphine, we believe our drugs will:

- enhance pain relief;
- reduce adverse side effects; and
- attenuate tolerance and addiction.

Clinical results from four studies involving a total of over 750 patients support our technology. For example, we recently completed a 200 patient Phase II clinical trial of our oral morphine product candidate. Results of this trial indicate that an optimal dose of our painkiller provided patients with 50% more pain relief than morphine alone during the first four hours after administration. This result is statistically significant at the level of $p=0.058$, which means the likelihood that this result occurred by chance is less than 1 in 17.

We have worldwide exclusive rights to our technology. Our proprietary position is based on five issued U.S. patents, one U.S. Notice of Allowance, two pending U.S. patent applications and ten corresponding pending foreign patent applications or issued patents.

OUR STRATEGY

Our goal is to build a speciality pharmaceutical company in pain management. We plan to achieve this goal by:

- Developing products with reduced clinical and regulatory risks compared to the development of new chemical entities. We believe this approach will enable us to commercialize our drugs rapidly and cost effectively.
- Focusing on clinical development and late-stage products. We believe this focus will enable us to generate product revenues earlier than if we were discovering new chemical entities.
- Retaining significant rights. In general, we intend to independently develop our product 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 have if we had outlicensed our drugs earlier in the development process.
- Leveraging our technology across multiple products and multiple indications. We are initially focusing our efforts on developing four opioid painkillers. However, we believe our technology can be broadly applied to other indications.
- Outsourcing key functions. We intend to outsource preclinical studies, clinical trials, formulation and manufacturing. We believe outsourcing will produce significant time savings and allow for more efficient deployment of our resources.

OTHER INFORMATION

We incorporated in Delaware in May 1998. Our principal executive office is located at 250 East Grand Avenue, Suite 70, South San Francisco, California 94080. Our telephone number at this location is (650) 624-8200.

THE OFFERING

Common stock offered by Pain Therapeutics, Inc.	shares
Common stock to be outstanding after this offering.....	shares
Use of proceeds.....	Working capital and general corporate purposes, including the continued development of existing product candidates, clinical research and development, formulation and manufacturing and commercialization activities.
Proposed Nasdaq National Market symbol.....	PTIE

The number of shares to be outstanding after this offering is based on 20,798,912 shares outstanding as of March 1, 2000. This number excludes:

- 1,710,200 shares of common stock issuable upon exercise of options then outstanding, at a weighted average exercise price of \$0.4355 per share;
- 190,000 shares of common stock issuable upon exercise of warrants then outstanding at a weighted average exercise price of \$3.53 per share;
- 150,000 shares of series A convertible preferred stock issuable upon exercise of warrants then outstanding at an exercise price of \$1 per share;
- 299,800 shares of common stock then available for issuance, under our 1998 Stock Plan, as amended; and
- 500,000 additional shares of common stock which will be available for issuance under our 2000 Employee Stock Purchase Plan immediately following the offering.

Except as otherwise indicated, all information in this prospectus assumes:

- the automatic conversion of all shares of series A, B, and C preferred stock into an aggregate 11,108,912 shares of common stock upon completion of this offering; and
- no exercise of the underwriters' over-allotment option.

SUMMARY FINANCIAL DATA

The following table presents summary financial information for Pain Therapeutics, Inc. The pro forma balance sheet data gives effect to: (1) the conversion of all series A convertible preferred stock and series B redeemable convertible preferred stock outstanding as of December 31, 1999 into 8,064,894 shares of common stock upon completion of the offering, (2) the issuance of 3,044,018 shares of series C redeemable convertible preferred stock in February 2000 and the conversion of all outstanding shares of our preferred stock into an aggregate 11,108,912 shares of common stock upon completion of the offering, and (3) the sale of _____ shares of common stock in the offering at an assumed initial offering price of \$ _____ per share, after deducting estimated underwriting discounts, commissions and offering expenses. The summary financial data as of December 31, 1999, for the period from May 4, 1998 (inception) through December 31, 1998, the year ended December 31, 1999 and the period from May 4, 1998 (inception) through December 31, 1999 are derived from our audited financial statements. You should read this information together with the financial statements and related notes included in this prospectus.

	PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1998 -----	YEAR ENDED DECEMBER 31, 1999 -----	PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1999 -----
STATEMENT OF OPERATIONS DATA:			
Operating expenses			
Licensing fees.....	\$ 100,000	\$ --	\$ 100,000
Research and development.....	200,000	2,092,119	2,292,119
General and administrative.....	122,168	1,341,181	1,463,349
	-----	-----	-----
Total operating expenses.....	422,168	3,433,300	3,855,468
	-----	-----	-----
Operating loss.....	(422,168)	(3,433,300)	(3,855,468)
Interest income.....	33,961	160,689	194,650
Income tax expense.....	800	800	1,600
	-----	-----	-----
Net loss.....	\$(389,007)	\$(3,273,411)	\$(3,662,418)
	=====	=====	=====
Basic and diluted loss per share.....	\$ (0.06)	\$ (0.35)	
	=====	=====	
Weighted average shares used in computing basic and diluted loss per share.....	6,948,637	9,322,441	
	=====	=====	

DECEMBER 31, 1999

	ACTUAL	PRO FORMA CONVERSION OF SERIES A AND SERIES B PREFERRED STOCK (UNAUDITED)	PRO FORMA ISSUANCE AND CONVERSION OF SERIES C PREFERRED STOCK (UNAUDITED)	PRO FORMA AS ADJUSTED (UNAUDITED)
BALANCE SHEET DATA:				
Cash and cash equivalents.....	\$9,339,669	\$ 9,339,669	\$24,534,759	\$
Working capital.....	9,095,831	9,095,831	24,290,921	
Total assets.....	9,441,173	9,441,173	24,636,263	
Series C redeemable convertible preferred stock.....	--	--	--	
Series B redeemable convertible preferred stock.....	9,703,903	--	--	
Series A convertible preferred stock.....	2,660	--	--	
Common stock.....	9,445	17,510	20,554	
Additional paid-in capital.....	4,235,317	13,933,815	29,125,861	
Deferred compensation.....	(1,073,921)	(1,073,921)	(1,073,921)	
Deficit accumulated during the development stage.....	(3,662,418)	(3,662,418)	(3,662,418)	
Total stockholders' equity (deficit).....	(563,317)	9,140,586	24,335,676	

RISK FACTORS

An investment in our common stock is very risky. You should carefully consider the risks described below before making an investment decision. Our business, operating results or financial condition could be materially adversely affected by any of the following risks, as well as by risks that we are unaware of or that we currently believe are immaterial. The market price of our common stock could decline due to any of such risks, and you might lose all or part of your investment.

RISKS RELATED TO OUR BUSINESS

OUR OPERATING HISTORY PROVIDES YOU WITH A LIMITED BASIS ON WHICH TO MAKE AN INVESTMENT DECISION.

The successful commercialization of any of our product candidates will require us to perform a variety of functions, including undertaking clinical trials, participating in regulatory approval processes, formulating and manufacturing product and conducting sales and marketing activities. However, we are a development stage company and we have not demonstrated our ability to perform these functions. So far our operations have been limited to organizing and staffing our company, acquiring, developing and securing our proprietary technology and undertaking preclinical studies and clinical trials of our four leading product candidates. These operations provide limited information for you to use in assessing our ability to commercialize our product candidates and the advisability of investing in our common stock. Consequently, any predictions you make about our future revenues and expenses may not be as accurate as they would 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, AND WE MAY NOT ACHIEVE OR MAINTAIN PROFITABILITY.

Since our inception, we have incurred significant net losses, including net losses of \$389,000 in the period from May 4, 1998 (inception) through December 31, 1998 and \$3.3 million in the year ended December 31, 1999. As a result of ongoing operating losses, we had an accumulated deficit of \$3.7 million as of December 31, 1999. We are not currently profitable. Even if we succeed in developing and commercializing one or more of our drugs, we expect to incur substantial losses for the foreseeable future and may never become profitable. We also expect to continue to incur significant operating and capital expenditures and anticipate that our expenses will increase substantially in the foreseeable future as we:

- continue to undertake preclinical and clinical trials for our product candidates;
- seek regulatory approvals for our product candidates;
- develop, formulate, manufacture and commercialize our drugs;
- implement additional internal systems and infrastructure; and
- hire additional personnel.

We also expect to experience negative cash flow for the foreseeable future as we fund our operating losses and capital expenditures. As a result, we will need to generate significant revenues to achieve and maintain profitability. We cannot be certain that we will be able to generate such revenues or that we will ever achieve profitability in the

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

WE CURRENTLY HAVE NO PRODUCT REVENUES. IF WE CANNOT RAISE ADDITIONAL CAPITAL ON ACCEPTABLE TERMS, WE MAY BE UNABLE TO COMPLETE PLANNED CLINICAL TRIALS AND OBTAIN FDA APPROVAL OF ANY OF OUR PRODUCT CANDIDATES.

All of our product candidates are still in the development stage and, before we may legally sell them, we will need to obtain approvals from the FDA and any applicable foreign regulatory authorities. Until we receive such approvals, we cannot sell our drugs and will not have product revenues. Therefore, for the foreseeable future, we will have to fund all of our operations and capital expenditures from the net proceeds of this offering and cash on hand. We expect that the net proceeds from this offering and cash on hand will be sufficient to meet our working capital and capital expenditure needs for at least the next twelve months. However, if we experience unanticipated cash requirements, we may need to raise additional funds much sooner and additional financing may not be available on favorable terms, if at all. Even if we succeed in selling additional equity 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.

IF WE ARE UNABLE TO DESIGN, CONDUCT AND COMPLETE CLINICAL TRIALS SUCCESSFULLY, WE WILL NOT BE ALLOWED TO SELL ANY OF OUR DRUGS AND WE WILL NOT GENERATE ANY PRODUCT REVENUES.

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 for humans and effective for its intended use. This demonstration requires significant research and animal tests, which are referred to as pre-clinical studies, as well as human tests, which are referred to as clinical trials. Our four product candidates are still in the early stages of clinical trials and we will have to commit substantial time and additional resources to conducting further pre-clinical and clinical studies in several types of pain before we can submit NDAs with respect to any of these product candidates. Our first clinical trials for our PTI-555, PTI-501 and PTI-601 product candidates were completed only recently, in the past six months. We intend to continue to conduct Phase II trials for these and our PTI-701 product candidate. We will not be able to proceed to Phase III trials for any product candidate until we determine appropriate dosages and submit such data to the FDA. Our other product candidates are at a much earlier stage of development and will require extensive pre-clinical testing before we can make any decision to proceed to clinical trials. In addition, before we can commence human clinical trials of these product candidates, we may have to submit an Investigational New Drug, or IND, application to the FDA.

Human 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. We estimate that clinical trials of our four leading product candidates will take a minimum of three years to complete and may take longer. Furthermore, 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. The commencement and completion of clinical trials may be delayed by several factors, including:

- lack of effectiveness during clinical trials;
- unforeseen safety issues;
- uncertain dosing issues;
- slower than expected rates of patient recruitment;
- inability to monitor patients adequately during or after treatment; and
- inability or unwillingness of medical investigators to follow our clinical protocols.

Our clinical trials will be subject to strict oversight by institutional review boards and the FDA. For example, our clinical trials:

- must be conducted in conformance with the FDA's good clinical practice regulations;
- must meet requirements for informed consent;
- may require large numbers of test subjects; and
- may be suspended by us or the FDA at any time if it appears that we are exposing participants to unacceptable health risks or if the FDA finds deficiencies in our IND submissions or the conduct of these trials.

In order to satisfy such requirements, we plan to incur substantial expenses for, and devote significant time and resources to, clinical trials of our product candidates. Even if our clinical trials are completed as planned, we cannot be certain that their results will support our product claims. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and we cannot be sure that the results of later clinical trials will replicate the results of prior clinical trials and pre-clinical testing. The clinical trial process may fail to demonstrate that our product candidates are safe for humans and effective for indicated uses. Such failure would cause us to abandon a product candidate and may delay development of other product candidates. Any delay in, or termination of, our clinical trials will delay the filing of our NDAs to the FDA and, ultimately, our ability to commercialize our drugs and generate product revenues.

IF WE FAIL TO OBTAIN THE NECESSARY REGULATORY APPROVALS, WE WILL NOT BE ALLOWED TO COMMERCIALIZE OUR DRUGS AND WILL NOT GENERATE PRODUCT REVENUES.

Even if we believe our clinical trials are successful, the FDA may delay approval of our NDAs. The FDA has substantial discretion in the drug approval process. Satisfaction of its 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. We cannot predict whether our research and clinical approaches will lead to drugs that the FDA considers safe for humans and effective for indicated uses. The FDA may require us to conduct additional clinical testing or to commit to perform post-marketing studies, in which cases we would have to expend additional unanticipated 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. We cannot predict with any certainty if or when we might submit a completed NDA for regulatory

approval of any of our current four product candidates. Delays in obtaining regulatory approvals may:

- delay commercialization of, and product revenues from, our product candidates;
- impose costly procedures on us; and
- diminish any competitive advantages that we may otherwise enjoy.

Even if we comply with all FDA requests, the FDA may ultimately deny one or more of our NDAs. We cannot be sure that we will ever obtain regulatory clearance for any of our product candidates. Failure to obtain FDA approval of any of our leading product candidates will severely undermine our business plan by reducing our number of salable products and corresponding product revenues.

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 risks associated with the FDA approval procedures described above.

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 health care 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 four 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 OUTSIDE RESEARCHERS FAIL TO DEVOTE SUFFICIENT TIME AND RESOURCES TO OUR DRUG DEVELOPMENT PROGRAMS, OR IF THEIR PERFORMANCE IS SUBSTANDARD, THE APPROVAL OF OUR FDA APPLICATIONS 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. Such 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 FDA applications and our introductions of new drugs will be delayed. These collaborators may also have relationships with other commercial entities, some of whom may compete with us. If outside collaborators assist our competitors at our expense, our competitive position could be harmed.

IF EXISTING AND FUTURE THIRD-PARTY MANUFACTURERS 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 RISE.

We have no manufacturing facilities and no experience in drug formulation or manufacturing. We lack the resources and expertise to formulate or manufacture our own products. We currently rely on a single contract manufacturer to supply, store and distribute drug supplies for our clinical trials. In addition, if any of our product candidates receive FDA approval, we will rely on one or more third-party contractors to manufacture our drugs. These third-party manufacturers may be unable to formulate and manufacture our drugs in the volume required for successful commercialization. Our current reliance on a single third-party manufacturer, and our anticipated future reliance on a limited number of third-party manufacturers, exposes us to the following risks, any of which could delay our clinical trials, the approval of our product candidates by the FDA, or the commercialization of our product candidates, result in higher costs or deprive us of potential product revenues:

- Contract manufacturers often encounter difficulties in achieving volume production problems involving production yields, quality control and quality assurance, as well as shortages of qualified personnel. Accordingly, if the pace of our clinical trials increases significantly or if there is unanticipated market demand for our products, our manufacturer might not be able to meet our clinical and commercial needs.
- Switching manufacturers may be difficult because the number of potential manufacturers is limited and the FDA must approve any replacement contractor. Such approval would require new testing and compliance inspections. In addition, a new manufacturer would have to be educated in, or develop substantially equivalent processes for, production of our products after receipt of FDA approval. It may be difficult or impossible for us to find a replacement manufacturer on acceptable terms quickly, or at all.
- Our existing and future contract manufacturers 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.
- Drug manufacturers are subject to ongoing periodic unannounced inspection by the FDA, the U.S. Drug Enforcement Agency, or DEA, and corresponding state agencies to ensure strict compliance with good manufacturing practice and other government regulations and corresponding foreign standards. We do not have control over third-party manufacturers' compliance with these regulations and standards.
- If 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.

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. On the other hand, 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 the efforts of our collaborators 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 and smaller companies that are collaborating with larger pharmaceutical companies, academic institutions, government agencies and other public and private research organizations. Many of these competitors have opioid 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 and selling drugs.

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

Companies that currently sell both generic and proprietary opioid formulations include Roxane Laboratories, Purdue Pharma, Janssen Pharmaceutica, Knoll Laboratories, Abbott Laboratories, Anesta, Endo Pharmaceuticals, Elkins-Sinn, Watson Laboratories, Alza Pharmaceuticals, Ortho-McNeil Pharmaceutical, Forest Pharmaceuticals and Astra Pharmaceutical. Alternative technologies 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. Such alternatives include Elan's SNX-111, as well as combination products from Endo Pharmaceuticals. In addition, companies pursuing different but related fields 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, parties for acquisitions, joint ventures or other collaborations.

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 for the products 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, are challenging the prices charged for medical products and services. 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 any such products, market acceptance of any such products will be reduced.

WE RELY ON OUR INTELLECTUAL PROPERTY, AND ANY FAILURE BY US TO PROTECT OUR INTELLECTUAL PROPERTY COULD ENABLE OUR COMPETITORS TO MARKET PRODUCTS WITH SIMILAR FEATURES THAT MAY REDUCE DEMAND FOR OUR PRODUCTS.

Our products are based on five issued U.S. patents, one U.S. Notice of Allowance, two pending U.S. patent applications and ten corresponding foreign patent applications or issued patents, all of which are held by Albert Einstein College of Medicine. We have an exclusive worldwide license to this patent portfolio. Our success, competitive position and potential future revenues will depend in part on our ability to:

- maintain and prosecute existing patents and patent applications;
- protect trade secrets;
- operate without infringing upon the proprietary rights of others; and
- prevent others from infringing on our proprietary rights.

We cannot be sure that the patents issued or licensed to us will provide protection against competitive products or otherwise be commercially viable. If either we or Albert Einstein College of Medicine fails to file, prosecute or maintain any of the 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. We intend to file additional patent applications relating to our technology, products and processes. We may direct Albert Einstein College of Medicine 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 these or future patents. These patents may also fail to provide us with meaningful competitive advantages. We cannot be sure what degree of protection any patents will afford, whether patents will be issued or whether we will be able to avoid violating or infringing upon patents issued to others.

We expect that we will rely upon trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. We cannot be sure that others will not 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. Moreover, we cannot be sure that our technology does not infringe upon any valid 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. There can be no assurance that, in that case, we would 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 we cannot assure you that any such action would be resolved in our favor. If such a dispute were to be resolved against us, we may 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. Despite the use of confidentiality agreements, which may be of limited effectiveness, we may not be able to protect our trade secrets.

WE RELY ON THE SERVICES OF OUR CHIEF EXECUTIVE OFFICER AND OTHER EXECUTIVE OFFICERS, AS WELL AS OUR PRINCIPAL SCIENTIFIC, MEDICAL AND MANAGEMENT ADVISORS AND EMPLOYEES, AND THOSE PERSONS' KNOWLEDGE OF OUR BUSINESS AND TECHNICAL EXPERTISE WOULD BE DIFFICULT TO REPLACE.

We are highly dependent on our president, chief executive officer and chairman, Remi Barbier, as well as our other executive officers and our principal scientific and medical advisors and employees. We have entered into an employment agreement with Mr. Barbier and employment offer letters with each of our other executive officers. We have only obtained key man life insurance covering Mr. Barbier. The loss of the technical knowledge and management and industry expertise of any of our key personnel could result in delays in product development, loss of customers and sales and diversion of management resources, which could adversely affect our operating results.

COMPETITION FOR QUALIFIED PERSONNEL IN THE PHARMACEUTICAL INDUSTRY IS INTENSE, AND IF WE ARE NOT SUCCESSFUL IN ATTRACTING AND RETAINING QUALIFIED PERSONNEL, OUR ABILITY TO GROW OUR BUSINESS MAY BE HARMED.

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 we cannot be certain that our

search for such personnel will be successful. Attracting and retaining qualified personnel will be critical to our success.

OUR DRUGS CONTAIN CONTROLLED SUBSTANCES, THE SUPPLY OF WHICH MAY BE LIMITED BY U.S. GOVERNMENT POLICY AND THE INCLUSION OF WHICH IN OUR DRUGS MAY GENERATE PUBLIC CONTROVERSY.

The active ingredients in our current product candidates, including morphine, tramadol and hydrocodone, are listed by the DEA as Schedule II or III substances under the Controlled Substances Act of 1970. Consequently, their manufacture, shipment, storage, sale and use are subject to the highest degree of regulation and accountability. For example, all regular Schedule II drug prescriptions must be signed by a physician and may not be refilled. 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 our business plan.

Furthermore, products containing controlled substances may generate public controversy. Opponents of these products may seek restrictions on marketing and withdrawal of any regulatory approvals. In addition, these opponents may seek to generate negative publicity in an effort to persuade the medical community to reject these products. Political pressures and adverse publicity could lead to delays and increased expenses and limit or restrict the introduction and marketing of our leading product candidates.

WE MAY INCUR SUBSTANTIAL LIABILITIES AND MAY BE REQUIRED TO LIMIT COMMERCIALIZATION OF OUR PRODUCTS IN RESPONSE TO PRODUCT LIABILITY LAWSUITS.

The testing and marketing of medical products entail an inherent risk of product liability. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization 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 pharmaceutical products we develop, alone or with corporate collaborators. We currently carry clinical trial insurance but do not carry product liability insurance. We, or any corporate collaborators, may not be able to obtain insurance at a reasonable cost, if at all. Even if our agreements with any future corporate collaborators entitle us to indemnification against losses, such indemnification may not be available or adequate should any claim arise.

RISKS RELATED TO THE OFFERING

WE HAVE BROAD DISCRETION IN HOW WE USE THE NET PROCEEDS OF THIS OFFERING, AND WE MAY NOT USE SUCH PROCEEDS EFFECTIVELY.

We have not designated the amount of net proceeds we will use for any particular purpose. Accordingly, our management will have broad discretion as to the application of the net proceeds and could use them for purposes other than those contemplated at the time of this offering. Our stockholders may not approve of the manner in which our management chooses to allocate and spend the net proceeds. Moreover, our management may use the net proceeds for corporate purposes that may not increase our profitability or our market value. Our primary purpose in conducting this offering is to create a public market for our common stock. As of the date of this prospectus, we plan to use the net proceeds from this offering for working capital and general corporate purposes, including

the continued development of existing product candidates, clinical research and development, formulation and manufacturing and commercialization activities.

OUR STOCK PRICE COULD BE VOLATILE WHICH MAY LEAD TO LOSSES BY INVESTORS.

Before this offering, there was no public market for our common stock. An active public market for our common stock may not develop or be sustained after this offering. We will determine the initial public offering price of our common stock based on negotiations between the representatives of the underwriters and our management concerning the valuation of our common stock, and such price may not be indicative of future market prices. The public market may not agree with or accept this valuation. The factors to be considered in determining the initial public offering price of our common stock, in addition to prevailing market conditions, include:

- estimates of our business potential and earnings prospects;
- an assessment of our management; and
- the consideration of the above factors in relation to market valuations of companies in related businesses.

After this offering, you may not be able to resell your shares at or above the initial public offering price. The trading price of our common stock is likely to be volatile.

The stock market in general, and the market prices for securities of biotechnology companies in particular, has experienced extreme volatility and may continue to be highly volatile in the future. 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:

- publicity regarding actual or potential clinical results relating to products under development by our competitors or us;
- announcements of technological innovations or new commercial products by our competitors or us;
- developments concerning proprietary rights, including patents;
- developments concerning our collaborations;
- regulatory developments in the United States and foreign countries;
- litigation;
- economic or other crises and other external factors; or
- period to period fluctuations in our financial results.

WE ARE AT RISK OF SECURITIES CLASS ACTION LITIGATION DUE TO OUR EXPECTED STOCK PRICE VOLATILITY.

In the past, securities class action litigation has often been brought against companies following periods of volatility in the market price of their securities. Due to the expected volatility of our stock price, we may be the target of securities litigation in the future. Securities litigation could result in substantial costs and divert management's attention and resources from our business.

OUR OFFICERS, DIRECTORS AND PERSONS AFFILIATED WITH OUR DIRECTORS WILL RETAIN SIGNIFICANT CONTROL OVER US AFTER THIS OFFERING, WHICH MAY LEAD TO CONFLICTS WITH OTHER STOCKHOLDERS ON CORPORATE GOVERNANCE ISSUES.

We anticipate that our officers, directors and individuals or entities affiliated with our directors will beneficially own approximately % of our outstanding common stock as a group after this offering closes. Acting together, these stockholders would be able to exercise significant influence over all matters that our stockholders vote upon, including the election of directors and the approval of significant corporate transactions. This concentration of ownership may also delay, deter or prevent a change in our control and may make some transactions more difficult or impossible to complete without the support of the stockholders.

THE PROVISIONS OF OUR CHARTER DOCUMENTS MAY INHIBIT POTENTIAL ACQUISITION BIDS THAT A STOCKHOLDER MAY BELIEVE ARE DESIRABLE, AND THE MARKET PRICE OF OUR COMMON STOCK MAY BE LOWER AS A RESULT.

Upon completion of this offering, our board of directors will have the authority to issue up to 10,000,000 shares of preferred stock. The board of directors can fix the price, rights, preferences, privileges and restrictions of the preferred stock without any further vote or action by our stockholders. The issuance of shares of preferred stock may delay or prevent a change in control transaction. As a result, the market price of our common stock and the voting and other rights of our stockholders may be adversely affected. The issuance of preferred stock may result in the loss of voting control to other stockholders. We have no current plans to issue any shares of preferred stock.

In addition to the foregoing, our charter documents contain the following anti-takeover devices:

- only one of the three classes of directors is elected each year;
- the ability of our stockholders to remove directors without cause is limited;
- the right of stockholders to act by written consent has been eliminated;
- the right of stockholders to call a special meeting of stockholders has been eliminated; and
- a requirement of advance notice to nominate directors or submit proposals for consideration at stockholder meetings.

These provisions could discourage potential acquisition proposals and could delay or prevent a change in control transaction. They could also have the effect of discouraging others from making tender offers for our common stock. As a result, these provisions may prevent the market price of our common stock from increasing substantially in response to actual or rumored takeover attempts. These provisions may also prevent changes in our management.

DELAWARE LAW MAY INHIBIT POTENTIAL ACQUISITION BIDS; THIS MAY ADVERSELY AFFECT THE MARKET PRICE OF OUR COMMON STOCK, DISCOURAGE MERGER OFFERS AND PREVENT CHANGES IN OUR MANAGEMENT.

Section 203 of the Delaware General Corporation Law may inhibit potential acquisition bids for our company. Upon completion of this offering, we will be subject to the anti-takeover provisions of the Delaware General Corporation Law, which regulate corporate acquisitions. Delaware law will prevent us from engaging, under certain

FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements under the captions "Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations," "Business," and elsewhere. These forward-looking statements include statements about the following:

- anticipated operating losses and capital expenditures;
- our clinical development efforts;
- the timing of regulatory processes for our product candidates; and
- our intention to rely on third parties for key functions.

When used in this prospectus, the words "believe," "anticipate," "estimate," "expect," "seek," "intend," "may," "will," "plan" and similar expressions are generally intended to identify "forward-looking statements." The matters discussed in our forward-looking statements are subject to known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements, or industry results, to be materially different from the results, performance or achievements expressed or implied by our forward-looking statements. These factors are discussed in more detail elsewhere in this prospectus, including under the captions "Summary," "Risk Factors," "Management's Discussion and Analysis of Financial Condition and Results of Operations," and "Business." Because of these uncertainties, you should not place undue reliance on our forward-looking statements. The safe harbor for forward-looking statements contained in the Securities Litigation Reform Act of 1995 is not available for forward-looking statements contained in this prospectus. We do not intend to update any of these factors or to publicly announce the result of any revisions to any of our forward-looking statements contained herein, whether as a result of new information, future events or otherwise.

Market data and forecasts used in this prospectus, including, for example, estimates of the size and growth rates of the pain management market, have been obtained from independent industry sources. We have not independently verified the data obtained from these sources and we cannot assure you of the accuracy of completeness of the data. Forecasts and other forward-looking information obtained from these sources are subject to the same qualifications and the additional uncertainties accompanying any estimates of future market size.

USE OF PROCEEDS

Our net proceeds from the sale of the shares of common stock we are offering are estimated to be \$ million (\$ million if the underwriters exercise their over-allotment option in full) assuming a public offering price of \$ per share and after deducting the underwriting discounts and commissions and our estimated offering expenses.

We will retain broad discretion in the allocation of the net proceeds of this offering. We currently anticipate using the net proceeds from this offering for working capital and general corporate purposes, including the continued development of existing product candidates, clinical research and development, formulation and manufacturing and commercialization activities. We may also, as opportunities arise, use a portion of the net proceeds to acquire or invest in businesses, products or technologies that are complementary to our own. While we periodically engage in preliminary discussions with respect to acquisitions, we are not currently a party to any agreements or commitments, and we have no understandings with respect to any acquisitions.

The amounts and timing of our actual expenditures for each purpose may vary significantly depending upon numerous factors, including:

- the size, scope and progress of our product candidate development efforts;
- regulatory approvals;
- competition;
- market acceptance of any of our drugs;
- marketing and sales activities;
- future revenue growth, if any; and
- the amount of cash, if any, we generate from operations.

The precise uses to which we will apply the net proceeds of this offering will be selected by management, under the supervision of our board of directors, in light of future circumstances and our business prospects. As a result, we will retain broad discretion in the allocation of the net proceeds of this offering. Pending the use of the net proceeds, we intend to invest the net proceeds in short-term, investment grade, interest bearing instruments.

DIVIDEND POLICY

We have never declared or paid cash dividends on our capital stock. We expect to retain our future earnings, if any, for use in the operation and expansion of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future declaration and payment of dividends will be subject to the discretion of our board of directors, will be subject to applicable law and will depend on our results of operations, earnings, financial condition, contractual limitations, cash requirements, future prospects and other factors deemed relevant by our board of directors.

CAPITALIZATION

The following table sets forth our capitalization as of December 31, 1999:

- on an actual basis derived from our financial statements;
- on a pro forma basis to give effect to the conversion of all of our series A convertible preferred stock and series B redeemable convertible preferred stock outstanding as of December 31, 1999 into 8,064,894 shares of common stock upon completion of the offering;
- on a pro forma basis to give effect to our sale of 3,044,018 shares of series C redeemable convertible preferred stock in February 2000, and the conversion of all outstanding shares of our preferred stock into an aggregate 11,108,912 shares of common stock upon completion of the offering; and
- on a pro forma as adjusted basis to give effect to the sale of shares of common stock in the offering at an assumed initial offering price of \$ per share, after deducting estimated underwriting discounts, commissions and offering expenses, and our amended and restated certificate of incorporation to be filed upon closing of this offering.

	AS OF DECEMBER 31, 1999			
	ACTUAL	PRO FORMA CONVERSION OF SERIES A AND SERIES B PREFERRED STOCK	PRO FORMA ISSUANCE AND CONVERSION OF SERIES C PREFERRED STOCK	PRO FORMA AS ADJUSTED
Redeemable convertible preferred stock, \$0.001 par value:				
Series B, 5,405,405 shares authorized, issued and outstanding actual; none issued and outstanding pro forma and pro forma as adjusted.....	\$ 9,703,903	\$ --	\$ --	
Series C, 3,200,000 shares authorized, none issued and outstanding actual, pro forma and pro forma as adjusted.....	--			
Total redeemable convertible preferred stock.....	9,703,903	--	--	
Stockholders' equity (deficit):				
Convertible preferred stock: series A, \$0.001 par value; 3,500,000 shares authorized and 2,659,489 issued and outstanding actual; none issued and outstanding pro forma; 10,000,000 undesignated shares authorized, none issued and outstanding pro forma as adjusted.....	2,660	--	--	
Common stock, \$0.001 par value; 20,000,000 shares authorized, 9,445,000 shares issued and outstanding actual; 17,509,894 issued and outstanding pro forma after conversion of series A convertible preferred stock and series B redeemable convertible preferred stock; 22,000,000 shares authorized and 20,553,912 shares issued and outstanding pro forma after issuance and conversion of series C redeemable convertible preferred stock; 120,000,000 shares authorized, issued and outstanding pro forma as adjusted.....	9,445	17,510	20,554	
Additional paid-in-capital.....	4,235,317	13,933,815	29,125,861	
Deferred compensation.....	(1,073,921)	(1,073,921)	(1,073,921)	
Notes receivable.....	(74,400)	(74,400)	(74,400)	
Deficit accumulated during the development stage.....	(3,662,418)	(3,662,418)	(3,662,418)	
Total stockholders' equity (deficit).....	(563,317)	9,140,586	24,335,676	
Total capitalization.....	\$ 9,140,586	\$ 9,140,586	\$24,335,676	

The data in the table above excludes:

- 1,295,200 shares of common stock issuable upon exercise of options outstanding as of December 31, 1999, at a weighted average exercise price of \$0.1234 per share;
- 259,800 shares of common stock available for issuance at December 31, 1999, under our 1998 Stock Plan, as amended (including 245,000 stock purchase rights granted but not yet purchased); and
- 70,000 shares of common stock issuable upon exercise of warrants outstanding as of December 31, 1999 at an exercise price of \$1 per share.
- 150,000 shares of series A convertible preferred stock issuable upon exercise of warrants outstanding at December 31, 1999 at an exercise price of \$1 per share.
- 120,000 shares of common stock issuable upon exercise of warrants issued in conjunction with the February 2000 sale of series C redeemable convertible preferred stock at an exercise price of \$5 per share.

See Note 3 to the Financial Statements.

DILUTION

Our pro forma net tangible book value as of December 31, 1999 was approximately \$24,335,676, or \$1.18 per share of common stock. Pro forma net tangible book value per share represents the amount of our total tangible assets less total liabilities, divided by the pro forma number of shares of common stock outstanding at December 31, 1999 and assumes the issuance of shares of series C redeemable convertible preferred stock in February 2000 and the conversion of all outstanding shares of preferred stock into an aggregate 11,108,912 shares of common stock automatically upon completion of this offering.

Dilution in net tangible book value per share represents the difference between the amount per share paid by purchasers of shares of common stock in this offering and the net tangible book value per share of our common stock immediately after the completion of this offering. After giving effect to the sale of the shares of our common stock in this offering at an assumed public offering price of \$ per share, after deducting underwriting discounts and commissions and estimated offering expenses, our pro forma as adjusted net tangible book value as of , 2000 would have been \$, or \$ per share. This represents an immediate increase in pro forma net tangible book value of \$ per share to existing stockholders and an immediate dilution of \$ per share to new investors, or approximately % of the assumed offering price of \$ per share. The following table illustrates this per share dilution:

Assumed offering price per share.....	\$
Pro forma net tangible book value per share at December 31, 1999.....	\$ 1.18
Increase per share attributable to new investors.....	\$

Pro forma as adjusted net tangible book value per share after this offering.....	\$

Dilution per share to new investors.....	\$
	=====

If the underwriters exercise their over-allotment option in full, the pro forma and adjusted net tangible book value per share to existing stockholders will be \$ per share, the increase in the net tangible book value per share to existing stockholders will be \$ per share and the dilution in net tangible book value to new investors will be \$ per share.

The following table summarizes, on a pro forma basis as of December 31, 1999 and after giving effect to the issuance of series C redeemable convertible preferred stock in February 2000 and the automatic conversion of all outstanding shares of preferred stock into common stock upon the closing of this offering, the total number of shares of common stock purchased from us, the total consideration paid to us and the average price per share paid to us by existing stockholders and by new investors before deducting the underwriting discounts and commissions and estimated offering expenses, at an assumed initial public offering price of \$ per share:

	SHARES PURCHASED		TOTAL CONSIDERATION		AVERAGE PRICE PER SHARE
	NUMBER	PERCENT	AMOUNT	PERCENT	
	-----	-----	-----	-----	-----
Existing stockholders.....	20,553,912	%	\$29,146,415	%	\$ 1.42
New investors.....	-----	-----	-----	-----	-----
Total.....	=====	100.0%	\$	100.0%	\$
	=====	=====	=====	=====	=====

The foregoing discussion assumes no exercise of any stock options or warrants to purchase common stock outstanding as of December 31, 1999. As of December 31, 1999, there were options outstanding to purchase 1,295,200 shares of common stock at a weighted average exercise price of \$0.1234 per share. To the extent any of these options are exercised, there will be further dilution to investors. In addition, there were 259,800 shares available for issuance upon the exercise of options which may be granted under our 1998 stock plan, as amended after December 31, 1999 (including 245,000 stock purchase rights granted but not yet purchased).

SELECTED FINANCIAL DATA

You should read the following selected financial data in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" on page 24 and the financial statements and related notes beginning on page F-1. The selected financial data for the period from May 4, 1998 (inception) through December 31, 1998, for the year ended December 31, 1999 and the period from May 4, 1998 (inception) through December 31, 1999 and the consolidated balance sheet data as of December 31, 1998 and 1999 are derived from our audited financial statements and notes appearing elsewhere in this prospectus. Historical results are not necessarily indicative of results that may be expected for any future period.

	PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1998 -----	YEAR ENDED DECEMBER 31, 1999 -----	PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1999 -----
SELECTED STATEMENT OF OPERATIONS DATA:			
Operating expenses:			
Licensing fees.....	\$ 100,000	\$ --	\$ 100,000
Research and development.....	200,000	2,092,119	2,292,119
General and administrative.....	122,168	1,341,181	1,463,349
	-----	-----	-----
Total operating expenses.....	422,168	3,433,300	3,855,468
	-----	-----	-----
Operating loss.....	(422,168)	(3,433,300)	(3,855,468)
Interest income.....	33,961	160,689	194,650
Income tax expense.....	800	800	1,600
	-----	-----	-----
Net loss.....	\$ (389,007)	\$(3,273,411)	\$(3,662,418)
	=====	=====	=====
Basic and diluted loss per share....	\$ (0.06)	\$ (0.35)	
	=====	=====	
Weighted average shares used in computing basic and diluted loss per share.....	6,948,637	9,322,441	
	=====	=====	

See Note 1 of Notes to Financial Statements for an explanation of the determination of the weighted-average common shares used to compute basic and diluted loss per share.

	DECEMBER 31, -----	
	1998	1999
	-----	-----
SELECTED BALANCE SHEET DATA:		
Cash and cash equivalents.....	\$ 2,333,512	\$ 9,339,669
Working capital.....	2,264,038	9,095,831
Total assets.....	2,382,600	9,441,173
Series B redeemable convertible preferred stock....	--	9,703,903
Series A convertible preferred stock.....	2,660	2,660
Additional paid-in-capital.....	2,686,839	4,235,317
Deferred compensation.....	--	(1,073,921)
Deficit accumulated during the development stage....	(389,007)	(3,662,418)
Total stockholders' equity (deficit).....	2,274,492	(563,317)

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

The following discussion and analysis should be read in conjunction with "Selected Financial Data" and our financial statements and the related notes included elsewhere in this prospectus. This discussion contains forward-looking statements that involve risks and uncertainties. Our actual results could differ materially from those anticipated in the forward-looking statements as a result of certain factors including the risks discussed in "Risk Factors" and elsewhere in this prospectus.

OVERVIEW

Pain Therapeutics is a clinical stage specialty pharmaceutical company engaged in the development of a new generation of opioid painkillers. We use our proprietary technology, to reformulate opioid drugs, such as morphine, into new opioid painkillers with improved clinical benefits. We currently have four product candidates in Phase II clinical trials. We believe our drugs offer enhanced pain relief, fewer adverse side effects and attenuated tolerance and addiction compared to existing opioid painkillers. If approved by the FDA, we believe our proprietary drugs could replace many existing opioid painkillers commonly used to relieve moderate to severe pain. Because our product candidates consist of component drugs each of which is individually FDA approved, we expect to encounter fewer clinical and regulatory hurdles than if we were developing new chemical entities.

We have yet to generate any revenues from product sales. We have not been profitable and, since our inception, we have incurred a cumulative net loss of approximately \$3.7 million through December 31, 1999. These losses have resulted principally from costs incurred in connection with research and development activities, including costs of clinical trials associated with our four product candidates and general and administrative expenses.

Product revenue will depend on our ability to receive regulatory approvals for, and successfully market, our product candidates. In the event that 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.

Sources of revenue for the foreseeable future may also include payments from potential collaborative arrangements, including license fees, funded research payments and milestone payments and royalties based on revenues received from products commercialized under such arrangements.

We expect to incur additional operating losses for the next several years. We also expect to continue to incur significant operating and capital expenditures and anticipate that our expenses will increase substantially in the foreseeable future as we:

- continue to undertake preclinical and clinical trials for our product candidates;
- seek to obtain regulatory approvals for our product candidates;
- develop, manufacture and market our product candidates and products;
- implement additional internal systems and infrastructure; and
- hire additional personnel.

Non-Cash Compensation

During the year ended December 31, 1999 we granted stock options to employees and non-employee consultants for which we recorded deferred compensation of approximately \$1.5 million as a reduction of stockholders' equity. No options were granted in 1998.

For employees, deferred compensation represents the difference between the exercise price of the option and the deemed fair value of our common stock on the date of grant in accordance with Accounting Principles Board Opinion No. 25 and its related interpretations. For non-employees, deferred compensation is recorded at the fair value of the options granted in accordance with Statement of Financial Accounting Standards No. 123 and Emerging Issues Task Force No. 96-18.

Compensation expense is being recognized over the vesting period for employees and the service period for non-employees in accordance with Financial Accounting Standards Board Interpretation No. 28. For the year ended December 31, 1999, amounts amortized to the statement of operations as compensation expense for employees and non-employees was \$188,000 and \$196,000, respectively.

RESULTS OF OPERATIONS

YEAR ENDED DECEMBER 31, 1999 AND PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1998

Licensing Fees

In May 1998, we entered into an exclusive, worldwide license agreement with Albert Einstein College of Medicine for all patents and pending patent applications relating to low-dose opioid antagonist technology. Pursuant to the terms of the license, we paid Albert Einstein College of Medicine a one time licensing fee and are required to pay clinical milestone payments and royalties based on a percentage of net sales. If a product is combined with a drug or other substance for which we are paying an additional royalty, the royalty rate we pay to Albert Einstein College of Medicine is reduced by one-half of the amount of such additional royalty. The licensing fee and milestone payments made through December 31, 1999 have been charged to research and development expense in accordance with Statement of Financial Accounting Standards No. 2, Accounting for Research and Development Costs, as this technology has no alternative future use.

Research and Development

Research and development expense consists of drug development work associated with our current product candidates, including costs of clinical trials and clinical supplies, and research payments to Albert Einstein College of Medicine. Research and development expenses increased to \$2.1 million for the year ended December 31, 1999 from \$200,000 for the period ended December 31, 1998. This increase was attributable to the initiation of clinical trials during 1999.

General and Administrative

General and administrative expense consists primarily of salaries and related benefit costs, amortization of deferred compensation for options granted to employees and consultants, facilities expenses, professional services expenses, travel and other general corporate expenses. General and administrative expenses increased to \$1.3 million for the year ended December 31, 1999 from \$122,000 for the period ended December 31, 1998. This increase was primarily attributable to the hiring of additional personnel, the

amortization of deferred compensation, increased professional services expenses and the longer period over which general corporate expenses were incurred in 1999. There will be future non-cash charges for options granted to employees and consultants.

Interest Income

Interest income increased to approximately \$161,000 for the year ended December 31, 1999 from \$34,000 for the period ended December 31, 1998. This increase resulted from higher average balances of cash and cash equivalents following the sale of our series B redeemable convertible preferred stock.

Income Taxes

We have incurred net operating losses since inception and, consequently, have not recorded any federal or state income taxes other than the minimum California state franchise tax. Our deferred tax assets primarily consist of net operating loss carryforwards and research and development tax credits. We have recorded a valuation allowance for the full amount of our deferred tax asset as the future realization of the tax benefit is not assured.

As of December 31, 1999, we had net operating loss carryforwards of approximately \$3.2 million for federal and state income tax purposes. These federal and state tax loss carryforwards are available to reduce future taxable income. If not utilized, the net operating loss carryforwards expire at various dates through 2019 for federal purposes and 2006 for state purposes. Annual limitations may result in the expiration of net operating loss and credit carryforwards before they are used. Under the provisions of the Internal Revenue Code, substantial changes in our ownership may limit the amount of net operating loss carryforwards that could be utilized annually in the future to offset taxable income.

LIQUIDITY AND CAPITAL RESOURCES

We have financed our operations primarily from the net proceeds generated from sales of our preferred stock. Through the date of this filing we have received total net proceeds of approximately \$27.5 million from the sales of:

- an aggregate 2,659,489 shares of our series A convertible preferred stock in August and October 1998 raising total net proceeds of approximately \$2.6 million;
- an aggregate 5,405,405 shares of our series B redeemable convertible preferred stock in October and November 1999 raising total net proceeds of approximately \$9.7 million; and
- an aggregate 3,044,018 shares of our series C redeemable convertible preferred stock in February 2000 raising total net proceeds of approximately \$15.2 million.

All of these shares of preferred stock will convert 1-for-1 into common stock upon completion of this offering. As of the date of this offering, there are warrants outstanding to purchase a total of 190,000 shares of our common stock at a weighted average exercise price of \$3.53 per share and 150,000 shares of our series A convertible preferred stock at an exercise price of \$1.

As of December 31, 1999, cash and cash equivalents were \$9.3 million, up from \$2.3 million at the end of 1998.

In 1999 we used approximately \$2.7 million of cash for operations principally as a result of the net loss of \$3.3 million offset by non-cash compensation of approximately \$383,000 and the increase in accounts payable of \$162,000. We used approximately \$319,000 of cash for operations in the 1998 period.

Our investing activities used cash of approximately \$39,000 in 1999 compared to approximately \$11,000 in 1998 and consisted of purchases of property and equipment. We expect to continue to make investments in our infrastructure, including the purchase of property and equipment to support our operations.

Our financing activities in 1999 and 1998 generated approximately \$9.7 million and \$2.6 million, respectively, of cash primarily from the private sales of preferred stock. Additionally, in February 2000 we raised approximately \$15.2 million from the sale of shares of our series C redeemable convertible preferred stock. Our series B and C redeemable convertible preferred stock have redemption features that may require us to make cash payments in the absence of certain events at set future dates in amounts equal to their purchase price plus unpaid, declared dividends.

We currently occupy approximately 3,250 square feet of leased space, for which the operating lease expires in September 2000. We are searching for additional space to meet our requirements as we implement internal systems and infrastructure and hire additional personnel. The combination of our need for additional square footage and increased rents in the San Francisco Bay Area will likely result in a significantly higher occupancy expense going forward.

We expect our cash requirements to increase significantly in 2000, as we continue our research and development efforts, hire and expand our product development personnel, grow our administrative support activities and expand our leased facilities. Additionally, as our clinical development efforts grow we anticipate a significant cash requirement for working capital growth, capital expenditures and investment in infrastructure. The amount and timing of cash requirements will depend on regulatory and market acceptance of our products, if any, and the resources we devote to researching and developing, formulating, manufacturing, commercializing and supporting our products. We believe that the net proceeds from this offering together with our current cash and cash equivalents should be sufficient to fund our operations for at least the next 12 months. However, we may require additional financing within this timeframe and such additional funding, if needed, will may not be available on terms acceptable to us or at all. Further, any additional equity financing may be dilutive to current stockholders.

RECENT ACCOUNTING PRONOUNCEMENT

In June 1998 the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 133, "Accounting for Derivative Instruments and Hedging Activities" (SFAS No. 133). SFAS No. 133 establishes accounting and reporting standards requiring that every derivative instrument be recorded in the balance sheet as either an asset or liability measured at its fair value. SFAS No. 133, as recently amended by SFAS No. 137, is effective for fiscal years beginning after June 15, 2000. Management believes the adoption of SFAS No. 133 will not have a material effect on the Company's financial position or results of operations.

QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

The primary objective of our investment activities is to preserve principal while at the same time maximizing the income we receive from investments without significantly

increasing risk. Some of the securities that we may invest in may be subject to market risk. This means that a change in prevailing interest rates may cause the value of the investment to fluctuate. For example, if we purchase a security that was issued with a fixed interest rate and the prevailing interest rate later rises, the value 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, money market funds and government and non-government debt 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. As of December 31, 1999, we neither had any holdings of derivative financial or commodity instruments, nor any foreign currency denominated transactions, and all of our cash and cash equivalents were in money market and checking funds.

Our series B and C redeemable convertible preferred stock is carried at its redemption value which approximates fair value and it is not subject to interest rate risk.

BUSINESS

Pain Therapeutics, Inc. is developing a new generation of opioid painkillers with improved clinical benefits. We use our proprietary technology to reformulate existing opioid painkillers into new drugs, which we believe offer enhanced pain relief, fewer adverse side effects and attenuated tolerance and addiction compared to existing opioid painkillers. If approved by the FDA, we believe our proprietary drugs could replace many existing opioid painkillers commonly used to treat moderate to severe pain. We believe our products will encounter fewer clinical and regulatory hurdles than new chemical entities, because they consist of component drugs that, individually, are already FDA approved.

BACKGROUND

Clinical Pain

Clinical pain is any unpleasant sensation that occurs as a result of injury or disease. Pain can have a protective role by warning of imminent or actual tissue damage, which can help prevent additional injury. Pain can also trigger a biological response that helps to preserve or regenerate damaged tissue. In this respect, pain is usually a normal, predictable response to events such as surgery, trauma and illness.

Types of Pain and Pain Relief

Drugs are often used to reduce or eliminate pain, especially when the pain is severe. The type of drug used to relieve pain depends on both the severity and the duration of the pain. Pain can be classified into three categories of severity:

- Mild Pain. Almost everyone experiences mild pain, such as headaches or joint pain, at one time or another. People typically treat mild pain with over-the-counter drugs such as aspirin and acetaminophen.
- Moderate Pain. Pain resulting from minor surgery or arthritis are examples of moderate pain. Physicians typically prescribe opioid painkillers to treat moderate pain. Opioid painkillers come in three varieties: weak opioids, strong opioids and synthetic opioids. Weak opioids such as hydrocodone or codeine are generally used to treat patients with moderate pain.
- Severe Pain. Patients experiencing severe pain often suffer from a serious underlying illness, such as AIDS or cancer. Severe pain can also result from major surgery, nerve damage or undetermined causes. Patients experiencing severe pain often require a strong opioid, such as morphine or fentanyl, to achieve adequate pain relief.

Pain can also be classified in terms of its duration as either acute or chronic. Acute pain, such as pain resulting from surgery, is brief and rarely results in long-term consequences. Most acute pain subsides within hours, days or weeks. Chronic pain persists long after an injury has healed, and typically results from a chronic illness or appears spontaneously and persists for undefined reasons. Examples of chronic pain include chronic lower back pain, and pain resulting from bone cancer or advanced arthritis. The effect of chronic pain tends to be more pervasive than that of acute pain. Chronic pain often affects a patient's mood, personality and social relationships. As a result, a patient with chronic pain commonly suffers from both their state of physical pain as well as a general decline in their quality of life.

In general, the more severe or chronic the pain, the more likely it is that an opioid painkiller is the appropriate treatment. The following diagram illustrates the types of pain which physicians may treat with opioid painkillers:

[GRAPHIC]

Pain Management Market

Medical efforts to treat pain, known as pain management, address a large market. Clinical pain is a worldwide problem with serious health and economic consequences. For example, in the United States:

- medical economists estimate that the effects of pain result in approximately \$100 billion of costs annually, including costs associated with an estimated 515 million lost work days;
- according to the National Institutes of Health, approximately 40 million Americans are unable to find relief from their pain;
- more than 30 million Americans suffer chronic pain for which they visit a doctor;
- approximately one million cancer patients suffer from severe pain at any given time; and
- an estimated 10% of the more than 200,000 AIDS patients suffer severe pain.

Drugs are the key element in the treatment of pain. The worldwide market for pain drugs totaled over \$16 billion in 1997. In the United States and Western Europe the corresponding market for pain drugs totaled nearly \$12 billion. The pain management market has grown significantly in recent years and is expected to continue to grow significantly. The pain market has grown by approximately 15% per year during the past five years due to a number of factors, including:

- a rapidly aging population;
- patients' demand for effective pain relief;
- increasing recognition of the therapeutic and economic benefits of effective pain management by physicians and healthcare providers and payers; and

- longer survival times for patients with painful chronic conditions, such as cancer and AIDS.

This accelerating growth rate appears to be attributable in part to recent innovations in the treatment of mild pain. For example, in 1999, two large pharmaceutical companies launched non-opioid prescription pain relievers approved for the treatment of certain types of pain called COX-2 inhibitors. These drugs achieved first-year sales exceeding \$1.0 billion in the United States. COX-2 inhibitors have fewer side effects than aspirin, and sell for more than twenty times its cost. The success of COX-2 inhibitors demonstrates the potential for rapid market acceptance and premium pricing of pain products with reduced side effects.

There has been little innovation in the opioid painkiller market for treatment of moderate to severe pain. Sales of opioid painkillers in the United States are primarily of older off-patent pain drugs, such as morphine and oxycodone. Notwithstanding the lack of novel drugs, U.S. opioid painkiller sales exceeded \$1.7 billion in 1998.

Approximately 90% of U.S. patients who receive opioids are treated on an outpatient basis. A portion of these patients receive care at one of the 3,400 specialty pain programs. The relatively low number of pain treatment centers allows for focused distribution channels for pain management products. This market structure permits midsize pharmaceutical companies to market and sell pain products cost-effectively.

OPIOID DRUGS

The history of opium use dates back more than 3,000 years. Today, the use of opioid drugs to treat patients with moderate to severe pain is widely accepted throughout the world. Opioids are the drugs of preference for many caregivers because they have an extensive clinical history, are easy to use and are available in a variety of doses and formulations. In the United States, Europe and Japan, physicians use a variety of strong, weak and synthetic opioids to manage patients' pain.

OPIOID DRUG SEGMENTS

MARKET SEGMENT	TYPICAL USE	EXAMPLES	REPRESENTATIVE BRAND	1998 U.S. SALES
Strong Opioids	Cancer pain	Morphine	MS Contin and others	\$760 million
Weak Opioids	Outpatient surgery	Hydrocodone and codeine	Vicodin and others	\$600 million
Synthetic Opioids	Back pain	Tramadol	Ultram	\$360 million
			Total	\$1.7 billion

Patients experiencing acute pain require fast acting, short-lived opioids and rapid delivery. The most common acute use of opioids is post-surgical pain. Opioid drugs used to treat acute pain include intravenous morphine, hydrocodone and oral oxycodone, which provide rapid pain relief.

In contrast, patients experiencing chronic severe pain often require long-term, regular use of opioid drugs. Because rapid dose adjustments are not necessary, patients experiencing chronic pain typically use opioid drugs in sustained release formulations. Such formulations include fentanyl patches and sustained release morphine. Although curing chronic pain is

possible, it is infrequent. The aim of using opioid drugs for patients with chronic pain is to decrease pain and suffering while improving overall physical and mental functions.

SHORTCOMINGS OF CURRENT PAIN MANAGEMENT

Despite widespread clinical use of opioids, pain management remains less than optimal. At all doses, opioid painkillers have significant adverse side effects that limit their usefulness. Adverse side effects include: respiratory depression, nausea, vomiting, dizziness, sedation, mental clouding, constipation, urinary retention and severe itching. In addition, chronic use of opioid painkillers can lead to the need for increasing dosage, and potentially, addiction. Concerns about addiction often influence clinicians to prescribe less than adequate doses of opioids. Many patients dislike the adverse side effects of opioid treatment and voluntarily take less than the prescribed dosage. In all cases, however, patients and clinicians must reach an appropriate balance between pain relief and adverse side effects. In addition, patients often use a process of trial and error with different opioids to identify an opioid that yields the optimal balance between pain relief and adverse side effects. Some patients may even prefer to endure pain rather than to withstand the side effects of opioid therapy. As a result, many patients are seriously undertreated and may be suffering from pain unnecessarily. In particular, infants and children receive disproportionately fewer and lower doses of opioid painkillers than adults.

Historically, there has been little innovation in the opioid painkillers used to treat moderate to severe pain. To date, product innovations have focused on increasing convenience, rather than improving clinical benefits. For example, novel dosing or delivery systems make it more convenient for patients to use opioid drugs, but neither enhance pain relief or reduce adverse side effects.

OUR SOLUTION

We are developing a new generation of proprietary drugs that address the shortcomings of existing opioid painkillers. We believe our drugs will:

- enhance pain relief;
- reduce adverse side effects; and
- attenuate tolerance and addiction.

If approved by the FDA, we believe our proprietary drugs could replace many commonly used opioid painkillers. We also believe our drugs could be used in chronic pain cases where physicians have been reluctant to prescribe opioid painkillers due to concerns about adverse side effects or addiction.

We have clinical results from four completed Phase II trials involving 750 patients, including two company-sponsored trials and two independent clinical trials. We believe the results of these clinical trials demonstrate that our product candidates offer superior pain relief as compared to equivalent dose levels of an opioid painkiller alone.

Our product candidates use a novel technology developed at Albert Einstein College of Medicine. Our technology combines very low doses of opioid inhibitors with standard opioid painkillers. We believe that the addition of a low dose of an opioid antagonist to opioid painkillers has an unexpected and beneficial effect. We believe that this effect includes enhancing potency, minimizing adverse side effects and attenuating tolerance and addiction.

Our technology has the added advantage of combining components which the FDA has individually approved for human use. We believe that we will encounter fewer clinical and regulatory hurdles than if we were developing new chemical entities because the safety and therapeutic profiles of these components are well-established.

STRATEGY

Our goal is to build a leading specialty pharmaceutical company in pain management. We intend to achieve this goal by:

Developing Products with Reduced Clinical and Regulatory Hurdles. We intend to develop proprietary drugs that we believe have lower clinical and regulatory risks compared to the development of new chemical entities. Our technology combines separate drugs, each independently approved by the FDA, whose safety and pharmacology are well established. We believe this approach will enable us to commercialize our drugs rapidly and cost effectively.

Focusing on Clinical Development and Late Stage Products. We continue to focus on managing clinical trials. All four of our current product candidates are in Phase II clinical trials. The conduct of human trials is a complex, highly regulated and highly specialized effort. We believe that our clinical development focus will enable us to generate product revenues earlier than if we were discovering new chemical entities.

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

Leveraging Technology Across Multiple Products and Multiple Indications. We are initially focusing our efforts on developing four opioid painkillers. However, we believe our technology can be broadly applied to additional segments of the pain market, as well as non-pain indications.

Outsourcing Key Functions. We intend to continue to outsource preclinical studies, clinical trials, formulation and manufacturing. We believe outsourcing will produce significant time savings and allow for more efficient deployment of our resources.

PRODUCTS IN DEVELOPMENT

We have four painkillers in Phase II clinical trials. Each painkiller is a proprietary combination of opioids. The first component is an opioid agonist, such as morphine. The second component is an opioid antagonist, such as naltrexone or naloxone. Normally, adding an antagonist to an agonist blocks the action of the agonist. This effect is clinically useful, for example, to reverse heroin overdose. At a very low-dose, however, studies indicate that this effect is reversed: a very low-dose of an opioid antagonist can enhance pain relief, reduce adverse side-effects and attenuate the development of tolerance and addiction. Our technology takes advantage of this effect by combining opioid agonists with low doses of opioid antagonists. The two individual components of our combination drugs have the advantage of having been previously approved by the FDA for human use at high

dose. However, the use of both components in combination, or the use of low-dose opioid antagonist alone, has not been approved by the FDA.

Our trials are designed to produce clinical information about how our painkillers perform compared to placebo and existing opioid painkillers. We plan to test each of our painkillers in several clinical models of pain in order to support a broad approval by the FDA for use of the drug for the relief of moderate to severe acute and chronic pain. FDA guidelines recommend that we demonstrate efficacy of our new painkillers in more than one clinical model of pain, typically including dental pain. Other acceptable clinical models of pain include post-operative pain, cancer pain and various types of trauma and arthritis pain. Because clinical models differ in their sensitivity to detect pain, we expect to complete Phase II studies in multiple clinical models of pain. We have designed all of our clinical trials to date as randomized, double-blind, placebo-controlled, dose-ranging studies. A randomized study is one in which patients are randomly assigned to the various study arms. A double-blind study is one in which the patient, the physician and the company's monitor are unaware if the patient is receiving placebo or study drug in order to preserve the integrity of the trial. A placebo-controlled study is one in which a subset of patients is purposefully not given study drug. Our initial clinical goals are to obtain regulatory approval of the following four combination opioid painkillers:

PRODUCT	STAGE OF DEVELOPMENT	FORMULATION
PTI-555	Phase II	Oral morphine/low-dose naltrexone
PTI-501	Phase II	Injectable morphine/low-dose naloxone
PTI-601	Phase II	Tramadol/low-dose naltrexone
PTI-701	Phase II	Hydrocodone-acetaminophen/low-dose naltrexone

PTI-555: oral morphine

PTI-555 is our proprietary substitute for oral morphine. We are developing this combination drug to treat moderate to severe pain in an acute or chronic setting. PTI-555 is a combination of oral morphine and low-dose naltrexone. If the FDA approves PTI-555, we believe it could be an effective substitute for oral morphine. The principal use of oral morphine is the treatment of patients suffering from chronic moderate to severe pain, such as cancer pain.

Clinical Results

In August 1999, we initiated a 200 patient Phase II clinical trial of PTI-555. This trial compared three different doses of PTI-555 with placebo and with oral morphine. Each dose of PTI-555 consisted of a fixed dose of morphine with a different low dose of naltrexone. The trial enrolled patients experiencing moderate to severe pain following dental surgery, in which two or more teeth were extracted. We completed patient enrollment on schedule in November 1999.

In December 1999 we completed the analysis of this Phase II clinical study. In this trial we demonstrated the following results:

- PTI-555 is safe in humans;
- three different doses of PTI-555 clearly provide patients with three different levels of pain relief;

- an optimal dose of PTI-555 provides patients with meaningful pain relief compared to placebo; this result is statistically significant at the level of $p < 0.001$, which means the likelihood that this result could have occurred by chance is less than 1 in 1,000; and
- an optimal dose of PTI-555 provides patients with 50% more pain relief than morphine alone in the first four hours of the study period; this result is statistically significant at the level of $p = 0.058$, which means the likelihood that this result could have occurred by chance is less than 1 in 17.

Based on these encouraging results, in January 2000 we initiated a new Phase II clinical trial with PTI-555. This trial is designed to confirm the safety, the efficacy and the optimal dose of PTI-555 in 300 patients suffering from moderate to severe pain following dental surgery. We expect to complete patient enrollment for this Phase II clinical trial by the third quarter of 2000.

PTI-501: injectable morphine

PTI-501 is our proprietary substitute for injectable morphine. We are developing this combination drug to treat moderate to severe pain in an acute or chronic setting. PTI-501 consists of a pre-mixed combination of injectable morphine and low-dose naloxone. If the FDA approves PTI-501, we believe it could be an effective substitute for injectable morphine. The principal use of injectable morphine is the treatment of patients with acute severe pain, such as trauma pain.

Clinical Results

Our clinical data on PTI-501 includes a company-sponsored Phase II clinical trial, as well as an independent clinical trial. The company-sponsored Phase II clinical trial enrolled 120 patients suffering from moderate to severe post-surgical pain. We completed patient enrollment for this clinical trial in December 1999, and we expect to unblind the results by the third quarter of 2000.

In 1997, independent researchers at Duke University Medical Center conducted a physician-sponsored, randomized, double-blind, placebo-controlled, dose-ranging clinical trial of 60 patients suffering from post-surgical pain. Published results of this trial indicated an approximate 50% reduction in certain morphine-related adverse side effects in patients who received an optimal dose of study drug compared to patients who received morphine without low-dose naloxone. This result is statistically significant at the level of $p < 0.05$, which means the likelihood that this result could have occurred by chance is less than 1 in 20.

PTI-601: tramadol

PTI-601 is our proprietary substitute for tramadol. In 1998, U.S. sales of tramadol exceeded \$360 million. We are developing this combination drug to treat patients with moderate pain in an acute or chronic setting. PTI-601 is a combination of tramadol and low-dose naltrexone. If the FDA approves PTI-601, we believe it could be an effective substitute for tramadol. Tramadol is principally used to treat patients with acute or chronic moderate pain, such as arthritis pain. Ortho-McNeil Pharmaceutical currently markets proprietary tramadol hydrochloride tablets under the brand-name Ultram. The relevant patent for Ultram expires in 2001.

Clinical Results

In August 1999, we initiated a 250 patient Phase II trial of PTI-601. This trial compared three different doses of PTI-601 with placebo and with tramadol. Each dose of PTI-601 consisted of a fixed dose of tramadol combined with a different low dose of naltrexone. The trial enrolled patients suffering from moderate to severe pain following dental surgery, in which three or more teeth were extracted. We completed patient enrollment on schedule in December 1999.

In January 2000 we completed the analysis of this Phase II clinical study. In this trial we demonstrated the following results:

- PTI-601 is safe in humans;
- different doses of PTI-601 clearly provide patients with different levels of pain relief; and
- an optimal dose of PTI-601 provides patients with meaningful pain relief compared to placebo; this result is statistically significant at the level of $p < 0.008$, which means the likelihood that this result could have occurred by chance is less than 1 in 125. By contrast patients who received tramadol alone did not achieve statistically meaningful pain relief compared to placebo.

PTI-701: hydrocodone

PTI-701 is our proprietary substitute for hydrocodone and similar weak opioids. In 1998, U.S. sales of such drugs exceeded \$600 million. We are developing PTI-701 to treat moderate to severe pain in an acute or chronic setting. PTI-701 is a combination of hydrocodone, acetaminophen and low-dose naltrexone. If the FDA approves PTI-701, we believe it could be an effective substitute for hydrocodone/acetaminophen. In the United States, all hydrocodone is sold in combination with acetaminophen. The principal use of hydrocodone is the treatment of patients with chronic moderate to severe pain, such as cancer pain. Hydrocodone combination products are currently sold under various trade names, including Knoll Laboratories' Vicodin, Forest Pharmaceuticals' Lorcet and Watson Laboratories' Norco.

In January 2000, we initiated a Phase II clinical trial with PTI-701. This trial is designed to demonstrate the safety, the efficacy and the optimal dose of PTI-701 in 300 patients suffering from moderate to severe pain following dental surgery. We expect to complete patient enrollment for this trial by the third quarter of 2000.

Other Product Candidates

We believe the use of low-dose opioid antagonists, either alone or in combination with existing opioid drugs, may have commercial applications beyond our four current product candidates. We believe that our technology can be broadly applied to additional segments of the pain market, as well as non-pain indications. Examples include certain drugs used in anesthesiology and those used to treat opioid and alcohol addiction. Until we undertake preclinical studies and clinical trials, we cannot be certain that our technology will have such additional applications.

We anticipate initiating several Phase I/II pilot studies in an effort to assess the clinical utility of our proprietary low-dose antagonist technology outside the field of pain management. In particular, in 2000, we may explore the use of our technology in patients

undergoing methadone maintenance treatment and in patients suffering from irritable bowel syndrome.

MANUFACTURING

We have no manufacturing facilities. We have entered into an agreement with a qualified third party for the formulation and manufacture of our clinical supplies. These supplies and the manufacturing facilities must comply with DEA regulations and current good manufacturing practices, or GMPs, reviewed by the FDA. We plan to continue to outsource formulation and manufacturing.

TECHNOLOGY OVERVIEW

According to the current understanding of pain mediation, opioid painkillers produce their pain relieving effect by activating an inhibitory pathway in the nervous system. Inhibitory pathways inhibit the transmission of pain signals into the brain. Scientists at Albert Einstein College of Medicine have published results suggesting that opioids also stimulate an excitatory pathway in the nervous system. The excitatory pathway partially counteracts pain inhibition and is believed to be a major cause of adverse side effects associated with opioid use, including the development of tolerance and addiction. In vitro studies on isolated nerve cells have helped researchers detect and analyze the unique properties of the inhibitory and excitatory pathways. At the normal clinical doses, the activation of the excitatory pathway was previously undetected probably due to masking by the inhibitory pathway.

Published results suggest that the selective blockade of the excitatory pathway promotes the pain relieving potency of morphine in mice by blocking the excitatory pain-enhancing effect. In addition, preclinical studies have demonstrated that co-treatment with a very low dose of an opioid antagonist, such as naloxone or naltrexone, preferentially blocks the excitatory pathway over the inhibitory pathway, thereby enhancing morphine's ability to inhibit pain.

We believe that the excitatory pathway plays an important role in modulating the adverse side effects of opioid use. After repeated administration of morphine or other opioid painkillers, increasing doses of opioids are required in order to obtain the same level of pain relief, a process known as tolerance. If chronic opioid treatment is terminated abruptly, withdrawal symptoms rapidly appear. Continued administration of opioids prevents the appearance of withdrawal symptoms, at which point a patient is considered dependent, and, potentially addicted. Published results also show that tolerance and dependence in mice are due to sustained activation of the excitatory pathway, and that tolerance and dependence can be prevented by co-administration of low-dose naltrexone, a pure opioid antagonist. At very low concentrations, we believe such opioid antagonists preferentially block excitatory pathways. These results provided the rationale for our human clinical trials.

The low-dose effect is the most important component of our technology wherein a very low dose of an opioid antagonist is combined with an opioid painkiller. Optimal dose ratios of low-dose opioid antagonist to opioid painkiller depend on their specific pharmacology and the mode of administration. Published preclinical and clinical dose response studies provide guidance in formulating optimal ratios of low-dose opioid antagonist to opioid painkiller for clinical development.

PROPRIETARY POSITION

Upon our formation in May 1998, we licensed our technology from Albert Einstein College of Medicine. We have worldwide exclusive rights to the technology. Pursuant to the terms of the license, we paid Albert Einstein College of Medicine a one time licensing fee and are required to pay clinical milestone payments and royalties based on a percentage of net drug sales. If a product is combined with a drug or other substance for which we are paying an additional royalty, the royalty that we pay to Albert Einstein College of Medicine will be reduced by one-half of the amount of such additional royalty.

We seek to protect our proprietary position by, among other methods, filing and prosecuting U.S. and foreign patents and patent applications with respect to our technology and products and their uses. We plan to prosecute and defend our patent applications, issued patents and proprietary information. We have an exclusive, worldwide license for five issued U.S. patents, one U.S. Notice of Allowance and two pending U.S. patent applications relating to the low-dose opioid antagonist technology under our license agreement with Albert Einstein College of Medicine, and ten corresponding pending foreign patent applications or issued patents.

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

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

GOVERNMENT REGULATION

Our product candidates will be subject to rigorous FDA regulation. The process of completing clinical trials and obtaining FDA approvals for any of our product candidates is likely to take a number of years and require the expenditure of substantial resources. We cannot be certain that any of our product candidates will receive FDA approval on a timely basis, if at all.

Regulation of combination products

Applicable FDA regulations treat our combination of opioid painkillers, such as morphine, and low-dose opioid antagonists, such as naloxone, as new drugs and require the filing of a NDA and approval by the FDA prior to commercialization in the U.S. Our clinical trials seek to demonstrate that an opioid painkiller/low-dose opioid antagonist combination produces greater beneficial effects than either drug alone. Because each component drug has been separately approved for human use by the FDA, we believe that we will encounter fewer regulatory hurdles than if we were developing new chemical entities.

The drug approval process

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

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

Preclinical studies consist of conducting animal studies to assess the potential safety and efficacy of the product candidate. We must submit the results of the preclinical studies to the FDA as a part of an IND for review by the FDA prior to the commencement of human clinical trials. Unless the FDA objects to, or otherwise responds to, an IND, the IND becomes effective 30 days following its receipt by the FDA.

We will continue to conduct human clinical trials in several phases that may overlap:

- Phase I: We initially introduce the product candidate into healthy human subjects or patients and test for safety, dosage tolerance, absorption, metabolism, distribution and excretion. In addition, we may, to the extent feasible, assess analgesic efficacy in our Phase I trials.
- Phase II: Involves studies in a limited patient population to identify possible adverse effects and safety risks, to determine the efficacy of the product candidate and to determine optimal dosage.
- Phase III: Once Phase II evaluations demonstrate that a dosage range of the product candidate is effective and has an acceptable safety profile, we can undertake Phase III trials to evaluate dosage and clinical efficacy further, and to test for safety in an expanded patient population at geographically dispersed clinical study sites.

The FDA publishes industry guidelines specifically for the clinical evaluation of painkillers. We rely in part on these guidelines to design a clinical strategy for the approval of each of our product candidates. In particular, FDA guidelines recommend that we demonstrate efficacy of our new painkillers in more than one clinical model of pain, typically including dental pain. Other acceptable clinical models of pain include post-operative pain, cancer pain and various types of trauma and arthritis pain. Since models differ in their pain intensity and their sensitivity to detect pain, we expect to complete several Phase II studies in multiple clinical models of pain. Upon a clear demonstration of the safety and efficacy of painkillers in multiple clinical models of pain, the FDA has historically approved pain killers with broad indications. Such general purpose labeling often takes the form of "for the management of moderate to severe pain."

Phase II efficacy studies have sometimes served as pivotal studies for painkiller product candidates. Phase III studies for these products normally focus greater attention on safety in larger patient populations rather than on efficacy. We cannot be certain that we will successfully complete Phase I, Phase II or Phase III testing within any specified time period, or at all, with respect to any of our product candidates. Furthermore, the

FDA may suspend clinical trials at any time in response to concerns that we are exposing participants to an unacceptable health risk.

We must submit the results of pharmaceutical development, preclinical studies, and clinical trials to the FDA in the form of a NDA for approval of the marketing and commercial shipment of the subject drug. The FDA may require additional testing or information before approving the NDA. The FDA may deny a NDA approval if we fail to satisfy safety, efficacy, or other regulatory requirements. Even if the FDA approves the drug, it may require post-marketing testing and surveillance to monitor the safety of the drug or may impose limitations on the indicated uses for which we may market the drug. In addition, the FDA may withdraw its approval if we fail to maintain compliance with regulatory standards or if problems occur following our initial marketing of the drug.

Other regulatory requirements

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

Whether or not the FDA grants approval, we must obtain similar approvals by comparable governmental regulatory authorities in foreign countries prior to the commencement of clinical trials and subsequent sales and marketing efforts in those countries. The approval procedure varies in complexity from country to country, and the time required may be longer or shorter than that required for FDA approval.

The Controlled Substances Act imposes various registration, record-keeping and reporting requirements, procurement and manufacturing quotas, labeling and packaging requirements, security controls and a restriction on prescription refills on certain pharmaceutical products. A principal factor in determining the particular requirements, if any, applicable to a product is its actual or potential abuse profile. The DEA regulates chemical compounds as Schedule I, II, III, IV or V substances, with Schedule I substances considered to present the highest risk of substance abuse and Schedule V substances the lowest risk. Any of our product candidates that contains a scheduled substance will be subject to regulation as a drug of that class.

COMPETITION

Our success will depend, in part, upon our ability to achieve market share at the expense of existing and established and future products in the relevant target markets. Existing and future products, therapies, technological approaches or delivery systems will compete directly with our products. Competing products may provide greater therapeutic benefits for a specific indication, or may offer comparable performance at a lower cost. Companies that currently sell generic or proprietary opioid formulations include Roxane

Laboratories, Purdue Pharma, Janssen Pharmaceutica, Knoll Laboratories, Abbott Laboratories, Anesta, Endo Pharmaceuticals, Elkins-Sinn, Watson Laboratories, Alza Pharmaceuticals, Ortho-McNeil Pharmaceutical, Forest Pharmaceuticals and Astra Pharmaceutical. Alternative technologies are being developed to increase opioid potency, as well as alternatives to opioid therapy for pain management, several of which are in clinical trials or are awaiting approval from the FDA. Such alternatives include Elan's SNX-111 and Endo Pharmaceuticals' Morphidex.

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

- developing drugs;
- undertaking 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.

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

EMPLOYEES

As of March 1, 2000, we had approximately twelve employees and five executive consultants, including three M.D./Ph.D.s, one M.D./D.D.S. and one Ph.D. We engage additional consultants from time to time to perform services on a per diem or hourly basis.

FACILITIES

Our executive office is located at 250 East Grand Avenue, Suite 70, South San Francisco, California 94080. Our leased property consists of approximately 3,250 square feet of office space. We believe that our facilities are sufficient to meet anticipated staffing up to the expiration of our lease in September 2000. We are searching for additional space to meet our future requirements as we implement internal systems and infrastructure and hire additional personnel.

LEGAL PROCEEDINGS

We are not a party to any legal proceedings.

MANAGEMENT

EXECUTIVE OFFICERS AND DIRECTORS

The following table presents information about our executive officers, key employees and directors. Upon completion of this offering our board of directors will be divided into three classes serving staggered three-year terms.

NAME ----	AGE ---	POSITION -----
Remi Barbier.....	40	President, Chief Executive Officer and Chairman of the Board
Barry M. Sherman, M.D.	58	Executive Vice President and Chief Medical Officer
Edmon R. Jennings.....	52	Chief Commercialization Officer
David L. Johnson.....	46	Chief Financial Officer
Gert Caspritz, Ph.D.(1).....	50	Director
Nadav Friedmann, M.D., Ph.D.(2).....	57	Director
Wilfred R. Konneker, Ph.D.(1).....	78	Director
Michael J. O'Donnell.....	41	Director and Secretary
Sanford R. Robertson(1)(2).....	68	Director

(1) Member of Audit Committee.

(2) Member of Compensation Committee.

Remi Barbier, our founder, has served as our President, Chief Executive Officer and Chairman since our 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. Prior to that, he was Vice President of Corporate Development and Clinical Project Manager of Xoma Corporation, a biotechnology company, from October 1993 to December 1995. Mr. Barbier received his B.A. from Oberlin College and his M.B.A. from the University of Chicago. He is a Director of Mendel Biotechnology, Inc.

Barry M. Sherman, M.D. has served as our Executive Vice President and Chief Medical Officer since April 1999. Prior to that time, Dr. Sherman was President and Chief Executive Officer of Anergen Inc., an immunology biotechnology company. From 1985 until 1996, Dr. Sherman held various positions at Genentech Inc., a biotechnology company, most recently serving as Senior Vice President and Chief Medical Officer with responsibility for Genentech's overall clinical development activities. Since 1986, Dr. Sherman has also been a Clinical Professor of Internal Medicine at Stanford University. From 1971 to 1985, Dr. Sherman was a Professor of Internal Medicine and Director of the Clinical Research Center at the University of Iowa College of Medicine. Dr. Sherman received his M.D., with honors, from the University of Michigan.

Edmon R. Jennings joined Pain Therapeutics, Inc. in February 2000. Prior to that time, Mr. Jennings held senior management positions at Genentech, including Vice President of Corporate Development from December 1995 to January 2000, Vice President of Sales and Marketing from January 1994 to December 1995 and Vice President of Sales from December 1990 to December 1993. Prior to Genentech, Mr. Jennings held positions with Bristol-Myers Oncology and Bristol Laboratories, both of which were divisions of Bristol-Myers (now Bristol-Myers Squibb), a pharmaceutical company, for approximately twelve years. Mr. Jennings received his B.A. from the University of Michigan.

David L. Johnson, CPA joined Pain Therapeutics, Inc. in January 2000. Prior to that time, Mr. Johnson was acting Chief Financial Officer at Aradigm, a drug delivery technology company. From October 1997 to November 1998, Mr. Johnson held positions as Vice President of Finance and Administration of Elan Pharmaceuticals North America and Vice President of Finance and Chief Financial Officer of Athena Neurosciences, both of which were divisions of Elan Pharmaceuticals, a pharmaceutical company. From September 1996 to October 1997, Mr. Johnson was Director of Finance at Gilead Sciences, a biopharmaceutical company. From June 1993 to December 1994, Mr. Johnson was Director of Financial Planning and Operational Analysis at Chiron, a biotechnology company. Mr. Johnson is a former member of the audit staff of KPMG LLP, our auditors. Mr. Johnson received his B.S. in Accounting from Oklahoma State University.

Gert Caspritz, Ph.D. has served as a director since November 1999. Dr. Caspritz has been the Investment Manager of TVM-Techno Venture Management, an international venture capital firm based in Germany, since June 1999. Prior to joining TVM he was employed with Hoechst Marion Roussel, a pharmaceutical company for over 15 years, most recently as Vice President of New Technologies Licensing. During his tenure at Hoechst Marion Roussel he was a member of various strategy task forces, including the group that negotiated many of Hoechst Marion Roussel's biotechnology collaborations. Dr. Caspritz serves on the board of Coley Pharmaceutical Group, PhytoMedica and Epicept. Dr. Caspritz received his undergraduate degree and his Ph.D. in Biology from the University of Mainz, Germany.

Nadav Friedmann, M.D., Ph.D. has served as a director since September 1998. Dr. Friedman has been President and Chief Executive Officer of Daiichi Pharmaceutical Corporation, a pharmaceutical company, since 1997 and before that was a Consultant to the Board 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 & Johnson, a healthcare company, including Vice President and Head of Research of 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.

Wilfred Konneker, Ph.D. has served as a director since November 1999. Dr. Konneker is currently a private investor. Prior to that he served as a director of Mallinckrodt, Inc., a healthcare company, and as Vice President of its radio pharmaceuticals division from 1966 to 1973. Dr. Konneker founded Nuclear Consultants, Inc., the first supplier of radio-isotopes to the pharmaceutical industry, in 1950, and served as its President and Chief Executive Officer until its merger with Mallinckrodt, Inc. in 1966. Dr. Konneker sits on the Board of Trustees for Washington University and the Board of Directors for Ohio University Foundation, the St. Louis Symphony, the Opera Theatre of St. Louis and the Chautauqua Foundation. Dr. Konneker received his Ph.D. in Nuclear Physics from Washington University and an undergraduate degree from Ohio University.

Michael J. O'Donnell has served as a director since June 1998. Mr. O'Donnell is a member of the law firm of Wilson Sonsini Goodrich & Rosati, Professional Corporation, our corporate counsel. Mr. O'Donnell serves as corporate counsel to numerous public and private biopharmaceutical and life science 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 currently a general partner of Francisco Partners, a technology investment fund. Mr. Robertson is the founder and former chairman of Robertson, Stephens, Inc. Mr. Robertson is also the founder of Robertson, Colman, Siebel & Weisel, later renamed Montgomery Securities. He is also a former director of AIM Management Group Inc. (now AMVESCAP) and BankAmerica Corporation. Mr. Robertson received his B.B.A. and M.B.A. degrees with distinction from the University of Michigan. He is also a director of Big Vine.com, Inc.

BOARD OF DIRECTORS

Our board of directors currently consists of six members. Each director holds office until his or her term expires or until his or her successor is duly elected and qualified. Upon completion of this offering, our amended and restated certificate of incorporation and bylaws will provide for a classified board of directors. In accordance with the terms of our certificate, our board of directors will be divided into three classes whose terms will expire at different times. The three classes will be comprised of the following directors:

- Class I consists of directors O'Donnell and Konneker, who will serve until the annual meeting of stockholders to be held in 2001;
- Class II consists of directors Caspritz and Friedmann, who will serve until the annual meeting of stockholders to be held in 2002; and
- Class III consists of directors Barbier and Robertson, who will serve until the annual meeting of stockholders to be held in 2003.

At each annual meeting of stockholders beginning with the 2001 annual meeting, the successors to directors whose terms will then expire will be elected to serve from the time of election and qualification until the third annual meeting following election and until their successors have been duly elected and qualified. Any additional directorships resulting from an increase in the number of directors will be distributed among the three classes so that, as nearly as possible, each class will consist of an equal number of directors.

Committees

Our board of directors has an executive committee, an audit committee and a compensation committee. The executive committee consists of directors Remi Barbier, Sanford Robertson and Nadav Friedmann. The audit committee consists of directors Gert Caspritz, Wilfred Konneker and Sanford Robertson. The audit committee reviews our internal accounting procedures, consults with and reviews the services provided by our independent accountants and makes recommendations to the board of directors regarding the selection of independent accountants. The compensation committee consists of directors Sanford Robertson and Nadav Friedmann. The compensation committee reviews and recommends to the board of directors the salaries, incentive compensation and benefits of our executive officers and administers our stock plans and employee benefit plans.

Compensation Committee Interlocks and Insider Participation

Our board of directors established the compensation committee in September 1999. Prior to establishing the compensation committee, our board of directors as a whole performed the functions delegated to the compensation committee. No member of our compensation committee has served as a member of the board of directors or compensation committee of any entity that has one or more executive officers serving as a

member of our board of directors or compensation committee. Since the formation of the compensation committee, none of its members has been an officer or employee.

Director Compensation

In March 2000, our board of directors approved guidelines for the grant of stock options under our 1998 Stock Plan, as amended, to directors who are not our officers or employees. These guidelines provide that such directors will receive 20,000 shares vesting annually over four years which are to be granted on the date of each annual stockholder meeting following the closing of this offering at the fair market value of our common stock on the date of grant.

SCIENTIFIC AND MEDICAL ADVISORS

We have established a scientific and medical advisory board to provide specific expertise in areas of research and development relevant to our business. Our scientific and medical advisory board meets periodically with our scientific and development personnel and management to discuss current and long-term research and development activities and initiatives. Our scientific and medical advisory board is comprised of:

Leslie Z. Benet, Ph.D.	Professor of Biopharmaceutical Sciences, University of California, San Francisco
Stanley Crain, Ph.D.	Professor of Neurosciences, Emeritus, Albert Einstein College of Medicine
Nadav Friedmann, M.D., Ph.D.	President & Chief Executive Officer, Daiichi Pharmaceuticals Corp.
Scott R. Hamann, M.D., Ph.D.	Department of Anesthesiology, University of Kentucky College of Medicine
Don R. Mehlich, M.D., D.D.S.	Independent Consultant, Co-founder, Scirex Corporation
Fredrick L. Minn, M.D., Ph.D.	Independent Consultant, formerly at Johnson & Johnson/Ortho-McNeil Pharmaceutical
Robert B. Raffa, Ph.D.	Associate Professor of Pharmacology, Temple University
Patrick Scannon, M.D., Ph.D.	Chief Medical and Scientific Officer, Xoma Corporation
Ke-Fei Shen, M.D., Ph.D.	Principal Associate, Albert Einstein College of Medicine
Barry M. Sherman, M.D.	Executive Vice President & Chief Medical Officer, Pain Therapeutics, Inc.
Eric J. Simon, Ph.D.	Professor of Psychiatry and Pharmacology, New York University School of Medicine
Frank Porreca, Ph.D.	Professor of Pharmacology and Anesthesiology, University of Arizona College of Medicine

EXECUTIVE OFFICERS

Our executive officers are appointed by our board of directors and serve until their successors are elected or appointed.

Compensation

The following table sets forth all compensation accrued during the year ended December 31, 1999 to our President and Chief Executive Officer, and our only other executive officer who was employed during the period. In accordance with the rules of the SEC, the compensation described in this table does not include perquisites and other personal benefits received by the executive officers named in the table below which do not exceed the lesser of \$50,000 or 10% of the total salary and bonus reported for these officers.

SUMMARY COMPENSATION TABLE

NAME AND PRINCIPAL POSITIONS	ANNUAL COMPENSATION (\$)			LONG-TERM COMPENSATION SECURITIES UNDERLYING OPTIONS (#)	ALL OTHER COMPENSATION
	SALARY	BONUS	OTHER		
Remi Barbier, President..... Chief Executive Officer and Chairman	\$176,042	--	--	--	--
Barry M. Sherman, M.D. Executive Vice President and Chief Medical Officer	\$132,275	--	--	600,000	--

Option Grants in 1999

The following table sets forth information concerning grants of stock options to each of the executive officers named in the table above during 1999. All options granted to these executive officers in 1999 were granted under the 1998 Stock Plan, as amended. Except as otherwise noted, one forty-eighth of the shares subject to each option vests and becomes exercisable on the first month after the vesting commencement date, and an additional one-forty-eighth of the shares subject to each option vests each month thereafter. The percent of the total options set forth below is based on an aggregate of 965,000 options granted to employees during 1999. All options were granted at fair market value as determined by our Board of Directors on the date of grant.

Potential realizable value represents hypothetical gains that could be achieved for the options if exercised at the end of the option term assuming that the initial public offering price of our common stock appreciates at 5% and 10% over the option term. The assumed 5% and 10% rates of stock price appreciation are provided in accordance with rules of the Securities and Exchange Commission and do not represent our estimate or projection of our future common stock price.

NAME	INDIVIDUAL GRANTS				POTENTIAL REALIZABLE VALUE AT ASSUMED ANNUAL RATES OF STOCK APPRECIATION FOR OPTION TERM(\$)	
	NUMBER OF UNDERLYING OPTIONS GRANTED	PERCENT OF TOTAL OPTIONS GRANTED TO EMPLOYEES DURING PERIOD(%)	EXERCISE PRICE PER SHARE	EXPIRATION DATE	5%	10%
Remi Barbier.....	--	--	--	--	--	--
Barry M. Sherman, M.D.....	250,000	25.9%	\$0.10	5/7/09		
	250,000	25.9%	\$0.10	9/10/09		
	100,000	10.4%	\$0.20	12/10/09		

Aggregate Option Exercises in 1999 and Values at December 31, 1999

The following table sets forth information concerning exercisable and unexercisable stock options held by the executive officers named in the summary compensation table at December 31, 1999. The value of unexercised in-the-money options is based on an assumed initial offering price of \$ per share minus the actual exercise prices. All options were granted under our 1998 Stock Plan, as amended. Except as otherwise noted, these options vest over four years and otherwise generally conform to the terms of our 1998 Stock Plan, as amended.

NAME	SHARES ACQUIRED ON EXERCISE	VALUE REALIZED(\$)(1)	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS AT DECEMBER 31, 1999(#)		VALUE OF UNEXERCISED IN-THE-MONEY OPTIONS AT DECEMBER 31, 1999(\$)(2)	
			EXERCISABLE	UNEXERCISABLE	EXERCISABLE	UNEXERCISABLE
Remi Barbier.....	--	\$--	--	--	\$--	\$--
Barry M. Sherman, M.D.	--	--	52,083	547,917		

(1) Based upon the assumed initial public offering price of \$ per share less the exercise price per share.

(2) Value is determined by subtracting the exercise price of an option from an assumed \$ per share fair market value of our common stock.

EMPLOYMENT AGREEMENTS

In July 1998, we entered into an employment agreement with Mr. Barbier. Under the terms of the agreement as amended by our board, Mr. Barbier receives an annual salary of \$275,000, and is eligible to receive an annual bonus in an amount to be determined by the board of directors. The term of the agreement is three years, and it automatically renews for consecutive one-year terms unless we or Mr. Barbier terminate the agreement earlier on sixty days' notice. The agreement entitles Mr. Barbier to serve on the board of directors for as long as he is our President and Chief Executive Officer. Thereafter, he will remain a member of our board of directors only if we terminate his employment without cause. The agreement also provides that if we terminate Mr. Barbier without cause, we must pay him

his salary for twelve months following the date of his termination and relinquish our right to repurchase any of his shares of our common stock.

In March 1999, we executed an employment offer letter for Dr. Sherman. Under the terms of the offer as amended by our Board, Dr. Sherman receives an annual salary of \$250,000. The offer letter provides that Dr. Sherman's employment may be terminated at any time by either Dr. Sherman or us upon thirty days' notice.

LIMITATIONS ON DIRECTORS' AND OFFICERS' LIABILITY AND INDEMNIFICATION

Our amended and restated certificate of incorporation to be filed upon completion of this offering limits the liability of our directors to the maximum extent permitted by Delaware law. Delaware law provides that directors of a corporation will not be personally liable for monetary damages for breach of their fiduciary duties as directors, except liability associated with any of the following:

- any breach of their duty of loyalty to the corporation or its stockholders;
- acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law;
- unlawful payments of dividends or unlawful stock repurchases or redemption; or
- any transaction from which the director derived an improper personal benefit.

The limitation of our directors' liability does not apply to liabilities arising under the federal securities laws and does not affect the availability of equitable remedies such as injunctive relief or rescission.

Our amended and restated certificate of incorporation and bylaws also provide that we shall indemnify our directors and executive officers and may indemnify our other officers and employees and other agents to the fullest extent permitted by law. We believe that indemnification under our bylaws covers at least negligence and gross negligence on the part of indemnified parties. Our bylaws also permit us to secure insurance on behalf of any officer, director, employee or other agent for any liability arising out of his or her actions in such capacity, regardless of whether our bylaws would permit indemnification.

We have entered into indemnification agreements with each of our officers and directors containing provisions that require us to, among other things, indemnify such officers and directors against liabilities that may arise by reason of their status or service as directors or officers (other than liabilities arising from willful misconduct of a culpable nature), to advance their expenses incurred as a result of any proceeding against them as to which they could be indemnified, and to cover our directors and officers under any of our liability insurance policies applicable to our directors and officers. We believe that these provisions and agreements are necessary to attract and retain qualified persons as directors and executive officers.

STOCK PLANS

1998 Stock Plan

Our 1998 Stock Plan, as amended, was approved by our board of directors in September 1998, and subsequently amended in May and September 1999 and February 2000. As of March 1, 2000, we had reserved a total of 3,200,000 shares of our common stock for issuance under the 1998 Stock Plan of which 299,800 shares were available for issuance. The 1998 Stock Plan, as amended, provides for the granting to our employees of

incentive stock options within the meaning of Section 422 of the United States tax code, and for the granting to employees, including officers and directors, non-employee directors and consultants of non-statutory stock options and stock purchase rights. Unless terminated sooner, the 1998 Stock Plan, as amended, will terminate automatically in 2008.

Our 1998 Stock Plan, as amended, is administered by our board of directors. Our board of directors determine the terms of the options or stock purchase rights granted, including the exercise price, the number of shares subject to each option or stock purchase right, the vesting and the form of consideration payable upon such exercise. In addition, the board of directors has the authority to amend, suspend or terminate the 1998 Stock Plan, provided that no such action may affect any share of common stock previously issued and sold or any option previously granted and then outstanding under the 1998 Stock Plan. Our board of directors has the exclusive authority to interpret and apply the provisions of the 1998 Stock Plan, as amended.

Options and stock purchase rights granted under our 1998 Stock Plan, as amended, are not generally transferable by the optionee, and each option and stock purchase right is exercisable during the lifetime of the optionee only by the optionee. Options granted under the 1998 Stock Plan, as amended, must generally be exercised within three months of the end of the optionee's status as our employee or consultant, or within twelve months after his or her termination by death or disability, but in no event later than the expiration of the option's ten year term. In the case of stock purchase rights, unless the board of directors determines otherwise, the agreement evidencing the grant shall provide that we have a repurchase option exercisable upon the voluntary or involuntary termination of his or her employment for any reason (including death or disability). In this event, the purchase price per share will be equal to the original price and may be paid by cancellation of his or her outstanding indebtedness to us, if any. Our repurchase option shall lapse at a rate determined by the board of directors. The exercise price of any incentive stock options granted under the 1998 Stock Plan, as amended, and any non-statutory stock options intended to qualify as "performance-based compensation" within the meaning of Section 162(m) of the United States tax code, must be at least equal to the fair market value of our common stock on the date of grant. With respect to any participant who owns stock possessing more than 10% of the voting power of all classes of our outstanding capital stock, the exercise price of any incentive stock option granted must equal at least 110% of the fair market value on the grant date and the term of such incentive stock option must not exceed five years. The term of all other options granted under the 1998 Stock Plan, as amended, may not exceed ten years.

Our 1998 Stock Plan, as amended, provides that in the event of our merger with or into another corporation or a sale of substantially all of our assets, each option or right shall be assumed or an equivalent option or right substituted by the successor corporation. If the outstanding options or rights are not assumed or substituted, the option or stock purchase right will immediately fully vest and become exercisable.

2000 Employee Stock Purchase Plan

Our 2000 Employee Stock Purchase Plan was adopted by our board of directors in March 2000. A total of 500,000 shares of common stock have been reserved for issuance under our 2000 Employee Stock Purchase Plan, plus annual increases equal to the lesser of 250,000 shares, 1% of the outstanding shares on such date, or a lesser amount determined by our board of directors.

Our 2000 Employee Stock Purchase Plan, which is intended to qualify under Section 423 of the United States tax code, contains consecutive six month offering and purchase periods. The offering periods generally start on the first trading day on or after May 1 and November 1 of each year, except for the first such offering period which commences on the first trading day on or after the effective date of this offering and ends on the last trading day on or before November 30, 2000.

Employees are eligible to participate if they are customarily employed by us or any participating subsidiary for at least 20 hours per week and more than five months in any calendar year. However, any employee who immediately after grant owns stock possessing 5% or more of the total combined voting power or value of all classes of our capital stock, or whose rights to purchase stock under all of our employee stock purchase plans accrues at a rate which exceeds \$25,000 worth of stock for each calendar year may not be granted an option to purchase stock under this plan. The 2000 Employee Stock Purchase Plan permits participants to purchase common stock through payroll deductions of up to 10% of the participant's "compensation." Compensation is defined as the participant's base straight time gross earnings and commissions but is exclusive of payments for overtime, shift premium payments, incentive compensation, incentive payments, bonuses and other compensation. The maximum number of shares a participant may purchase during a single purchase period is 2,000 shares.

Amounts deducted and accumulated by the participant are used to purchase shares of common stock at the end of each purchase period. The price of stock purchased under the 2000 Employee Stock Purchase Plan is generally 85% of the lower of the fair market value of the common stock at the beginning of the offering period or at the end of the purchase period. Participants may end their participation at any time during an offering period, and they will be paid their payroll deductions to date. Participation ends automatically upon termination of employment with us.

Rights granted under the 2000 Employee Stock Purchase Plan are not transferable by a participant other than by will, the laws of descent and distribution, or as otherwise provided under the plan. The 2000 Employee Stock Purchase Plan provides that, in the event of our merger with or into another corporation or a sale of substantially all our assets, each outstanding option may be assumed or substituted for by the successor corporation. If the successor corporation refuses to assume or substitute for the outstanding options, the offering period then in progress will be shortened and a new exercise date will be set. The 2000 Employee Stock Purchase Plan will terminate automatically in 2010, unless terminated earlier. Our board of directors has the authority to amend or terminate the purchase plan, except that no such action may adversely affect any outstanding rights to purchase stock under the 2000 Employee Stock Purchase Plan. Our board of directors has the exclusive authority to interpret and apply the provisions of the 2000 Employee Stock Purchase Plan.

CERTAIN RELATIONSHIPS AND RELATED TRANSACTIONS

PREFERRED STOCK

In August and October 1998, we sold a total of 2,659,489 shares of our series A convertible preferred stock at a price of \$1.00 per share. In October and November 1999, we sold a total of 5,405,405 shares of our series B redeemable convertible preferred stock at a price of \$1.85 per share. In February 2000, we sold a total of 3,044,018 shares of our series C redeemable convertible preferred stock at a price of \$5.00 per share. The following

officers, directors and 5% stockholders purchased shares of our preferred stock in these financings:

PURCHASER -----	SERIES A -----	SERIES B -----	SERIES C -----
John Griffin and entities and persons affiliated with Blue Ridge Limited Partnership.....	1,000,000	270,270	440,000
Cascade Investment LLC.....	--	--	2,000,000
GMS Capital Partners, L.P.....	--	1,000,000	146,070
TVM-Techno Venture Management III GmbH.....	--	1,459,449	184,655
Nadav Friedmann, M.D., Ph.D.....	20,000	--	--
Sanford R. Robertson.....	200,000	--	--
Entities affiliated with Michael J. O'Donnell.....	--	12,838	1,876

INVESTOR RIGHTS AGREEMENT

We have entered into an agreement pursuant to which these and other preferred stockholders will have registration rights with respect to their shares of common stock following this offering. For a description of these registration rights, see "Description of Capital Stock." Concurrently with the completion of this offering, all shares of our outstanding preferred stock will be automatically converted into an equal number of shares of common stock.

INDEMNIFICATION

We have entered into indemnification agreements with each of our directors and executive officers. Such indemnification agreements require us to indemnify our directors and officers to the fullest extent permitted by Delaware law. See "Limitation on Directors' Liability and Indemnification."

SEVERANCE ARRANGEMENTS

We executed employment offer letters for Mr. Johnson and Mr. Jennings in November and December 1999, respectively. Pursuant to these offer letters, Mr. Johnson and Mr. Jennings receive annual base salaries of \$155,000 and \$195,000, respectively. In addition, Mr. Johnson was permitted to purchase 190,000 shares of our common stock at a per share exercise price of \$0.20 subject to our repurchase right, and Mr. Jennings received an option to purchase 225,000 shares of our common stock at a per share exercise price of \$1.00. We may terminate either officer's employment at any time and for any reason or no reason. However, if we terminate Mr. Johnson's employment without cause after November 23, 2000, or Mr. Jennings' employment without cause after December 3, 2000, we must pay severance equal to the officer's base salary until the sooner of the date that he secures new employment, or the date that is three months after the date of his termination. Neither officer will receive any severance if we terminate his employment within the first year, if he voluntarily terminates his employment any time, or if we terminate him for cause at any time.

PRINCIPAL STOCKHOLDERS

The following table sets forth information known to us with respect to the beneficial ownership of our common stock as of March 1, 2000 and as adjusted to reflect the sale of common stock offered hereby by the following:

- each stockholder known by us to own beneficially more than 5% of our common stock;

- each of our executive officers named in the compensation table above;
- each of our directors; and
- all directors and executive officers as a group.

As of March 1, 2000, there would have been 20,798,912 shares of our common stock outstanding, assuming that all outstanding preferred stock has been converted into common stock. Except as otherwise indicated, we believe that the beneficial owners of the common stock listed below, on the information furnished by such owners, have sole voting power and investment power with respect to such shares. Beneficial ownership is determined in accordance with the rules of the Securities and Exchange Commission. In computing the number of shares beneficially owned by a person and the percent ownership of that person, shares of common stock subject to options or warrants held by that person that are currently exercisable or that will become exercisable within 60 days after March 1, 2000 are deemed outstanding, while such shares are not deemed outstanding for purposes of computing percent ownership of any other person. Unless otherwise indicated in the footnotes below, the persons and entities named in the table have sole voting and investment power with respect to all shares beneficially owned, subject to community property laws where applicable. The address for those individuals for which an address is not otherwise indicated is 250 Grand Avenue, Suite 70, South San Francisco, California 94080.

NAME OR GROUP OF BENEFICIAL OWNERS -----	SHARES BENEFICIALLY OWNED PRIOR TO OFFERING(1) -----	PERCENT OF SHARES OUTSTANDING(2)	
		PRIOR TO OFFERING -----	AFTER OFFERING -----
Cascade Investment, LLC..... 2365 Carillon Point Kirkland, WA 98033	2,000,000	9.6%	
TVM-Techno Venture Management III GmbH..... 101 Arch Street, Suite 1950 Boston, MA 02110	1,644,104	7.9%	
John Griffin(3)..... Blue Ridge Limited Partnership 660 Madison Avenue New York, NY 10021	1,710,270	8.2%	
GMS Capital Partners, L.P. 405 Park Avenue, 16th Floor New York, NY 10022	1,146,070	5.5%	
Remi Barbier.....	8,180,000	39.3%	
Gert Caspritz, Ph.D.(4)..... 101 Arch Street, Suite 1950 Boston, MA 02110	1,644,104	7.9%	
Sanford R. Robertson(5)..... 555 California Street, Suite 3130 San Francisco, CA 94104	256,771	1.2%	
David L. Johnson(6).....	190,000	*	*
Barry M. Sherman, M.D.(7).....	102,083	*	*

NAME OR GROUP OF BENEFICIAL OWNERS	SHARES BENEFICIALLY OWNED PRIOR TO OFFERING(1)	PERCENT OF SHARES OUTSTANDING(2)	
		PRIOR TO OFFERING	AFTER OFFERING
Nadav Friedmann, M.D., Ph.D.(8)..... 144 Fisher Road Mahwah, NJ 07430	126,771	*	*
Michael J. O'Donnell(9)..... Wilson Sonsini Goodrich & Rosati 650 Page Mill Road Palo Alto, CA 94304-1050	65,235	*	*
Edmon R. Jennings(10).....	9,375	*	*
Wilfred R. Konneker, Ph.D..... Konneker Development Corporation 142 Enchanted Parkway, Suite 200 Manchester, MO 63021	--	--	--
All directors and executive officers as a group (9 persons)(11).....	10,574,339	50.5%	

* Represents beneficial ownership of less than one percent (1%) of the outstanding shares of the Company's Common Stock.

- (1) Beneficial ownership is determined with the rules of the Securities and Exchange Commission and generally includes voting or investment power with respect to securities. Shares of Common Stock subject to stock options and warrants currently exercisable or exercisable within 60 days are deemed to be outstanding for computing the percentage ownership of the person holding such options and the percentage ownership of any group of which the holder is a member, but are not deemed outstanding for computing the percentage of any other person. Except as indicated by footnote, and subject to community property laws where applicable, the persons named in the table have sole voting and investment power with respect to all shares of Common Stock shown beneficially owned by them.
- (2) Applicable percentage of ownership is based on 20,798,912 shares of Common Stock outstanding prior to this offering.
- (3) Includes 1,090,270 shares held by Blue Ridge Limited Partnership, 40,000 shares held by Blue Ridge Private Equity Fund, and 580,000 shares held by John Griffin. All of the shares held by Blue Ridge Limited Partnership and Blue Ridge Private Equity Fund are beneficially owned by John Griffin.
- (4) Includes 1,644,104 shares held by TVM-Techno Venture Management III GmbH. Dr. Caspritz, a Director of the Company, is the Investment Manager of TVM-Techno Venture Management. Dr. Caspritz disclaims beneficial ownership of the shares held by TVM-Techno Venture Management III GmbH, except to the extent of his partnership interest in such shares.
- (5) Includes 6,771 shares issuable pursuant to options exercisable within 60 days of March 1, 2000.
- (6) All of these shares are subject to our right of repurchase which lapses over time.
- (7) Includes 102,083 shares issuable pursuant to options exercisable within 60 days of March 1, 2000.
- (8) Includes 6,771 shares issuable pursuant to options exercisable within 60 days of March 1, 2000.

- (9) Includes 45,000 shares held by WS Investment Company 98B, 12,162 shares held by WS Investment Company 99B, 1,777 shares held by WS Investment Company 2000A, 5,775 shares held by Michael J. O'Donnell and 521 shares issuable to Mr. O'Donnell pursuant to options exercisable within 60 days of March 1, 2000. Mr. O'Donnell, a Director of the Company, is a General Partner of WS Investment Company. Mr. O'Donnell disclaims beneficial ownership of the shares held by WS Investment Company, except to the extent of his partnership interest in such shares. Mr. O'Donnell is also a partner in Wilson Sonsini Goodrich & Rosati, our corporate counsel.
- (10) Includes 9,375 shares issuable pursuant to options exercisable within 60 days of March 1, 2000.
- (11) Includes 125,521 shares issuable pursuant to options exercisable within 60 days of March 1, 2000.

DESCRIPTION OF CAPITAL STOCK

Upon the completion of this offering, we will be authorized to issue shares, \$0.001 par value per share, to be divided into two classes to be designated common stock and preferred stock. Of the shares authorized, 120,000,000 shares shall be designated as common stock and 10,000,000 shares shall be designated as preferred stock. The following description of our capital stock is only a summary. For a complete description of our capital stock, you should refer to our certificate of incorporation and bylaws as in effect upon the completion of this offering, which are included as exhibits to the registration statement of which this prospectus forms a part, and to the provisions of applicable Delaware law.

COMMON STOCK

As of March 1, 2000, assuming the conversion of all outstanding shares of preferred stock into common stock, there were 20,798,912 shares of common stock outstanding which were held by approximately 85 stockholders. There will be shares of common stock outstanding (assuming no exercise of the underwriters' over-allotment option and no exercise of outstanding options after March 1, 2000) after giving effect to the sale of our common stock in this offering. In addition to 1,710,200 shares issuable upon exercise of outstanding options, and 299,800 shares available for issuance under our 1998 Stock Plan, as amended there are an aggregate of 500,000 shares reserved for issuance under our 2000 Employee Stock Purchase Plan. See "Management -- Stock Plans" for a description of our stock plans.

The holders of our common stock are entitled to one vote per share held of record on all matters submitted to a vote of the stockholders. Our amended and restated certificate of incorporation to be filed concurrently with completion of this offering, does not provide for cumulative voting in the election of directors. Subject to preferences that may be applicable to any outstanding preferred stock, the holders of common stock are entitled to receive ratably such dividends, if any, as may be declared from time to time by our board of directors out of funds legally available for that purpose. In the event of our liquidation, dissolution or winding up, holders of our common stock are entitled to share ratably in all assets remaining after payment of liabilities, subject to prior distribution rights of preferred stock, if any, then outstanding. Holders of our common stock have no preemptive or other subscription or conversion rights. There are no redemption or sinking fund provisions

applicable to our common stock. All outstanding shares of common stock are fully paid and non-assessable, and the shares of common stock to be issued upon the completion of this offering will be fully paid and non-assessable.

PREFERRED STOCK

Upon the completion of this offering and filing of our amended and restated certificate of incorporation, we will not have any shares of preferred stock outstanding, however, our board of directors will be authorized, without action by the stockholders, to issue up to 10,000,000 shares of preferred stock in one or more series and to fix the rights, preferences, privileges and restrictions of each series. These rights, preferences and privileges may include dividend rights, conversion rights, voting rights, terms of redemption, liquidation preferences, sinking fund terms and the number of shares constituting any series or the designation of any series, all or any of which may be greater than the rights of the common stock.

The issuance of preferred stock could adversely affect the voting power of holders of common stock and the likelihood that the holders of common stock will receive dividend payments and payments upon liquidation. In addition, the issuance of preferred stock could have the effect of delaying or preventing a change in our control without further action by the stockholders. We have no present plans to issue any shares of preferred stock.

WARRANTS TO PURCHASE COMMON STOCK

As of March 1, 2000, we had the following warrants outstanding to purchase a total of 340,000 shares of our capital stock:

- 70,000 shares of our common stock at an exercise price of \$1.00 per share, terminating 2005;
- 120,000 shares of our common stock at an exercise price of \$5.00 per share terminating 2005; and
- 150,000 shares of our series A convertible preferred stock which are convertible into 150,000 shares of our common stock at an exercise price of \$1.00 per share, terminating June 5, 2010.

REGISTRATION RIGHTS

Pursuant to a registration rights agreement we entered into with holders of 11,108,912 shares of our common stock (assuming conversion of all outstanding shares of preferred stock), the holders of these shares are entitled to certain registration rights regarding these shares. The registration rights provide that if we propose to register any securities under the Securities Act, either for our own account or for the account of other security holders exercising registration rights, they are entitled to notice of the registration and are entitled to include shares of their common stock in the registration. This right is subject to conditions and limitations, including the right of the underwriters in an offering to limit the number of shares included in the registration. The holders of these shares may also require us to file up to two registration statements under the Securities Act at our expense with respect to their shares of common stock. We are required to use our best efforts to effect this registration, subject to conditions and limitations. Furthermore, the holders of these shares may require us to file additional registration statements on Form S-3, subject to conditions and limitations. These rights terminate on the earlier of five years after the effective date of this offering, the date on which all securities subject to registration rights

have been sold, or when a holder is able to sell all its shares pursuant to Rule 144 under the Securities Act in any 90-day period.

DELAWARE ANTI-TAKEOVER LAW AND CERTAIN CHARTER AND BYLAW PROVISIONS

Certain provisions of Delaware law and our certificate of incorporation and bylaws could make the following transactions more difficult:

- the acquisition of us by means of a tender offer;
- the acquisition of us by proxy contest or other means; and
- the removal of our incumbent officers and directors.

These provisions, summarized below, are expected to discourage certain types of coercive takeover practices and inadequate takeover bids and to encourage persons seeking to acquire control of us to first negotiate with us. We believe that the benefits of increased protection of our potential ability to negotiate with the proponent of an unfriendly or unsolicited proposal to acquire or restructure our company outweighs the disadvantages of discouraging such proposals because, among other things, negotiation of such proposals could result in an improvement of their terms. The amendment of any of the following provisions would require approval by holders of at least 66 2/3% of our outstanding common stock.

Election and Removal of Directors. Effective with the first annual meeting of stockholders following completion of this offering, our amended and restated bylaws provide for the division of our board of directors into three classes, as nearly equal in number as possible, with the directors in each class serving for a three-year term, and one class being elected each year by our stockholders. This system of electing and removing directors may tend to discourage a third party from making a tender offer or otherwise attempting to obtain control of us and may maintain the incumbency of the board of directors, as it generally makes it more difficult for stockholders to replace a majority of the directors. Further, our amended and restated certificate of incorporation filed in connection with this offering and restated bylaws do not provide for cumulative voting in the election of directors.

Stockholder Meetings. Under our amended and restated certificate of incorporation and amended and restated bylaws, only our board of directors, chairman of the board or chief executive officer may call special meetings of stockholders. Our restated bylaws establish advance notice procedures with respect to stockholder proposals and the nomination of candidates for election as directors, other than nominations made by or at the direction of the board of directors or a committee thereof. In addition, our amended and restated certificate of incorporation eliminates the right of stockholders to act by written consent without a meeting and eliminates cumulative voting.

Undesignated Preferred Stock. The authorization of undesignated preferred stock makes it possible for the board of directors to issue preferred stock with voting or other rights or preferences that could impede the success of any attempt to change control of us. These and other provisions may have the effect of deterring or delaying hostile takeovers or delaying changes in control or management.

Section 203. We are subject to Section 203 of the Delaware General Corporation Law. In general, the statute prohibits a Delaware corporation from engaging in any

business combination with any interested stockholder for a period of three years following the date that the stockholder became an interested stockholder unless:

- prior to the date, the board of directors of the corporation approved either the business combination or the transaction that resulted in the stockholder becoming an interested stockholder;
- upon consummation of the transaction that resulted in the stockholder's becoming an interested stockholder, the interested stockholder owned at least 85% of the voting stock of the corporation outstanding at the time the transaction commenced, excluding those shares owned by persons who are directors and also officers, and employee stock plans in which employee participants do not have the right to determine confidentially whether shares held subject to the plan will be tendered in a tender or exchange offer; or
- on or subsequent to the date, the business combination is approved by the board of directors and authorized at an annual or special meeting of stockholders, and not by written consent, by the affirmative vote of at least two-thirds of the outstanding voting stock that is not owned by the interested stockholder.

Section 203 defines "business combination" to include:

- any merger or consolidation involving the corporation and the interested stockholder;
- any sale, transfer, pledge or other disposition involving the interested stockholder of 10% or more of the assets of the corporation;
- subject to exceptions, any transaction that results in the issuance or transfer by the corporation of any stock of the corporation to the interested stockholder; or
- the receipt by the interested stockholder of the benefit of any loans, advances, guarantees, pledges or other financial benefits provided by or through the corporation.

In general, Section 203 defines an interested stockholder as any entity or person beneficially owning 15% or more of the outstanding voting stock of the corporation and any entity or person affiliated with or controlling or controlled by the entity or person.

TRANSFER AGENT AND REGISTRAR

The transfer agent and registrar for the common stock is _____.

THE NASDAQ STOCK MARKET'S NATIONAL MARKET LISTING

We have applied to list our common stock on The Nasdaq Stock Market's National Market under the symbol "PTIE."

SHARES ELIGIBLE FOR FUTURE SALE

Prior to this offering, there has been no public market for our stock. After we complete this offering, based upon the number of shares outstanding at March 1, 2000, there will be _____ shares of our common stock outstanding. Of these outstanding shares, the _____ shares sold in this offering will be freely tradable without restriction or further registration under the Securities Act of 1933, except that any shares purchased by our "affiliates", as that term is defined in Rule 144 under the Securities Act, may generally only be sold in compliance with the limitations of Rule 144 described below.

LOCK-UP AGREEMENTS

The remaining shares of common stock outstanding after this offering are subject to lock-up agreements which expire 180 days after the date of this prospectus. Upon expiration of the 180-day lock-up period, all of these shares will be eligible for sale in the public market subject to the provisions of Rule 144 or Rule 701 under the Securities Act. The lock-up agreements were entered into by all holders of our securities, including all of our directors and executive officers, who in the aggregate hold:

- 10,448,818 shares of our common stock of record;
- options to purchase 950,000 shares of our common stock;
- warrants to purchase 70,000 shares of our common stock;
- warrants to purchase 150,000 shares of our series A preferred stock which are convertible into 150,000 shares of our common stock; and
- warrants to purchase 120,000 shares of our common stock.

In the lock-up agreements, these stockholders agreed that, for a period of 180 days after the date of this prospectus, they will not sell, contract to sell or otherwise dispose of any shares of our common stock, or any shares convertible into or exchangeable for shares of our common stock, owned directly by them or with respect to which they have the power of disposition, without the prior written consent of FleetBoston Robertson Stephens Inc.

SALES OF RESTRICTED SHARES

In addition to being subject to the lock-up agreements those shares are deemed "restricted securities" under Rule 144. In general under Rule 144 a stockholder, including one of our affiliates, who has beneficially owned his or her restricted securities for at least one year is entitled to sell, within any three-month period commencing 90 days after the date of this prospectus, a number of shares that does not exceed the greater of 1% of the then outstanding shares of common stock (approximately shares immediately after this offering) or the average weekly trading volume in our common stock during the four calendar weeks preceding the date on which notice of the sale was filed under Rule 144, provided requirements concerning availability of public information, manner of sale and notice of sale are satisfied. In addition, a stockholder that is not one of our affiliates at any time during the three months preceding a sale and who has beneficially owned the shares proposed to be sold for at least two years is entitled to sell the shares immediately under Rule 144(k) without compliance with the above described requirements of Rule 144.

In general, under Rule 701 of the Securities Act as currently in effect, any of our employees, consultants or advisors who purchase shares from us under a stock option plan or other written agreement can resell those shares 90 days after the effective date of this offering in reliance on Rule 144, but without complying with some of the restrictions, including the holding period, contained in Rule 144.

STOCK OPTIONS

We intend to file registration statements on Form S-8 under the Securities Act to register an aggregate of 3,700,000 shares of common stock issuable under our 1998 Stock Plan and the 2000 Employee Stock Purchase Plan. Shares issued upon exercise of stock options after the effective date of the Form S-8 registration statements will be eligible for

resale in the public market without restriction, subject to Rule 144 limitations applicable to affiliates and the lock-up agreements noted above, if applicable.

REGISTRATION RIGHTS

Upon completion of this offering, the holders of 11,108,912 shares of our common stock and of warrants to purchase 150,000 shares of our series A convertible preferred stock and warrants to purchase 120,000 shares of our common stock will be entitled to rights with respect to the registration of their shares under the Securities Act even if the shares would have been subject to Rule 144 restrictions. Please see "Description of Capital Stock -- Registration Rights" for a more detailed description of these registration rights. After registration, these shares will become freely tradable without restriction under the Securities Act. Any sales of securities by these shareholders could have a material adverse effect on the trading price of our common stock.

UNDERWRITING

We are offering the shares of common stock described in this prospectus through a number of underwriters. FleetBoston Robertson Stephens Inc., CIBC World Markets Corp. and Lazard Freres & Co. LLC will act as representatives of the underwriters. We have entered into an underwriting agreement with the representatives. Subject to the terms and conditions of the underwriting agreement, we have agreed to sell to the underwriters, and each underwriter has separately agreed to purchase from us, the number of shares of common stock listed next to its name below at the public offering price, less the underwriting discount described on the cover page of this prospectus:

UNDERWRITERS -----	NUMBER OF SHARES -----
FleetBoston Robertson Stephens Inc.	
CIBC World Markets Corp.	
Lazard Freres & Co. LLC.....	
INTERNATIONAL UNDERWRITER -----	
FleetBoston Robertson Stephens International Limited	
CIBC World Markets Corp.	
Lazard Capital Markets.....	
Total.....	----- =====

The underwriting agreement provides that the underwriters must buy all of these shares from us if they buy any of them. The underwriters will sell these shares to the public when and if the underwriters buy them from us. The underwriters are offering the common stock subject to a number of conditions, including:

- the underwriters' receipt and acceptance of the common stock from us; and
- the underwriters' right to reject orders in whole or in part.

Over-Allotment Option. We have granted to the underwriters an option to buy up to additional shares of our common stock at the same price per share as they are paying for the shares shown in the table above. The underwriters may exercise this option only to the extent that they sell more than the total number of shares shown in the table above. The underwriters may exercise this option at any time within 30 days after the date of this prospectus. To the extent that the underwriters exercise this option, the underwriters will be obligated to purchase the additional shares from us in the same proportions as they purchased the shares shown in the table above. If purchased, these additional shares will be sold by the underwriters on the same terms as those on which the other shares are being sold. We will be obligated, pursuant to this option, to sell shares to the extent the option is exercised. If the option is exercised in full, the total public offering price, underwriting discounts and commissions and proceeds to us will be \$, \$ and \$, respectively.

Stock Market Listing. We expect our common stock will be quoted on the Nasdaq National Market under the symbol "PTIE."

Determination of Offering Price. Before this offering, there has been no public market for our common stock. The initial public offering price will be determined through negotiations between us and the representatives. In addition to prevailing market

conditions, the factors to be considered in determining the initial public offering price will include:

- the valuation multiples of publicly-traded companies that the representatives believe are comparable to us;
- our financial information;
- our history and prospects and the outlook for our industry;
- an assessment of our management, our past and present operations, and the prospects for, and timing of, our future revenues;
- the present state of our development and the progress of our business plan; and
- the above factors in relation to market values and various valuation measures of other companies engaged in activities similar to ours.

An active trading market for our shares may not develop. Even if an active market does develop, the public price at which our shares trade in the future may be below the offering price.

Underwriting Discounts and Commissions. The underwriting discount is the difference between the price the underwriters pay to us and the price at which the underwriters initially offer the shares to the public. The underwriting discount will be determined through an arms-length negotiation between us and the representatives. The following table shows the per share and total underwriting discounts and commissions to be paid by us to the underwriters. These amounts are shown assuming no exercise and full exercise of the underwriters' over-allotment option described above:

	PER SHARE	WITHOUT OPTION	WITH OPTION
	-----	-----	-----
Public offering price.....	\$	\$	\$
Underwriting discounts and commissions.....	\$	\$	\$
Proceeds, before expenses, to us.....	\$	\$	\$

The expenses of this offering, not including the underwriting discount, are estimated to be approximately \$ and will be paid entirely by us. Expenses include the SEC filing fee, the NASD filing fee, Nasdaq listing fees, printing expenses, transfer agent and registrar fees and other miscellaneous fees. FleetBoston Robertson Stephens Inc. expects to deliver the shares of common stock to purchasers on , 2000.

Indemnification of the Underwriters. We will indemnify the underwriters against some civil liabilities, including liabilities under the Securities Act and liabilities arising from breaches of our representations and warranties contained in the underwriting agreement. If we are unable to provide this indemnification, we will contribute to payments the underwriters may be required to make in respect of those liabilities.

Dealers' Compensation. The underwriters initially will offer our shares to the public at the price specified on the cover page of this prospectus. The underwriters may allow to selected dealers a concession of not more than \$ per share. The underwriters may also allow, and any other dealers may reallow, a concession of not more than \$ per share to some other dealers. If all the shares are not sold at the public offering price, the underwriters may change the public offering price and the other selling terms. A change in the public offering price will not affect the amount of proceeds that we receive.

Discretionary Accounts. The underwriters do not expect to sell more than 5% of the shares of our common stock in the aggregate to accounts over which they exercise discretionary authority.

Directed Share Program. At our request, the underwriters have reserved for sale, at the initial public offering price, up to _____ shares, or 5%, of the shares of our common stock offered by this prospectus for sale to some of our directors, officers and employees and their family members, and other persons with relationships with us. The number of shares of our common stock available for sale to the general public will be reduced to the extent those persons purchase the reserved shares. Any reserved shares which are not orally confirmed for purchase within one day of the pricing of this offering may be offered by the underwriters to the general public on the same terms as the other shares offered by this prospectus.

Stabilization and Other Transactions. The rules of the SEC generally prohibit the underwriters from trading in our common stock on the open market during this offering. However, the underwriters are allowed to engage in some open market transactions and other activities during this offering that may cause the market price of our common stock to be above or below that which would otherwise prevail in the open market. These activities may include stabilization, short sales and over-allotments, syndicate covering transactions and penalty bids.

- Stabilizing transactions consist of bids or purchases made by the lead representative for the purpose of preventing or slowing a decline in the market price of our common stock while this offering is in progress.
- Short sales and over-allotments occur when the representatives, on behalf of the underwriting syndicate, sell more of our shares than they purchase from us in this offering. In order to cover the resulting short position, the representatives may exercise the over-allotment option described above and/or they may engage in syndicate covering transactions.
- Syndicate covering transactions are bids for or purchases of our common stock on the open market by the representatives on behalf of the underwriters in order to reduce a short position incurred by the representatives on behalf of the underwriters.
- A penalty bid is an arrangement permitting the representatives to reclaim the selling concession that would otherwise accrue to an underwriter if the common stock originally sold by that underwriter was later repurchased by the representatives and therefore was not effectively sold to the public by such underwriter.

If the underwriters commence these activities, they may discontinue them at any time without notice. The underwriters may carry out these transactions on the Nasdaq National Market, in the over-the-counter market or otherwise.

Passive Market Making. Prior to the pricing of this offering, and until the commencement of any stabilizing bid, underwriters and dealers who are qualified market makers on the Nasdaq National Market may engage in passive market making transactions. Passive market making is allowed during the period when the SEC's rules would otherwise prohibit market activity by the underwriters and dealers who are participating in this offering. Passive market makers must comply with applicable volume and price limitations and must be identified as such. In general, a passive market maker must display its bid at a price not in excess of the highest independent bid for our

common stock; but if all independent bids are lowered below the passive market maker's bid, the passive market maker must also lower its bid once it exceeds specified purchase limits. 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 our common stock during a specified period and must be discontinued when such limit is reached. Underwriters and dealers are not required to engage in passive market making and may end passive market making activities at any time.

Some of the underwriters have in the past and may in the future perform financial advisory services for us.

LEGAL MATTERS

The validity of the common stock offered hereby will be passed upon for us by Wilson Sonsini Goodrich & Rosati, Professional Corporation, Palo Alto, California. Legal matters will be passed upon for the underwriters by O'Melveny & Myers LLP, San Francisco, California. As of the date of this prospectus, investment partnerships composed of certain members of and persons associated with Wilson Sonsini Goodrich & Rosati, Professional Corporation, in addition to individual members of and persons associated with Wilson Sonsini Goodrich & Rosati, Professional Corporation, beneficially own an aggregate of 64,714 shares of our preferred and common stock.

EXPERTS

The financial statements of Pain Therapeutics, Inc. (a development stage enterprise) as of December 31, 1998 and 1999, and for the period from May 4, 1998 (inception) through December 31, 1998, the year ended December 31, 1999, and the period from May 4, 1998 (inception) through December 31, 1999 have been included herein and in the registration statement in reliance upon the report of KPMG LLP, independent certified public accountants, appearing elsewhere herein, and upon the authority of said firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We have filed with the Securities and Exchange Commission, Washington, D.C., a registration statement on Form S-1 under the Securities Act with respect to the shares of common stock offered hereby. This prospectus does not contain all the information set forth in the registration statement and the exhibits and schedules thereto. For further information with respect to us and our common stock, you should refer to the registration statement and to the exhibits and schedules filed therewith. Statements contained in this prospectus that describe the contents of any contract or other document are not necessarily complete, and in each instance reference is made to the copy of the contract or other document filed as an exhibit to the registration statement, each statement being qualified in all respects by this reference. A copy of the registration statement may be inspected by anyone without charge at the Public Reference Section of the Commission at Room 1024, Judiciary Plaza, 450 Fifth Street, N.W., Washington, D.C. 20549. Copies of all or any portion of the registration statement may be obtained from the Public Reference Section of the Commission, 450 Fifth Street, N.W., Washington, D.C. 20549, upon payment of prescribed fees. The public may obtain information on the operation of the public reference room by calling the SEC at 1-800-SEC-0330. The Commission maintains a Web site at <http://www.sec.gov> that contains reports, proxy and information statements and other information regarding registrants that file electronically with the Commission.

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

INDEX TO FINANCIAL STATEMENTS

	PAGE

Independent Auditors' Report.....	F-2
Balance Sheets.....	F-3
Statements of Operations.....	F-4
Statements of Stockholders' Equity (Deficit).....	F-5
Statements of Cash Flows.....	F-6
Notes to Financial Statements.....	F-7

INDEPENDENT AUDITORS' REPORT

The Board of Directors
Pain Therapeutics, Inc.:

We have audited the accompanying balance sheets of Pain Therapeutics, Inc. (a development stage enterprise) as of December 31, 1998 and 1999, and the related statements of operations, stockholders' equity (deficit) and cash flows for the period from May 4, 1998 (inception) through December 31, 1998, for the year ended December 31, 1999 and for the period from May 4, 1998 (inception) through December 31, 1999. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

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

In our opinion, the financial statements referred to above present fairly, in all material respects, the financial position of Pain Therapeutics, Inc. (a development stage enterprise) as of December 31, 1998 and 1999 and the results of its operations and its cash flows for the period from May 4, 1998 (inception) through December 31, 1998, for the year ended December 31, 1999 and for the period from May 4, 1998 (inception) through December 31, 1999, in conformity with generally accepted accounting principles.

San Francisco, California
February 26, 2000, except as to note 7
which is as of March 9, 2000

/s/ KPMG LLP

F-2

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

BALANCE SHEETS

	DECEMBER 31, 1999		
	DECEMBER 31, 1998	ACTUAL	PRO FORMA STOCKHOLDERS' EQUITY (NOTE 1)
			(UNAUDITED)
ASSETS			
Current assets:			
Cash and cash equivalents.....	\$2,333,512	\$ 9,339,669	
Interest receivable.....	3,138	15,362	
Prepaid expenses.....	35,496	41,387	
	2,372,146	9,396,418	
Property and equipment, net.....	10,454	44,755	
	\$2,382,600	\$ 9,441,173	
	=====	=====	
LIABILITIES AND STOCKHOLDERS' EQUITY			
(DEFICIT)			
Liabilities:			
Accounts payable.....	\$ 108,108	\$ 300,587	
	108,108	300,587	
Commitments and contingencies			
Redeemable convertible preferred stock -- Series B \$.001 par value; 5,405,405 shares authorized; 5,405,405 shares designated, issued and outstanding in 1999; none pro forma; liquidation preference and redemption value of \$1.85 per share.....	--	9,703,903	--
Stockholders' equity:			
Convertible preferred stock -- Series A \$.001 par value; 3,500,000 shares authorized; 2,659,489 shares issued and outstanding in 1998 and 1999; none pro forma; liquidation preference of \$1.00 per share.....	2,660	2,660	--
Common stock, \$.001 par value; 20,000,000 shares authorized and 9,000,000 and 9,445,000 shares issued and outstanding as of December 31, 1998 and 1999, respectively; 17,509,894 shares pro forma.....	9,000	9,445	17,510
Additional paid-in-capital.....	2,686,839	4,235,317	13,933,815
Deferred compensation.....	--	(1,073,921)	(1,073,921)
Notes receivable.....	(35,000)	(74,400)	(74,400)
Deficit accumulated during the development stage.....	(389,007)	(3,662,418)	(3,662,418)
	2,274,492	(563,317)	\$ 9,140,586
	-----	-----	=====
Total liabilities and stockholders' equity (deficit).....	\$2,382,600	\$ 9,441,173	
	=====	=====	

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

STATEMENTS OF OPERATIONS

	PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1998	YEAR ENDED DECEMBER 31, 1999	MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1999
	-----	-----	-----
Operating expenses:			
Licensing fees.....	\$ 100,000	\$ --	\$ 100,000
Research and development.....	200,000	2,092,119	2,292,119
General and administrative.....	122,168	1,341,181	1,463,349
	-----	-----	-----
Total expenses.....	422,168	3,433,300	3,855,468
	-----	-----	-----
Operating loss.....	(422,168)	(3,433,300)	(3,855,468)
Other income:			
Interest income.....	33,961	160,689	194,650
	-----	-----	-----
Net loss before income taxes.....	(388,207)	(3,272,611)	(3,660,818)
Income tax expense.....	800	800	1,600
	-----	-----	-----
Net loss.....	\$(389,007)	\$(3,273,411)	\$(3,662,418)
	=====	=====	=====
Basic and diluted loss per share.....	\$ (0.06)	\$ (0.35)	
	=====	=====	
Weighted-average shares used in computing basic and diluted loss per share.....	6,948,637	9,322,441	
	=====	=====	

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT)
FOR THE PERIOD MAY 4, 1998 (INCEPTION) THROUGH
DECEMBER 31, 1998 AND THE YEAR ENDED DECEMBER 31, 1999

	SERIES A CONVERTIBLE PREFERRED STOCK		COMMON STOCK		ADDITIONAL PAID-IN CAPITAL	DEFERRED COMPENSATION	NOTE RECEIVABLE FOR STOCK
	SHARES	PAR VALUE	SHARES	PAR VALUE			
Balance -- May 4, 1998 (inception).....	--	\$ --	--	\$ --	\$ --	\$ --	\$ --
Common stock issued on June 22, 1998 at \$.001 per share.....	--	--	8,500,000	8,500	--	--	--
Series A convertible preferred stock issued between August 14, 1998 and October 28, 1998 at \$1.00 per share (net of issuance costs of \$19,490).....	2,659,489	2,660	--	--	2,637,339	--	--
Common stock issued on September 23, 1998 at \$.10 per share for notes receivable.....	--	--	350,000	350	34,650	--	(35,000)
Common stock issued on September 23, 1998 at \$.10 per share for cash.....	--	--	150,000	150	14,850	--	--
Net loss.....	--	--	--	--	--	--	--
Balance -- December 31, 1998.....	2,659,489	2,660	9,000,000	9,000	2,686,839	--	(35,000)
Payment on note receivable.....	--	--	--	--	--	--	5,000
Common stock issued between April 1 and August 1, 1999 at \$.10 per share for notes receivable.....	--	--	444,000	444	43,956	--	(44,400)
Issuance of common stock pursuant to exercise of stock options.....	--	--	1,000	1	99	--	--
Issuance of warrants in connection with lease in August 1999.....	--	--	--	--	33,810	--	--
Deferred compensation with respect to options issuances during 1999.....	--	--	--	--	1,457,144	(1,457,144)	--
Amortization of deferred compensation.....	--	--	--	--	--	383,223	--
Compensation expense with respect to non-employee option grants....	--	--	--	--	13,469	--	--
Net loss.....	--	--	--	--	--	--	--
Balance -- December 31, 1999.....	2,659,489	\$2,660	9,445,000	\$9,445	\$4,235,317	\$(1,073,921)	\$(74,400)

	DEFICIT ACCUMULATED DURING DEVELOPMENT STAGE		STOCKHOLDERS' EQUITY (DEFICIT)
Balance -- May 4, 1998 (inception).....	\$ --	\$ --	--
Common stock issued on June 22, 1998 at \$.001 per share.....	--	--	8,500
Series A convertible preferred stock issued between August 14, 1998 and October 28, 1998 at \$1.00 per share (net of issuance costs of \$19,490).....	--	2,639,999	--
Common stock issued on September 23, 1998 at \$.10 per share for notes receivable.....	--	--	--
Common stock issued on September 23, 1998 at \$.10 per share for cash.....	--	15,000	--
Net loss.....	(389,007)	(389,007)	--
Balance -- December 31, 1998.....	(389,007)	2,274,492	--
Payment on note receivable.....	--	5,000	--
Common stock issued between April 1 and August 1, 1999 at \$.10 per share for notes receivable.....	--	--	--
Issuance of common stock pursuant to exercise of stock options.....	--	100	--
Issuance of warrants in connection with lease in August 1999.....	--	33,810	--
Deferred compensation with respect	--	--	--

to options issuances during 1999.....	--	--
Amortization of deferred compensation.....	--	383,223
Compensation expense with respect to non-employee option grants....	--	13,469
Net loss.....	(3,273,411)	(3,273,411)
	-----	-----
Balance -- December 31, 1999.....	<u>\$(3,662,418)</u>	<u>\$ (563,317)</u>
	=====	=====

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

STATEMENTS OF CASH FLOWS

	PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1998 -----	YEAR ENDED DECEMBER 31, 1999 -----	MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1999 -----
Cash flows from operating activities:			
Net loss.....	\$ (389,007)	\$(3,273,411)	\$(3,662,418)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation and amortization.....	518	4,244	4,762
Amortization of deferred compensation.....	--	383,223	383,223
Noncash expense for options and warrants issued.....	--	36,009	36,009
Changes in operating assets and liabilities:			
Interest receivable.....	(3,138)	(12,224)	(15,362)
Prepaid expenses.....	(35,496)	5,379	(30,117)
Accounts payable.....	108,108	162,479	270,587
	-----	-----	-----
Net cash used in operating activities.....	(319,015)	(2,694,301)	(3,013,316)
	-----	-----	-----
Cash flows used in investing activities -- purchase of property and equipment.....	(10,972)	(38,545)	(49,517)
	-----	-----	-----
Cash flows from financing activities:			
Proceeds from issuance of series B redeemable convertible preferred stock (net of issuance costs of \$296,096).....	--	9,733,903	9,733,903
Stock subscription received.....	--	5,000	5,000
Proceeds from issuance of series A convertible preferred stock (net of issuance costs of \$19,490).....	2,639,999	--	2,639,999
Proceeds from issuance of common stock.....	23,500	100	23,600
	-----	-----	-----
Net cash provided by financing activities.....	2,663,499	9,739,003	12,402,502
	-----	-----	-----
Net increase in cash.....	2,333,512	7,006,157	9,339,669
Cash and cash equivalents at beginning of period.....	--	2,333,512	--
	-----	-----	-----
Cash and cash equivalents at end of period.....	\$2,333,512	\$ 9,339,669	\$ 9,339,669
	=====	=====	=====
Supplemental cash flow information:			
Cash paid for income taxes.....	\$ --	\$ 1,600	\$ 1,600
	=====	=====	=====

See accompanying notes to financial statements.

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS

(1) THE COMPANY AND SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

The Company

Pain Therapeutics, Inc. (a development stage enterprise) is a clinical-stage specialty pharmaceutical company which was incorporated on May 4, 1998. Since our inception in May 1998, we have licensed proprietary technology from Albert Einstein College of Medicine and have devoted substantially all of our resources to the development of a new generation of opioid painkillers with improved clinical benefits, which are based on the acquired technology.

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

On March 9, 2000, our Board of Directors authorized our management to file a Registration Statement with the Securities and Exchange Commission to sell shares of our common stock to the public.

Cash and Cash Equivalents

We consider all highly liquid financial instruments with original maturities of three months or less to be cash equivalents. We maintain our cash at one financial institution. Our balances are in excess of federal depository insurance limitations.

Use of Estimates

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

Income Taxes

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

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

Property and Equipment

Property and equipment are stated at cost, net of accumulated depreciation and amortization. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, generally three to five years.

Fair Value of Financial Instruments

Interest and stock subscriptions receivables are considered to have carrying amounts that approximate fair value because of the short maturity of these financial instruments. Notes receivable are considered to have carrying amounts that approximate fair value as they bear a market rate of interest. The series B redeemable, convertible preferred stock has a carrying amount that approximates fair value as the redemption amount equals the carrying amount.

Research and Development Costs

Research and development costs and the costs of obtaining licenses used in research and development are charged to expense as incurred.

Impairment of Long-Lived Assets

We review, as circumstances dictate, the carrying amount of our long-lived assets. The purpose of these reviews is to determine whether the carrying amounts are recoverable. Recoverability is determined by comparing the projected undiscounted net cash flows of the long-lived assets against their respective carrying amounts. The amount of impairment, if any, is measured based on the excess of the carrying value over the fair value. No such events have occurred with respect to the Company's long-lived assets.

Stock-Based Compensation

Statement of Financial Accounting Standards (SFAS) No. 123, Accounting for Stock-Based Compensation, establishes a fair-value method of accounting for stock options and similar equity instruments. The fair-value method requires compensation cost to be measured at the grant date based on the value of the award, and is recognized over the service period. SFAS No. 123 allows companies to either account for stock-based compensation to employees under the provisions of SFAS No. 123 or under the provisions of Accounting Principles Board (APB) Opinion No. 25 and its related interpretations. We have elected to account for our stock-based compensation to employees in accordance with the provisions of APB Opinion No. 25 and provide the pro forma disclosures required under SFAS No. 123.

We have recorded deferred compensation for the difference between the exercise price and the deemed fair market value of the common stock for financial reporting purposes of stock options granted to employees. The compensation expense related to such grants is amortized over the vesting period of the related stock options in accordance with Financial Accounting Standards Board Interpretation No. 28 (FIN 28).

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

We account for equity instruments issued to nonemployees in accordance with the provisions of SFAS No. 123 and Emerging Issues Task Force (EITF) Issue No. 96-18 Accounting for Equity Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services.

Comprehensive Loss

We have no components of other comprehensive loss other than our net loss and, accordingly, our comprehensive loss is equivalent to our net loss for all periods presented.

Business Segments

SFAS No. 131, Disclosures about Segments of an Enterprise and Related Information, requires an enterprise to report segment information based on how management internally evaluates the operating performance of its business units (segments). Our operations are confined to one business segment: the discovery and development of new opioid painkillers.

Loss per Share

Basic loss per share is computed on the basis of the weighted-average number of shares outstanding for the reporting period. Diluted loss per share is computed on the basis of the weighted-average number of common shares plus dilutive potential common shares outstanding using the treasury-stock method. Potential dilutive common shares consist of convertible preferred stock, shares issuable to holders of unexercised employee stock options and outstanding warrants. Convertible preferred stock, options and warrants equivalent to, in the aggregate, 2,879,489 and 9,382,094 shares of common stock as of December 31, 1998 and 1999, respectively, were not included in the calculation of diluted loss per share because the representative share increments would be antidilutive.

Pro Forma Stockholders' Equity (Unaudited)

The unaudited pro forma stockholders' equity gives effect to the conversion of 8,064,894 shares of series A convertible preferred stock and B redeemable convertible preferred stock outstanding as of December 31, 1999 into shares of common stock, at a conversion rate of 1 common share for each preferred share of series A convertible preferred stock and B redeemable convertible preferred stock, upon the closing of our initial public offering.

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

(2) PROPERTY AND EQUIPMENT

Property and equipment consisted of the following as of December 31:

	1998	1999
	-----	-----
Machinery and equipment.....	\$ 7,195	\$14,703
Fixtures.....	3,777	34,814
	-----	-----
Less accumulated depreciation.....	10,972 (518)	49,517 (4,762)
	-----	-----
Property and equipment, net.....	\$10,454	\$44,755
	=====	=====

(3) STOCKHOLDERS' EQUITY (DEFICIT)

Common Stock

On June 22, 1998, we issued 8,500,000 shares of common stock at \$0.001 per share. Of these shares, 8,480,000 were issued subject to a repurchase option. The shares are released from our repurchase option over a four-year vesting period at the rate of 1/48 at the end of each month from the date of purchase until all shares are released. Our repurchase option is exercisable only within 90 days following the termination of the purchaser's employment, at which time we are able to repurchase the unvested shares at the original purchase price of \$0.001 per share. As of December 31, 1999 4,416,667 shares of common stock were not vested and, therefore, were subject to repurchase by us in the event of termination of the purchaser's employment.

On September 23, 1998, under the terms of the 1998 Stock Plan (see below), we granted stock purchase rights to and subsequently issued 500,000 shares of common stock at \$0.10 per share in exchange for \$35,000 in promissory notes and \$15,000 in cash. Such shares were issued pursuant to a restricted stock purchase agreement. The shares are released from our repurchase option over a four-year vesting period at the rate of 1/48 at the end of each month from the date of purchase until all shares are released. Our repurchase option is exercisable only within 90 days following the termination of the purchaser's employment or provision of services, at which time we are able to repurchase the unvested shares at the original purchase price of \$0.10 per share. As of December 31, 1999, 350,000 shares of common stock were not vested and, therefore, were subject to repurchase by us in the event of termination of the purchaser's employment or provision of services to us.

Between April and August 1999, under the terms of the 1998 Stock Plan (see below), we granted stock purchase rights to and subsequently issued 444,000 additional shares of common stock at \$0.10 per share in exchange for promissory notes. Such shares were issued pursuant to a restricted stock purchase agreement. The shares are released from our repurchase option over a two-year vesting period at the rate of 1/24 at the end of each month from the date of purchase until all shares are released. Our repurchase option is exercisable only within 90 days following the termination of the purchaser's employment or provision of services, at which time we are able to repurchase the unvested shares at the original repurchase price per share. As of December 31, 1999, 190,500 shares of common stock were not vested and, therefore, subject to repurchase by us in the event of termination of the purchaser's employment or provision of services to us.

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

Preferred Stock

We are authorized to issue 10,000,000 shares of preferred stock.

We issued 2,659,489 shares of series A convertible preferred stock at \$1.00 per share during August and October 1998.

We issued 5,405,405 shares of series B redeemable convertible, preferred stock at \$1.85 per share during October and November 1999.

A summary of the rights, preferences, privileges and restrictions relative to the series A convertible preferred stock and series B redeemable convertible preferred stock (Preferred Stock) follows:

Dividends. The holders of both the series A convertible preferred stock and series B redeemable convertible preferred stock are entitled to receive dividends, prior and in preference to holders of common stock and on a pari passu basis, at the rate of \$0.06 per annum, when and if declared by the Board of Directors. Such dividends are not cumulative. No dividends have been declared to date.

Liquidation. In the event that we liquidate, dissolve or wind up, the holders of preferred stock shall be entitled to receive, prior and in preference to the holders of common stock, an amount per share equal to (i) \$1.00 per share for each share of series A convertible preferred stock, plus declared but unpaid dividends; and (ii) \$1.85 per share for each outstanding share of series B redeemable convertible preferred stock, plus declared but unpaid dividends. If, upon the occurrence of such event, the assets and funds thus distributed are insufficient to pay the full preferential amounts to all the holders of the preferred stock, then our entire assets legally available for distribution shall be distributed ratably among the holders of the preferred stock in proportion to the preferential amount each such holder is otherwise entitled to receive. After the liquidation preference has been paid to the holders of the preferred stock, all remaining assets and funds shall be distributed ratably among the holders of common stock. A merger, consolidation or sale of all or substantially all of our assets, which will result in our stockholders immediately prior to such transaction not holding at least 50% of the voting power of the surviving corporation, shall be treated as a liquidation.

Conversion. Each share of preferred stock shall be convertible, at the option of the holder thereof, at any time after the date of issuance of such share for such preferred stock. Each share of preferred stock shall be convertible into the number of shares of common stock as is determined by dividing (i) \$1.00 in the case of series A convertible preferred stock; or (ii) \$1.85 in the case of series B redeemable convertible preferred stock by the conversion price applicable to such shares. The initial conversion price is \$1.00 per share of series A convertible preferred stock and \$1.85 per share of series B redeemable convertible preferred stock. The preferred stock shall be automatically converted into shares of common stock at the then applicable conversion rate upon the Company's sale of its common stock in a firm commitment underwritten public offering with a sales price per share (as adjusted) of at least \$5.00 per share and with aggregate gross proceeds to the Company of at least \$15,000,000.

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

Antidilution Adjustments. The conversion price of each series of preferred stock is subject to adjustment upon the occurrence of certain events described in our Certificate of Incorporation, including the issuance of common stock for a consideration per share less than the conversion price in effect for each respective series of preferred stock, common stock dividends, common stock splits and recapitalizations.

Redemption. The series A convertible preferred stock is not redeemable. Each holder of series B redeemable convertible preferred stock has the right to require us to redeem up to one-third of such series B redeemable convertible preferred stock on each of October 1, 2005, October 1, 2006 and October 1, 2007, with the right to carryforward such redemption onto subsequent anniversaries to the extent it is not exercised in full on the applicable redemption date. The redemption price per share shall be equal to the original series B redeemable convertible preferred stock purchase price (subject to adjustment) plus all declared but unpaid dividends.

Voting. Except as otherwise provided or required by law, the holders of both series of preferred stock shall be entitled to vote on an as-converted basis on all matters with the holders of common stock. Consent of more than 50% of the holders of preferred stock, voting together as a class, shall be required in order to (i) amend the Certificate of Incorporation or Bylaws; (ii) liquidate, dissolve or wind up the Company; or (iii) sell or otherwise dispose of all or substantially all of the Company's assets or merge into or consolidate with another entity, as a result of which the holders of the outstanding shares of the Company prior to the transaction hold less than 50% of the voting power of the surviving corporation and which generates gross proceeds to the Company and its stockholders of \$50,000,000 or more. Consent of two-thirds of the holders of series B redeemable convertible preferred stock, voting as a class, is required to consummate a change of control involving gross proceeds to us and our stockholders of less than \$50,000,000.

Registration Rights. The holders of both series of preferred stock have certain registration rights with respect to the preferred stock and the common stock into which the preferred stock is convertible.

Piggyback Registration Rights. The holders of both series of preferred stock have the right to request that shares of common stock issued or issuable upon conversion of said preferred stock be included in any registration of common stock that we perform. In any such registration, the underwriters may, for marketing reasons, exclude all or part of the shares requested to be registered on behalf of the holder. Notwithstanding the foregoing, we have the right to terminate any such registration prior to its effectiveness regardless of any request for inclusion by a holder.

Warrants

In June 1998, we issued a warrant to purchase 150,000 shares of series A convertible preferred stock at an exercise price of \$1.00 per share to one of the holders of the series A convertible preferred stock, in consideration of such holder's advance of funds to us prior to the closing of the series A convertible preferred stock financing. The warrant expires on June 5, 2010. The shares of Series A convertible preferred stock underlying this warrant

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

are entitled to the benefits of the registration rights granted by us to the holders of series A convertible preferred stock.

In August 1999, we issued a warrant to purchase 70,000 shares of common stock at an exercise price of \$1.00 per share to the Company's landlord in connection with the commercial lease of the Company's facilities. The warrant will expire on the fifth anniversary of the Company's initial public offering (or sooner under certain circumstances). The shares of common stock underlying this warrant are not entitled to any registration rights. The fair value of these warrants of \$33,810 was estimated using a Black-Scholes model and the following assumptions: estimated volatility of 60%, a risk-free interest rate of 5.27%, no dividend yield, and an expected life equal to the contractual terms of 5 years. This fair value is being amortized to rent expense over the lease term.

1998 Stock Plan

Pursuant to approval by the board of directors, effective September 23, 1998 we adopted the 1998 Stock Plan, allowing issuance of up to 1,500,000 shares of common stock. The board of directors subsequently amended the 1998 Stock Plan to increase the number of shares of common stock reserved for issuance under the 1998 Stock Plan to 2,500,000. The 1998 Stock Plan will terminate on September 23, 2008 or an earlier date as determined by the board of directors.

Under the 1998 Stock Plan, employees, directors and consultants (Service Providers) may be granted options that allow for the purchase of shares of our common stock. Nonstatutory stock options and stock purchase rights (see above) may be granted to all Service Providers. Incentive stock options may only be granted to employees.

Nonstatutory stock options may be granted under the 1998 Stock Plan at a price not less than 110% and 85% of the fair value of the stock on the date the option is granted where (a) the options are granted to Service Providers who, at the time of grant, own stock representing more than 10% of the voting power of all classes of stock, and (b) the options are granted to any other Service Provider, respectively. Incentive stock options may be granted under the 1998 Stock Plan at a price not less than 110% and 100% of the fair market value of the stock on the date the option is granted where (a) the options are granted to employees who, at the time of the grant, own stock representing more than 10% of the voting power of all classes of stock, and (b) the options are granted to any other employee, respectively. The term of the nonstatutory and incentive stock options granted is ten years or less from the date of the grant, as provided for in the individual option agreement.

Vesting provisions of individual options may vary, except in the case of options granted to officers, directors and consultants where vesting is at a rate of no less than 20% per year over five years from the date of grant. Forfeited options become available for reissuance under the 1998 Stock Plan.

There were no options granted during the period from May 4, 1998 (inception) through December 31, 1998.

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

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

	RANGE OF EXERCISE PRICES	NUMBER OF OPTIONS	WEIGHTED- AVERAGE EXERCISE PRICE
	-----	-----	-----
Options outstanding as of December 31, 1998.....	\$ --	--	\$ --
Granted.....	0.10 - 0.20	1,361,200	0.12
Exercised.....	0.10	(1,000)	0.10
Forfeited.....	0.10	(65,000)	0.10
	-----	-----	-----
Options outstanding as of December 31, 1999.....	\$0.10 - 0.20	1,295,200	\$0.12
	-----	-----	-----
Total number of shares exercisable as of December 31, 1999.....	\$0.10 - 0.20	133,213	\$0.11
	=====	=====	=====

As of December 31, 1999, 14,800 shares of common stock were available for issuance under the 1998 Stock Plan either under stock options or stock purchase rights.

Pursuant to SFAS No. 123, Accounting for Stock-Based Compensation, we are required to disclose the pro forma effects on net loss and net loss per share as if we had elected to use the fair value approach to account for all of our employee stock-based compensation plans. Had compensation cost of our plans been determined in a manner consistent with the fair value approach of SFAS No. 123, our pro forma net loss and pro forma net loss per share would have been reduced to the pro forma amounts indicated below:

Pro forma net loss:

	YEARS ENDED DECEMBER 31,	
	-----	-----
	1998	1999
	-----	-----
Net loss as reported.....	\$389,007	\$3,273,411
Adjusted pro forma net loss.....	389,007	3,279,228
Net loss per share basic and diluted as reported.....	0.06	0.35
Adjusted pro forma.....	0.06	0.35

The per share weighted-average fair value of stock options granted during 1999 was \$1.13 on the date of grant using the minimum value method with the following weighted-average assumptions for grants during the period ended December 31, 1999:

Expected dividend yield.....	0%
Risk-free interest rate range.....	5.49 - 6.20%
Expected life.....	5 years

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

The following table summarizes information about stock options outstanding as of December 31, 1999:

EXERCISE PRICES	OPTIONS OUTSTANDING			OPTIONS EXERCISABLE	
	NUMBER OF OPTIONS	WEIGHTED-AVERAGE REMAINING CONTRACTUAL LIFE (YEARS)	WEIGHTED-AVERAGE EXERCISE PRICE	NUMBER OF VESTED OPTIONS	WEIGHTED-AVERAGE EXERCISE PRICE
\$0.10..	992,200	9.48	\$0.10	124,588	\$0.10
0.20..	303,000	9.94	0.20	8,625	0.20
	1,295,200	9.59	\$0.12	133,213	\$0.11

During the year ended December 31, 1999 we granted stock options under the 1998 Stock Plan to employees and non-employee consultants for which we recorded deferred compensation of \$836,641 and \$620,502, respectively. No options were granted in 1998.

For employees, deferred compensation represents the difference between the exercise price of the option and the deemed fair value of our common stock on the date of grant in accordance with APB No. 25 and its related interpretations. For non-employees, deferred compensation is recorded at the fair value of the options granted in accordance with SFAS No. 123 and EITF 96-18. The fair value for non-employee options was determined using a Black-Scholes model and the following assumptions: estimated volatility of 60%, a risk free interest rate ranging from 5.54 - 6.28%, no dividend yield, and an expected life of the option equal to the options contractual life of ten years from the date of grant.

Compensation expense is being recognized over the vesting period for employees and the service period for non-employees in accordance with FIN No. 28. For the year ended December 31, 1999, amounts amortized to the statement of operations as compensation expense for employees and non-employees was \$188,000 and \$196,000, respectively.

(4) INCOME TAXES

Income tax expense and for the period from May 4, 1998 (inception) through December 31, 1998 and for the year ended December 31, 1999 is comprised of the following:

	CURRENT	DEFERRED	TOTAL
1998:			
Federal.....	\$ --	--	\$ --
State.....	800	--	800
	\$800	--	\$800
	====	====	====
1999:			
Federal.....	\$ --	--	\$ --
State.....	800	--	800
	----	----	----
Total	\$800	--	\$800
	====	====	====

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

Tax expense differed from the amounts computed by applying the U.S. federal income tax rate of 34% to pretax income for the period from May 4, 1998 (inception) through December 31, 1998 and for the year ended December 31, 1999 as a result of the following:

	1998	1999
	-----	-----
Computed "expected" tax expense (benefit).....	\$(131,990)	\$(1,112,688)
Current NOLs for which no benefit was realized....	130,098	1,111,542
Permanent differences.....	1,892	1,146
State taxes.....	800	800
	-----	-----
	\$ 800	\$ 800
	=====	=====

The tax effect of temporary differences that give rise to significant portions of the deferred tax assets as of December 31, 1998 and 1999 is as follows:

	1998	1999
	-----	-----
Deferred tax assets:		
Intangible assets.....	\$ 11,275	\$ 8,817
Issuance of options and warrants.....	--	194,633
Net operating loss carryforward.....	141,451	1,275,414
State taxes.....	272	571
Research and development credit.....	13,000	120,247
	-----	-----
Gross deferred tax assets.....	165,998	1,599,682
Valuation allowance.....	(165,998)	(1,599,682)
	-----	-----
Net deferred tax assets.....	\$ --	\$ --
	=====	=====

We have recorded a valuation allowance of \$165,998 and \$1,599,682 against the deferred tax assets related to temporary differences and credits for federal and state income tax purposes as of December 31, 1998 and 1999, respectively. We believe that realization of these deferred tax assets is not assured, and therefore we have not recognized the related deferred tax benefits. The change in the valuation allowance for the years ended December 31, 1998 and 1999 was approximately \$166,000 and \$1,433,684, respectively.

As of December 31, 1999, we have operating loss carryforwards (expiring through 2019 for federal purposes and 2006 for state purposes) of approximately \$3,202,000 and \$3,201,000 for federal and state income tax purposes, respectively. We have federal research credits (expiring through 2019) of approximately \$114,000. We have California research credits (carrying forward indefinitely) of approximately \$9,000.

Under provisions of the Internal Revenue Code, should substantial changes in our ownership occur, the utilization of net operating loss carryforwards may be limited.

(5) AGREEMENT WITH ALBERT EINSTEIN COLLEGE OF MEDICINE

On May 5, 1998, we entered into an exclusive, worldwide license agreement (the Agreement) with Albert Einstein College of Medicine (AECOM) to gain exclusive rights to certain intellectual property developed and patented by AECOM. In consideration for the terms of the Agreement, we paid AECOM a one-time licensing fee. In addition, we have paid

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

the first three of four research funding installments to be paid over the first two years of the Agreement. We are not obligated to pay the remaining research funding payments in the event that the Agreement is terminated. We are also required to make milestone payments upon achievement of certain events with respect to licensed intellectual property. Royalties for the life of the agreement equal 4% of net product sales. If a product is combined with a drug or other substance for which we are paying an additional royalty, the royalty rate we pay to AECOM is reduced by one-half the amount of such additional royalty.

(6) LEASES

We lease office space and equipment pursuant to noncancelable operating leases that will expire at various dates through 2002.

Minimum annual rentals are as follows:

Through December 31, 2000.....	\$25,325
Through December 31, 2001.....	1,992
Through December 31, 2002.....	1,328
Through December 31, 2003.....	--
Through December 31, 2004 and thereafter.....	--

Total.....	\$28,645
	=====

Rent expense under noncancelable operating leases was \$9,428 and \$36,992 for the period from May 4, 1998 through December 31, 1998 and for the year ended December 31, 1999, respectively.

(7) SUBSEQUENT EVENTS

Series C Redeemable Convertible Preferred Stock

On February 1, 2000, we issued 3,044,018 shares of series C redeemable convertible preferred stock for \$15,195,000, net of issuance costs. The series C redeemable convertible Preferred Stock has the same rights, preferences and privileges as the series B redeemable convertible preferred stock. In connection with the issuance of the series C redeemable convertible preferred stock, we issued warrants to purchase 120,000 shares of common stock at \$5 a share.

Board Resolutions

In February 1999 our stockholders approved an amendment to our 1998 Stock Plan increasing the number of shares of common stock available for issuance under the plan by 700,000 to 3,200,000.

On March 9, 2000, our board of directors approved, subject to stockholder approval, and effective upon the closing of our proposed initial public offering the following resolutions:

- an amendment to our Certificate of Incorporation to increase the number of authorized shares of common stock to 120,000,000, and
- an amendment to our 1998 Stock Plan providing non-employee directors with an annual grant of options to purchase 20,000 shares of common stock.

PAIN THERAPEUTICS, INC.
(A DEVELOPMENT STAGE ENTERPRISE)

NOTES TO FINANCIAL STATEMENTS (CONTINUED)

Employee Stock Purchase Plan

Our 2000 Employee Stock Purchase Plan was adopted by our board of directors in March 2000 subject to stockholder approval. A total of 500,000 shares of common stock have been reserved for issuance under our 2000 Employee Stock Purchase Plan, plus annual increases equal to the lesser of (i) 250,000 shares, (ii) 1% of the outstanding shares on such date, or (iii) a lesser amount determined by our board of directors.

Our 2000 Employee Stock Purchase Plan, which is intended to qualify under Section 423 of the United States tax code, contains consecutive six month offering and purchase periods. The offering periods generally start on the first trading day on or after May 1 and November 1 of each year, except for the first such offering period which commences on the first trading day on or after the effective date of this offering and ends on the last trading day on or before November 30, 2000.

Employees are eligible to participate if they are customarily employed by us or any participating subsidiary for at least 20 hours per week and more than five months in any calendar year. However, any employee who immediately after grant owns stock possessing 5% or more of the total combined voting power or value of all classes of our capital stock, or whose rights to purchase stock under all of our employee stock purchase plans accrues at a rate which exceeds \$25,000 worth of stock for each calendar year may not be granted an option to purchase stock under this plan. The 2000 Employee Stock Purchase Plan permits participants to purchase common stock through payroll deductions of up to 10% of the participant's "compensation." Compensation is defined as the participant's base straight time gross earnings and commissions but is exclusive of payments for overtime, shift premium payments, incentive compensation, incentive payments, bonuses and other compensation. The maximum number of shares a participant may purchase during a single purchase period is 2,000 shares.

Amounts deducted and accumulated by the participants are used to purchase shares of common stock at the end of each purchase period. The price of stock purchased under the 2000 Employee Stock Purchase Plan is generally 85% of the lower of the fair market value of the common stock at the beginning of the offering period or at the end of the purchase period. Participants may end their participation at any time during an offering period, and they will be paid their payroll deductions to date. Participation ends automatically upon termination of employment with us.

Rights granted under the 2000 Employee Stock Purchase Plan are not transferable by a participant other than by will, the laws of descent and distribution, or as otherwise provided under the plan. The 2000 Employee Stock Purchase Plan provides that, in the event of our merger with or into another corporation or a sale of substantially all our assets, each outstanding option may be assumed or substituted for by the successor corporation. If the successor corporation refuses to assume or substitute for the outstanding options, the offering period then in progress will be shortened and a new exercise date will be set. The 2000 Employee Stock Purchase Plan will terminate automatically in 2010, unless terminated earlier. The Board of Directors has the authority to amend or terminate the purchase plan, except that no such action may adversely affect any outstanding rights to purchase stock under the 2000 Employee Stock Purchase Plan. Our Board of Directors has the exclusive authority to interpret and apply the provisions of the purchase plan.

DESCRIPTION OF ARTWORK:

INSIDE FRONT COVER PAGE:

The following words will appear across the top of the page in large, bold type letters:

"Pain Therapeutics, Inc. is developing a new generation of opioid painkillers. Our goal is to build a leading specialty pharmaceutical company in pain management."

Below, there will be an outline of an opium poppy plant with an overlay of a table depicting our clinical development progress for product candidates PTI-555, PTI-501, PTI-601 and PTI-701. The following text will appear in the far left column of the table:

PTI-555

- o Treatment of moderate to severe pain
- o Substitute for oral morphine

PTI-501

- o Treatment of moderate to severe pain
- o Substitute for injectable morphine

PTI-601

- o Treatment of moderate pain
- o Substitute for tramadol

PTI-701

- o Treatment of moderate pain
- o Substitute for hydrocodone and other weak opioids

The following words appear at the bottom of the page:

"All of our drug combinations are derived from the opium poppy plant."

BUSINESS SECTION:

On page 30, we have included a diagram depicting the types of pain, with examples of each type, that are typically treated with opioid drugs.

On page 31, we have included a table describing the three segments of the pain management market and 1998 U.S. sales for typical opioid pain killers in each segment.

On page 34, we have included a table summarizing our current four product candidates and the stage of development and a description of the formulation of each product candidate.

INSIDE BACK COVER PAGE:

The page is titled "Technology Overview" and is comprised of two diagrams. The first diagram depicts the effect of an opioid agonist on inhibitory and excitatory pathways in the nervous system. The following text appears below the first diagram:

"Opioid agonists, such as morphine, activate an inhibitory pathway in the nervous system, which leads to pain relief. Simultaneously, opioid agonists activate an excitatory pathway, leading to a partial blocking of pain relief as well as adverse side effects, tolerance, and potentially, addiction."

The second diagram depicts the effect of our opioid agonist/low-dose opioid antagonist drugs on inhibitory and excitatory pathways in the nervous system. The following text appears below the second diagram:

"When an opioid agonist is combined with a low-dose opioid antagonist, such as naloxone or naltrexone, the low-dose antagonist preferentially blocks the excitatory pathway. Studies indicate this results in enhanced pain relief, a reduction in adverse side effects, and attenuated tolerance, and, potentially addiction."

LOGO

UNTIL _____, 2000, ALL DEALERS THAT EFFECT TRANSACTIONS IN THESE SECURITIES, WHETHER OR NOT PARTICIPATING IN THIS OFFERING, MAY BE REQUIRED TO DELIVER A PROSPECTUS. THIS IS IN ADDITION TO THE DEALER'S OBLIGATION TO DELIVER A PROSPECTUS WHEN ACTING AS AN UNDERWRITER AND WITH RESPECT TO UNSOLD ALLOTMENTS OR SUBSCRIPTIONS.

THE INFORMATION IN THIS PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. WE MAY NOT SELL THESE SECURITIES UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THIS PROSPECTUS IS NOT AN OFFER TO SELL THESE SECURITIES AND IT IS NOT SOLICITING AN OFFER TO BUY THESE SECURITIES IN ANY STATE WHERE THE OFFER OR SALE IS NOT PERMITTED.

SUBJECT TO COMPLETION, DATED MARCH 13, 2000

LOGO

SHARES

COMMON STOCK

Pain Therapeutics, Inc. is offering _____ shares of its common stock. This is our initial public offering, and no public market currently exists for our shares. We have applied to have our common stock approved for quotation on the Nasdaq Stock Market's National Market under the symbol "PTIE." We anticipate that the initial public offering price will be between \$ _____ and \$ _____ per share.

 INVESTING IN OUR COMMON STOCK INVOLVES RISKS.
 SEE "RISK FACTORS" BEGINNING ON PAGE 6.

	PER SHARE	TOTAL
	-----	-----
Public Offering Price.....	\$	\$
Underwriting Discounts and Commissions.....	\$	\$
Proceeds to Pain Therapeutics, Inc.....	\$	\$

THE SECURITIES AND EXCHANGE COMMISSION AND STATE SECURITIES REGULATORS HAVE NOT APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

Pain Therapeutics, Inc. has granted the underwriters a 30-day option to purchase up to an additional _____ shares of common stock to cover over-allotments. FleetBoston Robertson Stephens Inc. expects to deliver the shares to the purchasers on _____, 2000.

ROBERTSON STEPHENS INTERNATIONAL
 CIBC WORLD MARKETS

LAZARD FRERES & CO. LLC

THE DATE OF THIS PROSPECTUS IS _____, 2000.

PART II

INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 13. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION

The following table sets forth the costs and expenses, other than underwriting discounts and commissions, payable by Pain Therapeutics, Inc. in connection with the sale of common stock being registered. All amounts are estimates except the SEC registration fee and the NASD filing fee.

SEC registration fee.....	\$19,800
NASD filing fee.....	8,000
Nasdaq National Market listing fee.....	
Printing and engraving costs.....	
Legal fees and expenses.....	
Accounting fees and expenses.....	
Blue Sky fees and expenses.....	
Transfer Agent and Registrar fees.....	
Miscellaneous expenses.....	

Total.....	\$ =====

ITEM 14. INDEMNIFICATION OF DIRECTORS AND OFFICERS

Section 145 of the Delaware General Corporation Law permits a corporation to include in its charter documents, and in agreements between the corporation and its directors and officers, provisions expanding the scope of indemnification beyond that specifically provided by the current law.

Article VIII of the Registrant's Amended and Restated Certificate of Incorporation provides for the indemnification of directors to the fullest extent permissible under Delaware law.

Article VI of the Registrant's Amended and Restated Bylaws provides for the indemnification of officers, directors and third parties acting on behalf of the Registrant if such person acted in good faith and in a manner reasonably believed to be in and not opposed to the best interest of the Registrant, and, with respect to any criminal action or proceeding, the indemnified party had no reason to believe his or her conduct was unlawful.

The Registrant has entered into indemnification agreements with its directors and executive officers, in addition to indemnification provided for in the Registrant's Amended and Restated Bylaws, and intends to enter into indemnification agreements with any new directors and executive officers in the future.

ITEM 15. RECENT SALES OF UNREGISTERED SECURITIES

Since inception, we have issued unregistered securities to a limited number of persons as described below:

Common Stock:

- (1) In June 1998, we sold 8,480,000 shares of our common stock at a price of \$0.001 per share to a founder for \$8,480.

- (2) In June 1998, we sold an aggregate of 20,000 shares of our common stock at a price of \$0.001 per share to investors for an aggregate purchase price of \$20.
- (3) In September 1998, we sold 100,000 shares of our common stock at a price of \$0.10 per share to an investor for a purchase price of \$10,000.
- (4) In September 1998, we sold an aggregate of 400,000 shares of our common stock at a price of \$0.10 per share to investors for an aggregate purchase price of \$40,000.
- (5) In April 1999, we sold 300,000 shares of our common stock to an investor at a price of \$0.10 per share for a purchase price of \$30,000.
- (6) In May 1999, we sold an aggregate of 144,000 shares of our common stock to investors at a price of \$0.10 per share for an aggregate purchase price of \$14,400.
- (7) In June 1999, we sold 1,000 shares of our common stock to a consultant at a price of \$0.10 per share for a total value of \$100.
- (8) In February 2000, we sold an aggregate of 245,000 shares of our common stock at a price of \$0.20 per share for an aggregate purchase price of \$49,000.

Preferred Stock:

- (1) In August 1998, we sold an aggregate of 1,100,000 shares of our series A convertible preferred stock to investors at a price of \$1.00 per share for an aggregate purchase price of \$1,100,000.
- (2) In October 1998, we sold an aggregate of 1,559,489 shares of our series A convertible preferred stock to investors at a price of \$1.00 per share for an aggregate purchase price of \$1,559,489.
- (3) In October 1999, we sold an aggregate of 4,846,320 shares of our series B redeemable convertible preferred stock to investors at a price of \$1.85 per share for an aggregate purchase price of \$8,956,692.
- (4) In November 1999, we sold an aggregate of 559,085 shares of our series B redeemable convertible preferred stock to investors at a price of \$1.85 per share for an aggregate purchase price of \$1,034,307.
- (5) In February 2000, we sold an aggregate of 3,044,018 shares of our series C redeemable convertible preferred stock to investors at a price of \$5.00 per share for an aggregate purchase price of \$15,220,090.

Stock Options and Stock Purchase Rights:

- (1) From inception through March 2000, we granted stock options and stock purchase rights to acquire an aggregate of 2,965,200 shares of our common stock at prices ranging from \$0.10 to \$2.00 per share to employees, consultants and directors pursuant to our 1998 Stock Plan.
- (2) From inception through March 2000, we issued an aggregate of 1,190,000 shares of our common stock to employees, consultants and directors pursuant to the exercise of stock options and stock purchase rights under our 1998 Stock Plan, for aggregate consideration of \$143,500.

Warrants:

- (1) In June 1998, we issued a warrant to acquire 150,000 shares of our series A convertible preferred stock at an exercise price of \$1.00 per share to an investor.
- (2) In August 1998, we issued a warrant to acquire 70,000 shares of our common stock at an exercise price of \$1.00 per share to our landlord.
- (3) In February 2000, we issued a warrant to acquire 120,000 shares of our common stock at an exercise price of \$5.00 per share to an investor.

For additional information concerning these equity investment transactions, reference is made to the information contained under the caption "Certain Transactions" in the form of prospectus included herein. The sales of the above securities were deemed to be exempt from registration in reliance on Rule 701 promulgated under Section 3(b) under the Securities Act as transactions pursuant to a compensatory benefit plan or a written contract relating to compensation, or in reliance on Section 4(2) of the Securities Act or Regulation D promulgated thereunder as transactions by an issuer not involving any public offering. The recipients of securities in each such transaction represented their intention to acquire the securities for investment only and not with a view to or for sale in connection with any distribution thereof and appropriate legends were affixed to the share certificates and other instruments issued in such transactions. All recipients either received adequate information about Pain Therapeutics, Inc. or had access, through employment or other relationships, to such information.

ITEM 16. EXHIBITS AND FINANCIAL STATEMENT SCHEDULES

(a) EXHIBITS

EXHIBIT INDEX

EXHIBIT
NUMBER

- - - - -

1.1*	Form of Underwriting Agreement
3.1	Form of Amended and Restated Certificate of Incorporation of the Registrant to be in effect upon closing of this offering
3.2	Form of Bylaws of the Registrant to be in effect upon closing of this offering
4.1*	Form of stock certificates
5.1*	Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation
10.1	Form of Indemnification Agreement between the Registrant and each of its directors and officers
10.2+	License Agreement, dated May 5, 1998, between Registrant and Albert Einstein College of Medicine
10.3	Research Agreement dated May 14, 1999 between the Registrant and KP Pharmaceutical Technology, Inc.
10.4	Lease Agreement dated August 25, 1998 between the Registrant and Britannia Pointe Grand Limited Partnership
10.5	1998 Stock Plan, as amended, and form of agreements thereunder between the Registrant and certain securityholders
10.6*	2000 Employee Stock Purchase Plan
10.7	Second Amended and Restated Investors' Rights Agreement dated as of February 1, 2000 between Registrant and the holders of its series B and series C redeemable convertible preferred stock
10.8	Employment Agreement dated July 1, 1998 between the Registrant and Mr. Barbier
10.9	Employment Offer Letter dated December 3, 1999 between the Registrant and Mr. Jennings

EXHIBIT
NUMBER

10.10	Employment Offer Letter dated November 23, 1999 between the Registrant and Mr. Johnson
10.11	Employment Offer Letter dated March 29, 1999 between the Registrant and Dr. Sherman
23.1	Consent of KPMG LLP, Independent Certified Public Accountants
23.2*	Consent of Counsel (see Exhibit 5.1)
24.1	Power of Attorney (see page II-6)
27.1	Financial Data Schedule

+ Confidential treatment has been requested for certain portions of this agreement. The omitted portions will be separately filed with the Securities and Exchange Commission.

* To be filed by amendment.

Schedules not listed above have been omitted because the information required to be set forth therein is not applicable or is shown in the financial statements or notes thereto.

ITEM 17. UNDERTAKINGS

The undersigned Registrant hereby undertakes to provide to the Underwriters at the closing specified in the Underwriting Agreement certificates in such denominations and registered in such names as required by the Underwriters to permit prompt delivery to each purchaser.

Insofar as indemnification by the Registrant for liabilities arising under the Securities Act may be permitted to directors, officers and controlling persons of the Registrant pursuant to the provisions referenced in Item 14 of this Registration Statement 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 a director, officer or controlling person in connection with the securities being registered hereunder, 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.

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 any 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, as amended, the registrant has duly caused this Registration Statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of Palo Alto, State of California, on the 13th day of March, 2000.

PAIN THERAPEUTICS, INC.

By: /s/ REMI BARBIER

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

POWER OF ATTORNEY

KNOW ALL PERSONS BY THESE PRESENTS, that each person whose signature appears below constitutes and appoints Remi Barbier and David L. Johnson, and each of them, his attorneys-in-fact, each with the power of substitution, for him and in his name, place and stead, in any and all capacities, to sign any and all amendments (including post-effective amendments) to this Registration Statement, and to sign any registration statement for the same offering covered by this Registration Statement that is to be effective upon filing pursuant to Rule 462(b) promulgated under the Securities Act of 1933, as amended, and all post-effective amendments thereto, and to file the same, with all exhibits thereto and all documents in connection therewith, with the Securities and Exchange Commission, granting unto said attorneys-in-fact and agents, and each of them, full power and authority to do and perform each and every act and thing requisite and necessary to be done in and about the premises, as fully to all intents and purposes as he might or could do in person, hereby ratifying and confirming all that such attorneys-in-fact and agents or any of them, or his or their substitute or substitutes, may lawfully do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Act of 1933, as amended, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated:

SIGNATURE -----	TITLE -----	DATE ----
/s/ REMI BARBIER ----- Remi Barbier	President, Chief Executive Officer and Chairman of the Board of Directors (Principal Executive Officer)	March 13, 2000
/s/ DAVID L. JOHNSON ----- David L. Johnson	Vice President, Finance and Chief Financial Officer (Principal Financial and Accounting Officer)	March 13, 2000

SIGNATURE -----	TITLE -----	DATE -----
/s/ GERT CASPRITZ, PH.D. ----- Gert Caspritz, Ph.D.	Director	March 13, 2000
/s/ NADAV FRIEDMANN, M.D., PH.D. ----- Nadav Friedmann, M.D., Ph.D.	Director	March 13, 2000
/s/ WILFRED R. KONNEKER, PH.D. ----- Wilfred R. Konneker, Ph.D.	Director	March 13, 2000
/s/ MICHAEL J. O'DONNELL ----- Michael J. O'Donnell	Director	March 13, 2000
/s/ SANFORD R. ROBERTSON ----- Sanford R. Robertson	Director	March 13, 2000

EXHIBIT INDEX

EXHIBIT
NUMBER

- 1.1* Form of Underwriting Agreement
- 3.1 Form of Amended and Restated Certificate of Incorporation of the Registrant to be in effect upon closing of this offering
- 3.2 Form of Bylaws of the Registrant to be in effect upon closing of this offering
- 4.1* Form of stock certificates
- 5.1* Opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation
- 10.1 Form of Indemnification Agreement between the Registrant and each of its directors and officers
- 10.2+ License Agreement, dated May 5, 1998, between Registrant and Albert Einstein College of Medicine
- 10.3 Research Agreement dated May 14, 1999 between the Registrant and KP Pharmaceutical Technology, Inc.
- 10.4 Lease Agreement dated August 25, 1998 between the Registrant and Britannia Pointe Grand Limited Partnership
- 10.5 1998 Stock Plan, as amended, and form of agreements thereunder between the Registrant and certain securityholders
- 10.6* 2000 Employee Stock Purchase Plan
- 10.7 Second Amended and Restated Investors' Rights Agreement dated as of February 1, 2000 between Registrant and the holders of its series B and C redeemable convertible preferred stock
- 10.8 Employment Agreement dated July 1, 1998 between the Registrant and Mr. Barbier
- 10.9 Employment Offer Letter dated December 3, 1999 between the Registrant and Mr. Jennings
- 10.10 Employment Offer Letter dated November 23, 1999 between the Registrant and Mr. Johnson
- 10.11 Employment Offer Letter dated March 29, 1999 between the Registrant and Dr. Sherman
- 23.1 Consent of KPMG LLP, Independent Certified Public Accountants
- 23.2* Consent of Counsel (see Exhibit 5.1)
- 24.1 Power of Attorney (see page II-6)
- 27.1 Financial Data Schedule

+ Confidential treatment has been requested for certain portions of this agreement. The omitted portions will be separately filed with the Securities and Exchange Commission.

* To be filed by amendment.

AMENDED AND RESTATED CERTIFICATE OF INCORPORATION

OF

PAIN THERAPEUTICS, INC.

Pain Therapeutics, Inc., a corporation organized and existing under the laws of the State of Delaware (the "Corporation"), hereby certifies that:

A. The name of this Corporation is Pain Therapeutics, Inc.

B. The date of filing of this Corporation's original Certificate of Incorporation with the Secretary of State of Delaware was May 4, 1998.

C. Pursuant to Sections 242 and 245 of the Delaware General Corporation law, this Restated Certificate of Incorporation restates, integrates and amends the provisions of the Corporation's Amended and Restated Certificate of Incorporation as follows:

FIRST: The name of this Corporation is Pain Therapeutics, Inc.

SECOND: The address of the Corporation's registered office in the State of Delaware is 1209 Orange Street, Wilmington, County of New Castle, Delaware 19801. The name of its registered agent at such address is The Corporation Trust Company.

THIRD: The purpose of this Corporation is to engage in any lawful act or activity for which corporations may be organized under the General Corporation Law of Delaware.

FOURTH: This Corporation is authorized to issue two classes of shares to be designated, respectively, Common Stock and Preferred Stock. The total number of shares of Common Stock which this corporation is authorized to issue is 120,000,000, with a par value of \$0.001, and the total number of shares of Preferred Stock which this corporation is authorized to issue is 10,000,000, with a par value of \$0.001.

The Preferred Stock may be issued from time to time in one or more series pursuant to a resolution or resolutions providing for such issue duly adopted by the Board of Directors (authority to do so being hereby expressly vested in the Board). The Board of Directors is further authorized to determine or alter the rights, preferences, privileges and restrictions granted to or imposed upon any wholly unissued series of Preferred Stock and, to fix the number of shares of any such series of Preferred Stock and the designation of any such series of Preferred Stock. The Board of Directors is authorized, within the limits and restrictions stated in any resolution or resolutions of the Board of Directors originally fixing the number of shares constituting any series, to increase or decrease (but not below the number of shares thereof then outstanding) the number of shares of any such series

subsequent to the issue of shares of that series, to determine the designation of any series, and to fix the number of shares of any series.

FIFTH: The Corporation is to have perpetual existence.

SIXTH: Elections of directors need not be by written ballot unless a stockholder demands election by written ballot at the meeting and before voting begins or unless the Bylaws of the Corporation shall so provide.

SEVENTH: The management of the business and the conduct of the affairs of the Corporation shall be vested in its Board of Directors. The number of directors which shall constitute the whole Board of Directors shall be designated in the Bylaws of the Corporation.

The Board of Directors shall be divided into three classes designated as Class I, Class II, and Class III, respectively. Directors shall be assigned to each class in accordance with a resolution or resolutions adopted by the Board of Directors. At the first annual meeting of stockholders following the date hereof, the term of office of the Class I directors shall expire, and Class I directors shall be elected for a full term of three years. At the second annual meeting of stockholders following the date hereof, the term of office of the Class II directors shall expire, and Class II directors shall be elected for a full term of three years. At the third annual meeting of stockholders following the date hereof, the term of office of the Class III directors shall expire, and Class III directors shall be elected for a full term of three years. At each succeeding annual meeting of stockholders, directors shall be elected for a full term of three years to succeed the directors of the class whose terms expire at such annual meeting.

Notwithstanding the foregoing provisions of this Article, each director shall serve until his or her successor is duly elected and qualified or until his or her death, resignation, or removal. No decrease in the number of directors constituting the Board of Directors shall shorten the term of any incumbent director.

Any vacancies on the Board of Directors resulting from death, resignation, disqualification, removal, or other causes shall be filled by either (i) the affirmative vote of the holders of a majority of the voting power of the then-outstanding shares of voting stock of the Corporation entitled to vote generally in the election of directors (the "Voting Stock") voting together as a single class; or (ii) by the affirmative vote of a majority of the remaining directors then in office, even though less than a quorum of the Board of Directors. Newly created directorships resulting from any increase in the number of directors shall, unless the Board of Directors determines by resolution that any such newly created directorship shall be filled by the stockholders, be filled only by the affirmative vote of the directors then in office, even though less than a quorum of the Board of Directors. Any director elected in accordance with the preceding sentence shall hold office for the remainder of the full term of the class of directors in which the new directorship was created or the vacancy occurred and until such director's successor shall have been elected and qualified.

The affirmative vote of sixty-six and two-thirds percent (66-2/3%) of the voting power of the then outstanding shares of Voting Stock, voting together as a single class, shall be required for the

adoption, amendment or repeal of the following sections of the Corporation's Bylaws by the stockholders of the Corporation: 2.2 (Annual Meeting) and 2.3 (Special Meeting).

No action shall be taken by the stockholders of the Corporation except at an annual or special meeting of the stockholders called in accordance with the Bylaws.

Any director, or the entire Board of Directors, may be removed from office at any time (i) with cause by the affirmative vote of the holders of at least a majority of the voting power of all of the then-outstanding shares of the Voting Stock, voting together as a single class; or (ii) without cause by the affirmative vote of the holders of at least sixty-six and two-thirds percent (66-2/3%) of the voting power of all of the then-outstanding shares of the Voting Stock.

EIGHTH: A. To the fullest extent permitted by the Delaware General Corporation Law as the same exists or as may hereafter be amended, a director of the Corporation or any subsidiary of the Corporation shall not be personally liable to the Corporation or its stockholders and shall otherwise be indemnified by the Corporation for monetary damages for breach of fiduciary duty as a director of the Corporation, any predecessor of the Corporation or any subsidiary of the Corporation.

B. The Corporation shall indemnify to the fullest extent permitted by law any person made or threatened to be made a party to an action or proceeding, whether criminal, civil, administrative or investigative, by reason of the fact that he, his testator or intestate is or was a director or officer of the Corporation, any predecessor of the Corporation or any subsidiary of the Corporation or serves or served at any other enterprise as a director or officer at the request of the Corporation, any predecessor to the Corporation or any subsidiary of the Corporation.

C. Neither any amendment nor repeal of this Article EIGHTH, nor the adoption of any provision of the Corporation's Certificate of Incorporation inconsistent with this Article EIGHTH, shall eliminate or reduce the effect of this Article EIGHTH, in respect of any matter occurring, or any action or proceeding accruing or arising or that, but for this Article EIGHTH, would accrue or arise, prior to such amendment, repeal, or adoption of an inconsistent provision.

NINTH: Notwithstanding any other provisions of this Certificate of Incorporation or any provision of law which might otherwise permit a lesser vote or no vote, but in addition to any affirmative vote of the holders of any particular class or series of the Voting Stock required by law, this Certificate of Incorporation or any rights of designation of Preferred Stock conferred on the Board of Directors pursuant to Article FOURTH, the affirmative vote of the holders of at least sixty-six and two-thirds percent (66-2/3%) of the voting power of all of the then-outstanding shares of the Voting Stock, voting together as a single class, shall be required to alter, amend or repeal Article SEVENTH or this Article NINTH.

TENTH: The Corporation reserves the right to amend, alter, change or repeal any provision contained in this Certificate of Incorporation, in the manner now or hereafter prescribed by statute, except as provided in Article NINTH of this Certificate, and all rights conferred upon the stockholders herein are granted subject to this right.

ELEVENTH: In furtherance and not in limitation of the powers conferred by statute, the Board of Directors is expressly authorized to make, alter, amend or repeal the Bylaws of the Corporation.

TWELFTH: Meetings of stockholders may be held within or without the State of Delaware, as the Bylaws may provide. The books of the Corporation may be kept (subject to any provision contained in the statutes) outside of the State of Delaware at such place or places as may be designated from time to time by the Board of Directors or in the Bylaws of the Corporation.

THIRTEENTH: Advance written notice of new business and stockholder nominations for the election of directors shall be given in the manner and to the extent provided in the Bylaws of the Corporation.

FOURTEENTH: Stockholders shall not be entitled to cumulative voting rights for the election of directors.

This Amended and Restated Certificate of Incorporation has been duly adopted by the stockholders of the Corporation in accordance with the provisions of Sections 242 and 245 of the General Corporation Law of the State of Delaware, as amended.

IN WITNESS WHEREOF, Pain Therapeutics, Inc. has caused this Amended and Restated Certificate of Incorporation to be signed by Remi Barbier, its President, and attested by Michael O'Donnell, its Secretary, this ____ day of _____, 2000.

Pain Therapeutics, Inc.

Remi Barbier, President

Attested:

Michael O'Donnell, Secretary

AMENDED AND RESTATED BYLAWS

OF

PAIN THERAPEUTICS, INC.
A DELAWARE CORPORATION

TABLE OF CONTENTS

	PAGE

ARTICLE I - STOCKHOLDERS.....	1
1. ANNUAL MEETINGS.....	1
2. SPECIAL MEETINGS.....	1
3. NOTICE OF MEETINGS.....	1
4. ADJOURNMENTS.....	1
5. QUORUM.....	2
6. ORGANIZATION.....	2
7. VOTING; PROXIES.....	2
8. FIXING DATE FOR DETERMINATION OF STOCKHOLDERS OF RECORD.....	3
9. LIST OF STOCKHOLDERS ENTITLED TO VOTE.....	3
10. ACTION BY CONSENT OF STOCKHOLDERS.....	4
ARTICLE II - BOARD OF DIRECTORS.....	4
1. NUMBER; QUALIFICATIONS.....	4
2. ELECTION; RESIGNATION; REMOVAL; VACANCIES.....	4
3. REGULAR MEETINGS.....	5
4. SPECIAL MEETINGS.....	5
5. TELEPHONIC MEETINGS PERMITTED.....	5
6. QUORUM; VOTE REQUIRED FOR ACTION.....	5
7. ORGANIZATION.....	5
8. INFORMAL ACTION BY DIRECTORS.....	5
ARTICLE III - COMMITTEES.....	6
1. COMMITTEES.....	6
2. COMMITTEE RULES.....	6
ARTICLE IV - OFFICERS.....	7
1. EXECUTIVE OFFICERS; ELECTION; QUALIFICATIONS; TERM OF OFFICE; RESIGNATION; REMOVAL; VACANCIES.....	7
2. POWERS AND DUTIES OF EXECUTIVE OFFICERS.....	7
ARTICLE V - STOCK.....	7
1. CERTIFICATES.....	7
2. LOST, STOLEN OR DESTROYED STOCK CERTIFICATES; ISSUANCE OF NEW CERTIFICATES.....	8

ARTICLE VI - INDEMNIFICATION.....	8
1. THIRD PARTY ACTIONS.....	8
2. ACTIONS BY OR IN THE RIGHT OF THE CORPORATION.....	8
3. SUCCESSFUL DEFENSE.....	9
4. DETERMINATION OF CONDUCT.....	9
5. PAYMENT OF EXPENSES IN ADVANCE.....	9
6. INDEMNITY NOT EXCLUSIVE.....	9
7. INSURANCE INDEMNIFICATION.....	10
8. THE CORPORATION.....	10
9. EMPLOYEE BENEFIT PLANS.....	10
10. INDEMNITY FUND.....	10
11. INDEMNIFICATION OF OTHER PERSONS.....	11
12. SAVINGS CLAUSE.....	11
13. CONTINUATION OF INDEMNIFICATION AND ADVANCEMENT OF EXPENSES.....	11
ARTICLE VII - MISCELLANEOUS.....	11
1. FISCAL YEAR.....	11
2. SEAL.....	11
3. WAIVER OF NOTICE OF MEETINGS OF STOCKHOLDERS, DIRECTORS AND COMMITTEES.....	12
4. INTERESTED DIRECTORS; QUORUM.....	12
5. FORM OF RECORDS.....	12
6. AMENDMENT OF BY-LAWS.....	13

AMENDED AND RESTATED BYLAWS

OF

PAIN THERAPEUTICS, INC.
a Delaware corporationARTICLE I
STOCKHOLDERS

1. ANNUAL MEETINGS

An annual meeting of stockholders shall be held for the election of directors at such date, time and place, either within or without the state of Delaware, as may be designated by resolution of the Board of Directors from time to time. Any other proper business may be transacted at the annual meeting.

2. SPECIAL MEETINGS

Special meetings of stockholders for any purpose or purposes may be called at any time by the Board of Directors, or by a committee of the Board of Directors which has been duly designated by the Board of Directors and whose powers and authority, as expressly provided in a resolution of the Board of Directors, include the power to call such meetings, or by one or more shareholders holding shares in the aggregate entitled to cast not less than ten percent (10%) of the votes at that meeting, but such special meetings may not be called by any other person or persons.

3. NOTICE OF MEETINGS

Whenever stockholders are required or permitted to take any action at a meeting, a written notice of the meeting shall be given which shall state the place, date and hour of the meeting, and, in the case of a special meeting, the purpose or purposes for which the meeting is called. Unless otherwise provided by law, the certificate of incorporation or these by-laws, the written notice of any meeting shall be given not less than ten nor more than sixty days before the date of the meeting to each stockholder entitled to vote at such meeting. If mailed, such notice shall be deemed to be given when deposited in the mail, postage prepaid, directed to the stockholder at his address as it appears on the records of the corporation.

4. ADJOURNMENTS

Any meeting of stockholders, annual or special, may adjourn from time to time to reconvene at the same or some other place, and notice need not be given of any such adjourned meeting if the

time and place thereof are announced at the meeting at which the adjournment is taken. At the adjourned meeting the corporation may transact any business which might have been transacted at the original meeting. If the adjournment is for more than thirty days, or if after the adjournment a new record date is fixed for the adjourned meeting, a notice of the adjourned meeting shall be given to each stockholder of record entitled to vote at the meeting.

5. QUORUM

Except as otherwise provided by law, the certificate of incorporation or these by-laws, at each meeting of stockholders the presence in person or by proxy of the holders of shares of stock having a majority of the votes which could be cast by the holders of all outstanding shares of stock entitled to vote at the meeting shall be necessary and sufficient to constitute a quorum. In the absence of a quorum, the stockholders so present may, by majority vote, adjourn the meeting from time to time in the manner provided in Section 1.4 of these by-laws until a quorum shall attend. Shares of its own stock belonging to the corporation or to another corporation, if a majority of the shares entitled to vote in the election of directors of such other corporation is held, directly or indirectly, by the corporation, shall neither be entitled to vote nor be counted for quorum purposes; provided, however, that the foregoing shall not limit the right of the corporation to vote stock, including but not limited to its own stock, held by it in a fiduciary capacity.

6. ORGANIZATION

Meetings of stockholders shall be presided over by the Chairman of the Board, if any, or in his absence by the Vice Chairman of the Board, if any, or in his absence by the President, or in his absence by a Vice President, or in the absence of the foregoing persons by a chairman designated by the Board of Directors, or in the absence of such designation by a chairman chosen at the meeting. The Secretary shall act as secretary of the meeting, but in his absence the chairman of the meeting may appoint any person to act as secretary of the meeting.

7. VOTING; PROXIES

Except as otherwise provided by the certificate of incorporation, each stockholder entitled to vote at any meeting of stockholders shall be entitled to one vote for each share of stock held by him which has voting power upon the matter in question. Each stockholder entitled to vote at a meeting of stockholders may authorize another person or persons to act for him by proxy, but no such proxy shall be voted or acted upon after three years from its date, unless the proxy provides for a longer period. A duly executed proxy shall be irrevocable if it states that it is irrevocable and if, and only as long as, it is coupled with an interest sufficient in law to support an irrevocable power. A stockholder may revoke any proxy which is not irrevocable by attending the meeting and voting in person or by filing an instrument in writing revoking the proxy or another duly executed proxy bearing a later date with the Secretary of the corporation. Voting at meetings of stockholders need not be by written ballot and need not be conducted by inspectors of election unless so determined by the holders of shares of stock having a majority of the votes which could be cast by the holders of all

outstanding shares of stock entitled to vote thereon which are present in person or by proxy at such meeting. At all meetings of stockholders for the election of directors a plurality of the votes cast shall be sufficient to elect. All other elections and questions shall, unless otherwise provided by law, the certificate of incorporation or these by-laws, be decided by the vote of the holders of shares of stock having a majority of the votes which could be cast by the holders of all shares of stock entitled to vote thereon which are present in person or represented by proxy at the meeting.

8. FIXING DATE FOR DETERMINATION OF STOCKHOLDERS OF RECORD

In order that the corporation may determine the stockholders entitled to notice of or to vote at any meeting of stockholders or any adjournment thereof, or to express consent to corporate action in writing without a meeting, or entitled to receive payment of any dividend or other distribution or allotment of any rights, or entitled to exercise any rights in respect of any change, conversion or exchange of stock or for the purpose of any other lawful action, the Board of Directors may fix a record date, which record date shall not precede the date upon which the resolution fixing the record date is adopted by the Board of Directors and which record date: (1) in the case of determination of stockholders entitled to vote at any meeting of stockholders or adjournment thereof, shall, unless otherwise required by law, not be more than sixty nor less than ten days before the date of such meeting; (2) in the case of determination of stockholders entitled to express consent to corporate action in writing without a meeting, shall not be more than ten days from the date upon which the resolution fixing the record date is adopted by the Board of Directors; and (3) in the case of any other action, shall not be more than sixty days prior to such other action. If no record date is fixed: (1) the record date for determining stockholders entitled to notice of or to vote at a meeting of stockholders shall be at the close of business on the day next preceding the day on which notice is given, or, if notice is waived, at the close of business on the day next preceding the day on which the meeting is held; (2) the record date for determining stockholders entitled to express consent to corporate action in writing without a meeting when no prior action of the Board of Directors is required by law, shall be the first date on which a signed written consent setting forth the action taken or proposed to be taken is delivered to the corporation in accordance with applicable law, or, if prior action by the Board of Directors is required by law, shall be at the close of business on the day on which the Board of Directors adopts the resolution taking such prior action; and (3) the record date for determining stockholders for any other purpose shall be at the close of business on the day on which the Board of Directors adopts the resolution relating thereto. A determination of stockholders of record entitled to notice of or to vote at a meeting of stockholders shall apply to any adjournment of the meeting; provided, however, that the Board of Directors may fix a new record date for the adjourned meeting.

9. LIST OF STOCKHOLDERS ENTITLED TO VOTE

The Secretary shall prepare and make, at least ten days before every meeting of stockholders, a complete list of the stockholders entitled to vote at the meeting, arranged in alphabetical order, and showing the address of each stockholder and the number of shares registered in the name of each stockholder. Such list shall be open to the examination of any stockholder, for any purpose germane to the meeting, during ordinary business hours, for a period of at least ten days prior to the meeting,

either at a place within the city where the meeting is to be held, which place shall be specified in the notice of the meeting, or, if not so specified, at the place where the meeting is to be held. The list shall also be produced and kept at the time and place of the meeting during the whole time thereof and may be inspected by any stockholder who is present. Upon the willful neglect or refusal of the directors to produce such a list at any meeting for the election of directors, they shall be ineligible for election to any office at such meeting. The stock ledger shall be the only evidence as to who are the stockholders entitled to examine the stock ledger, the list of stockholders or the books of the corporation, or to vote in person or by proxy at any meeting of stockholders.

10. ACTION BY CONSENT OF STOCKHOLDERS

Unless otherwise restricted by the certificate of incorporation, any action required or permitted to be taken at any annual or special meeting of the stockholders may be taken without a meeting, without prior notice and without a vote, if a consent in writing, setting forth the action so taken, shall be signed by the holders of outstanding stock having not less than the minimum number of votes that would be necessary to authorize or take such action at a meeting at which all shares entitled to vote thereon were present and voted. Prompt notice of the taking of the corporate action without a meeting by less than unanimous written consent shall be given to those stockholders who have not consented in writing.

ARTICLE II BOARD OF DIRECTORS

1. NUMBER; QUALIFICATIONS

The Board of Directors shall consist of one or more members, the number thereof to be determined from time to time by resolution of the Board of Directors. Directors need not be stockholders.

2. ELECTION; RESIGNATION; REMOVAL; VACANCIES

The Board of Directors shall initially consist of the persons named as directors in the certificate of incorporation, and each director so elected shall hold office until the first annual meeting of stockholders or until his successor is elected and qualified. At the first annual meeting of stockholders and at each annual meeting thereafter, the stockholders shall elect directors each of whom shall hold office for a term of one year or until his successor is elected and qualified. Any director may resign at any time upon written notice to the corporation. Any newly created directorship or any vacancy occurring in the Board of Directors for any cause may be filled by a majority of the remaining members of the Board of Directors, although such majority is less than a quorum, or by a plurality of the votes cast at a meeting of stockholders, and each director so elected

shall hold office until the expiration of the term of office of the director whom he has replaced or until his successor is elected and qualified.

3. REGULAR MEETINGS

Regular meetings of the Board of Directors may be held at such places within or without the State of Delaware and at such times as the Board of Directors may from time to time determine, and if so determined notices thereof need not be given.

4. SPECIAL MEETINGS

Special meetings of the Board of Directors may be held at any time or place within or without the State of Delaware whenever called by the President, any Vice President, the Secretary, or by any member of the Board of Directors. Notice of a special meeting of the Board of Directors shall be given by the person or persons calling the meeting at least twenty-four hours before the special meeting.

5. TELEPHONIC MEETINGS PERMITTED

Members of the Board of Directors, or any committee designated by the Board of Directors, may participate in a meeting thereof by means of conference telephone or similar communications equipment by means of which all persons participating in the meeting can hear each other, and participation in a meeting pursuant to this by-law shall constitute presence in person at such meeting.

6. QUORUM; VOTE REQUIRED FOR ACTION

At all meetings of the Board of Directors a majority of the whole Board of Directors shall constitute a quorum for the transaction of business. Except in cases in which the certificate of incorporation or these by-laws otherwise provide, the vote of a majority of the directors present at a meeting at which a quorum is present shall be the act of the Board of Directors.

7. ORGANIZATION

Meetings of the Board of Directors shall be presided over by the Chairman of the Board, if any, or in his absence by the Vice Chairman of the Board, if any, or in his absence by the President, or in their absence by a chairman chosen at the meeting. The Secretary shall act as secretary of the meeting, but in his absence the chairman of the meeting may appoint any person to act as secretary of the meeting.

8. INFORMAL ACTION BY DIRECTORS

Unless otherwise restricted by the certificate of incorporation or these by-laws, any action required or permitted to be taken at any meeting of the Board of Directors, or of any committee thereof, may be taken without a meeting if all members of the Board of Directors or such committee,

as the case may be, consent thereto in writing, and the writing or writings are filed with the minutes of proceedings of the Board of Directors or such committee.

ARTICLE III COMMITTEES

1. COMMITTEES

The Board of Directors may, by resolution passed by a majority of the whole Board of Directors, designate one or more committees, each committee to consist of one or more of the directors of the corporation. The Board of Directors may designate one or more directors as alternate members of any committee, who may replace any absent or disqualified member at any meeting of the committee. In the absence or disqualification of a member of the committee, the member or members thereof present at any meeting and not disqualified from voting, whether or not he or they constitute a quorum, may unanimously appoint another member of the Board of Directors to act at the meeting in place of any such absent or disqualified member. Any such committee, to the extent permitted by law and to the extent provided in the resolution of the Board of Directors, shall have and may exercise all the powers and authority of the Board of Directors in the management of the business and affairs of the corporation, and may authorize the seal of the corporation to be affixed to all papers which may require it.

2. COMMITTEE RULES

Unless the Board of Directors otherwise provides, each committee designated by the Board of Directors may make, alter and repeal rules for the conduct of its business. In the absence of such rules each committee shall conduct its business in the same manner as the Board of Directors conducts its business pursuant to Article III of these by-laws.

ARTICLE IV
OFFICERS1. EXECUTIVE OFFICERS; ELECTION; QUALIFICATIONS; TERM OF OFFICE;
RESIGNATION; REMOVAL; VACANCIES

The Board of Directors shall elect a President and Secretary, and it may, if it so determines, choose a Chairman of the Board and a Vice Chairman of the Board from among its members. The Board of Directors may also choose one or more Vice Presidents, one or more Assistant Secretaries, a Treasurer and one or more Assistant Treasurers. Each such officer shall hold office until the first meeting of the Board of Directors after the annual meeting of stockholders next succeeding his election, and until his successor is elected and qualified or until his earlier resignation or removal. Any officer may resign at any time upon written notice to the corporation. The Board of Directors may remove any officer with or without cause at any time, but such removal shall be without prejudice to the contractual rights of such officer, if any, with the corporation. Any number of offices may be held by the same person. Any vacancy occurring in any office of the corporation by death, resignation, removal or otherwise may be filled for the unexpired portion of the term by the Board of Directors at any regular or special meeting.

2. POWERS AND DUTIES OF EXECUTIVE OFFICERS

The officers of the corporation shall have such powers and duties in the management of the corporation as may be prescribed by the Board of Directors and, to the extent not so provided, as generally pertain to their respective offices, subject to the control of the Board of Directors. The Board of Directors may require any officer, agent or employee to give security for the faithful performance of his duties.

ARTICLE V
STOCK

1. CERTIFICATES

Every holder of stock shall be entitled to have a certificate signed by or in the name of the corporation by the Chairman or Vice Chairman of the Board of Directors, if any, or the President or Vice President, and by the Treasurer or an Assistant Treasurer, or the Secretary or an Assistant Secretary, of the corporation, certifying the number of shares owned by him in the corporation. Any of or all the signatures on the certificate may be a facsimile. In case any officer, transfer agent, or registrar who has signed or whose facsimile signature has been placed upon a certificate shall have ceased to be such officer, transfer agent, or registrar before such certificate is issued, it may be issued

by the corporation with the same effect as if he were such officer, transfer agent, or registrar at the date of issue.

2. LOST, STOLEN OR DESTROYED STOCK CERTIFICATES; ISSUANCE OF NEW CERTIFICATES

The corporation may issued a new certificate of stock in the place of any certificate theretofore issued by it, alleged to have been lost, stolen or destroyed, and the corporation may require the owner of the lost, stolen or destroyed certificate, or his legal representative, to give the corporation a bond sufficient to indemnify it against any claim that may be made against it on account of the alleged loss, theft or destruction of any such certificate or the issuance of such new certificate.

ARTICLE VI INDEMNIFICATION

1. THIRD PARTY ACTIONS

The corporation shall indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending, or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the corporation) by reason of the fact that he is or was a director or officer of the corporation, or that such director or officer is or was serving at the request of the corporation as a director, officer, employee or agent of another corporation, partnership, joint venture trust or other enterprise (collectively "Agent"), against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement (if such settlement is approved in advance by the Company, which approval shall not be unreasonably withheld) actually and reasonably incurred by him in connection with such action, suit or proceeding if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the corporation, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful. The termination of any action, suit or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that the person did not act in good faith and in a manner which he reasonably believed to be in or not opposed to the best interest of the corporation, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his conduct was unlawful.

2. ACTIONS BY OR IN THE RIGHT OF THE CORPORATION

The corporation shall indemnify any person who was or is a party or is threatened to be made a party to any threatened, pending or completed action or suit by or in the right of the corporation to procure a judgment in its favor by reason of the fact that he is or was an Agent (as defined in Section 6.1) against expenses (including attorneys' fees) actually and reasonably incurred by him in

connection with the defense or settlement of such action or suit if he acted in good faith and in manner he reasonably believed to be in or not opposed to the best interests of the corporation and except that no indemnification shall be made in respect of any claim, issue or matter as to which such person shall have been adjudged to be liable to the corporation unless and only to the extent that the Delaware Court of Chancery or the court in which such action or suit was brought shall determine upon application that, despite the adjudication of liability but in view of all the circumstances of the case, such person is fairly and reasonably entitled to indemnity for such expenses which the Delaware Court of Chancery or such other court shall deem proper.

3. SUCCESSFUL DEFENSE

To the extent that an Agent of the corporation has been successful on the merits or otherwise in defense of any action, suit or proceeding referred to in Sections 6.1 and 6.2, or in defense of any claim, issue or matter therein, he shall be indemnified against expenses (including attorneys' fees) actually and reasonably incurred by him in connection therewith.

4. DETERMINATION OF CONDUCT

Any indemnification under Sections 6.1 and 6.2 (unless ordered by a court) shall be made by the corporation only as authorized in the specific case upon a determination that the indemnification of the Agent is proper in the circumstances because he has met the applicable standard of conduct set forth in Sections 6.1 and 6.2. Such determination shall be made (1) by the Board of Directors or an executive committee by a majority vote of a quorum consisting of directors who were not parties to such action, suit or proceeding, or (2) or if such quorum is not obtainable or, even if obtainable, a quorum of disinterested directors so directs, by independent legal counsel in a written opinion, or (3) by the stockholders.

5. PAYMENT OF EXPENSES IN ADVANCE

Expenses incurred in defending a civil or criminal action, suit or proceeding shall be paid by the corporation in advance of the final disposition of such action, suit or proceeding upon receipt of an undertaking by or on behalf of the director, officer, employee or agent to repay such amount if it shall ultimately be determined that he is not entitled to be indemnified by the corporation as authorized in this Article VI.

6. INDEMNITY NOT EXCLUSIVE

The indemnification and advancement of expenses provided or granted pursuant to the other subsections of this section shall not be deemed exclusive of any other rights to which those seeking indemnification or advancement of expenses may be entitled under any by-law, agreement, vote of stockholders or disinterested directors or otherwise, both as to action in his official capacity and as to action in another capacity while holding such office.

7. INSURANCE INDEMNIFICATION

The corporation shall have the power to purchase and maintain insurance on behalf of any person who is or was an Agent of the corporation, or is or was serving at the request of the corporation, as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise against any liability asserted against him and incurred by him in any such capacity, or arising out of his status as such, whether or not the corporation would have the power to indemnify him against such liability under the provisions of this Article VI.

8. THE CORPORATION

For purposes of this Article VI, references to "the corporation" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors and officers, so that any person who is or was a director or Agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, shall stand in the same position under and subject to the provisions of this Article VI (including, without limitation the provisions of Section 6.4) with respect to the resulting or surviving corporation as he would have with respect to such constituent corporation if its separate existence had continued.

9. EMPLOYEE BENEFIT PLANS

For purposes of this Article VI, references to "other enterprises" shall include employee benefit plans; references to "fines" shall include any excise taxes assessed on a person with respect to an employee benefit plan; and references to "serving at the request of the corporation" shall include any service as a director, officer, employee or agent of the corporation which imposes duties on, or involves services by, such director, officer, employee, or agent with respect to an employee benefit plan, its participants, or beneficiaries; and a person who acted in good faith and in a manner he reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan shall be deemed to have acted in a manner "not opposed to the best interests of the corporation" as referred to in this Article VI.

10. INDEMNITY FUND

Upon resolution passed by the Board, the corporation may establish a trust or other designated account, grant a security interest or use other means (including, without limitation, a letter of credit), to ensure the payment of certain of its obligations arising under this Article VI and/or agreements which may be entered into between the corporation and its officers and directors from time to time.

11. INDEMNIFICATION OF OTHER PERSONS

The provisions of this Article VI shall not be deemed to preclude the indemnification of any person who is not an Agent (as defined in Section 6.1), but whom the corporation has the power or obligation to indemnify under the provisions of the General Corporation Law of the State of Delaware or otherwise. The corporation may, in its sole discretion, indemnify an employee, trustee or other agent as permitted by the General Corporation Law of the State of Delaware. The corporation shall indemnify an employee, trustee or other agent where required by law.

12. SAVINGS CLAUSE

If this Article or any portion thereof shall be invalidated on any ground by any court of competent jurisdiction, then the corporation shall nevertheless indemnify each Agent against expenses (including attorney's fees), judgments, fines and amounts paid in settlement with respect to any action, suit, proceeding or investigation, whether civil, criminal or administrative, and whether internal or external, including a grand jury proceeding and an action or suit brought by or in the right of the corporation, to the full extent permitted by any applicable portion of this Article that shall not have been invalidated, or by any other applicable law.

13. CONTINUATION OF INDEMNIFICATION AND ADVANCEMENT OF EXPENSES

The indemnification and advancement of expenses provided by, or granted pursuant to, this Article VI shall, unless otherwise provided when authorized or ratified, continue as to a person who has ceased to be a director, officer, employee or agent and shall inure to the benefit of the heirs, executors and administrators of such a person.

ARTICLE VII
MISCELLANEOUS

1. FISCAL YEAR

The fiscal year of the corporation shall be determined by resolution of the Board of Directors.

2. SEAL

The corporate seal shall have the name of the corporation inscribed thereon and shall be in such form as may be approved from time to time by the Board of Directors.

3. WAIVER OF NOTICE OF MEETINGS OF STOCKHOLDERS, DIRECTORS AND COMMITTEES

Any written waiver of notice, signed by the person entitled to notice, whether before or after the time stated therein, shall be deemed equivalent to notice. Attendance of a person at a meeting shall constitute a waiver of notice of such meeting, except when the person attends a meeting for the express purpose of objecting, at the beginning of the meeting, to the transaction of any business because the meeting is not lawfully called or convened. Neither the business to be transacted at, nor the purpose of any regular or special meeting of the stockholders, directors, or members of a committee of directors need be specified in any written waiver of notice.

4. INTERESTED DIRECTORS; QUORUM

No contract or transaction between the corporation and one or more of its directors or officers, or between the corporation and any other corporation, partnership, association, or other organization in which one or more of its directors or officers are directors or officers, or have a financial interest, shall be void or voidable solely for this reason, or solely because the director or officer is present at or participates in the meeting of the Board of Directors or committee thereof which authorizes the contract or transaction, or solely because his or their votes are counted for such purpose, if: (1) the material facts as to his relationship or interest and as to the contract or transaction are disclosed or are known to the Board of Directors or the committee, and the Board of Directors or committee in good faith authorizes the contract or transaction by the affirmative votes of a majority of the disinterested directors, even though the disinterested directors be less than a quorum; or (2) the material facts as to his relationship or interest and as to the contract or transaction are disclosed or are known to the stockholders entitled to vote thereon, and the contract or transaction is specifically approved in good faith by vote of the stockholders; or (3) the contract or transaction is fair as to the corporation as of the time it is authorized, approved or ratified, by the Board of Directors, a committee thereof, or the stockholders. Common or interested directors may be counted in determining the presence of a quorum at a meeting of the Board of Directors or of a committee which authorizes the contract or transaction.

5. FORM OF RECORDS

Any records maintained by the corporation in the regular course of its business, including its stock ledger, books of account, and minute books, may be kept on, or be in the form of, punch cards, magnetic tape, photographs, microphotographs, or any other information storage device, provided that the records so kept can be converted into clearly legible form within a reasonable time. The corporation shall so convert any records so kept upon the request of any person entitled to inspect the same.

6. AMENDMENT OF BY-LAWS

These by-laws may be altered or repealed, and new by-laws made, by the Board of Directors, but the stockholders may make additional by-laws and may alter and repeal any by-laws whether adopted by them or otherwise.

PAIN THERAPEUTICS, INC.
INDEMNIFICATION AGREEMENT

THIS INDEMNIFICATION AGREEMENT ("AGREEMENT") is made as of this _____ day of _____, _____, by and between PAIN THERAPEUTICS, INC., a Delaware corporation (the "COMPANY"), and ("INDEMNITEE").

WHEREAS, the Company and Indemnitee recognize the increasing difficulty in obtaining directors' and officers' liability insurance, the significant increases in the cost of such insurance and the general reductions in the coverage of such insurance;

WHEREAS, the Company and Indemnitee further recognize the substantial increase in corporate litigation in general, subjecting officers and directors to expensive litigation risks at the same time as the availability and coverage of liability insurance has been severely limited;

WHEREAS, Indemnitee does not regard the current protection available as adequate under the present circumstances, and Indemnitee and other officers and directors of the Company may not be willing to continue to serve as officers and directors without additional protection; and

WHEREAS, the Company desires to attract and retain the services of highly qualified individuals, such as Indemnitee, to serve as officers and directors of the Company and to indemnify its officers and directors so as to provide them with the maximum protection permitted by law.

NOW, THEREFORE, the Company and Indemnitee hereby agree as follows:

1. INDEMNIFICATION.

(a) Third Party Proceedings. The Company shall indemnify Indemnitee if Indemnitee is or was a party or is threatened to be made a party to any threatened, pending or completed action or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the Company) by reason of the fact that Indemnitee is or was a director, officer, employee or agent of the Company, or any subsidiary of the Company, by reason of any action or inaction on the part of Indemnitee while an officer or director or by reason of the fact that Indemnitee is or was serving at the request of the Company as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees), judgments, fines and amounts paid in settlement (if such settlement is approved in advance by the Company, which approval shall not be unreasonably withheld) actually and reasonably incurred by Indemnitee in connection with such action or proceeding if Indemnitee acted in good faith and in a manner Indemnitee reasonably believed to be in or not opposed to the best interests of the Company, and, with respect to any criminal action or proceeding, had no

reasonable cause to believe Indemnitee's conduct was unlawful. The termination of any action or proceeding by judgment, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that (i) Indemnitee did not act in good faith and in a manner which Indemnitee reasonably believed to be in or not opposed to the best interests of the Company, or (ii) with respect to any criminal action or proceeding, Indemnitee had reasonable cause to believe that Indemnitee's conduct was unlawful.

(b) Proceedings By or in the Right of the Company. The Company shall indemnify Indemnitee if Indemnitee was or is a party or is threatened to be made a party to any threatened, pending or completed action or proceeding by or in the right of the Company or any subsidiary of the Company to procure a judgment in its favor by reason of the fact that Indemnitee is or was a director, officer, employee or agent of the Company, or any subsidiary of the Company, by reason of any action or inaction on the part of Indemnitee while an officer or director or by reason of the fact that Indemnitee is or was serving at the request of the Company as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, against expenses (including attorneys' fees) and, to the fullest extent permitted by law, amounts paid in settlement, in each case to the extent actually and reasonably incurred by Indemnitee in connection with the defense or settlement of such action or proceeding if Indemnitee acted in good faith and in a manner Indemnitee reasonably believed to be in or not opposed to the best interests of the Company and its stockholders, except that no indemnification shall be made in respect of any claim, issue or matter as to which Indemnitee shall have been finally adjudicated by court order or judgment to be liable to the Company in the performance of Indemnitee's duty to the Company and its stockholders unless and only to the extent that the court in which such action or proceeding is or was pending shall determine upon application that, in view of all the circumstances of the case, Indemnitee is fairly and reasonably entitled to indemnity for expenses and then only to the extent that the court shall determine.

2. EXPENSES; INDEMNIFICATION PROCEDURE.

(a) Advancement of Expenses. The Company shall advance all expenses incurred by Indemnitee in connection with the investigation, defense, settlement or appeal of any civil or criminal action or proceeding referenced in Section 1(a) or (b) hereof (but not amounts actually paid in settlement of any such action or proceeding). Indemnitee hereby undertakes to repay such amounts advanced only if, and to the extent that, it shall ultimately be determined that Indemnitee is not entitled to be indemnified by the Company as authorized hereby. The advances to be made hereunder shall be paid by the Company to Indemnitee within twenty (20) days following delivery of a written request therefor by Indemnitee to the Company.

(b) Notice/Cooperation by Indemnitee. Indemnitee shall, as a condition precedent to his right to be indemnified under this Agreement, give the Company notice in writing as soon as practicable of any claim made against Indemnitee for which indemnification will be sought under this Agreement. Notice to the Company shall be directed to the Chief Executive Officer of the Company at the address shown on the signature page of this Agreement (or such other address as the

Company shall designate in writing to Indemnitee). Notice shall be deemed received three business days after the date postmarked if sent by domestic certified or registered mail, properly addressed; otherwise notice shall be deemed received when such notice shall actually be received by the Company. In addition, Indemnitee shall give the Company such information and cooperation as it may reasonably require and as shall be within Indemnitee's power.

(c) Procedure. Any indemnification and advances provided for in Section 1 and this Section 2 shall be made no later than forty-five (45) days after receipt of the written request of Indemnitee. If a claim under this Agreement, under any statute, or under any provision of the Company's Certificate of Incorporation or By-laws providing for indemnification, is not paid in full by the Company within forty-five (45) days after a written request for payment thereof has first been received by the Company, Indemnitee may, but need not, at any time thereafter bring an action against the Company to recover the unpaid amount of the claim and, subject to Section 12 of this Agreement, Indemnitee shall also be entitled to be paid for the expenses (including attorneys' fees) of bringing such action. It shall be a defense to any such action (other than an action brought to enforce a claim for expenses incurred in connection with any action or proceeding in advance of its final disposition) that Indemnitee has not met the standards of conduct which make it permissible under applicable law for the Company to indemnify Indemnitee for the amount claimed, but the burden of proving such defense shall be on the Company and Indemnitee shall be entitled to receive interim payments of expenses pursuant to Subsection 2(a) unless and until such defense may be finally adjudicated by court order or judgment from which no further right of appeal exists. It is the parties' intention that if the Company contests Indemnitee's right to indemnification, the question of Indemnitee's right to indemnification shall be for the court to decide, and neither the failure of the Company (including its Board of Directors, any committee or subgroup of the Board of Directors, independent legal counsel, or its stockholders) to have made a determination that indemnification of Indemnitee is proper in the circumstances because Indemnitee has met the applicable standard of conduct required by applicable law, nor an actual determination by the Company (including its Board of Directors, any committee or subgroup of the Board of Directors, independent legal counsel, or its stockholders) that Indemnitee has not met such applicable standard of conduct, shall create a presumption that Indemnitee has or has not met the applicable standard of conduct.

(d) Notice to Insurers. If, at the time of the receipt of a notice of a claim pursuant to Section 3(b) hereof, the Company has director and officer liability insurance in effect, the Company shall give prompt notice of the commencement of such proceeding to the insurers in accordance with the procedures set forth in the respective policies. The Company shall thereafter take all necessary or desirable action to cause such insurers to pay, on behalf of the Indemnitee, all amounts payable as a result of such proceeding in accordance with the terms of such policies.

(e) Selection of Counsel. In the event the Company shall be obligated under Section 2(a) hereof to pay the expenses of any proceeding against Indemnitee, the Company, if appropriate, shall be entitled to assume the defense of such proceeding, with counsel approved by Indemnitee, which approval shall not be unreasonably withheld, upon the delivery to Indemnitee of written notice of its election so to do. After delivery of such notice, approval of such counsel by

Indemnatee and the retention of such counsel by the Company, the Company will not be liable to Indemnatee under this Agreement for any fees of counsel subsequently incurred by Indemnatee with respect to the same proceeding, provided that (i) Indemnatee shall have the right to employ his counsel in any such proceeding at Indemnatee's expense; and (ii) if (A) the employment of counsel by Indemnatee has been previously authorized by the Company, (B) Indemnatee shall have reasonably concluded that there may be a conflict of interest between the Company and Indemnatee in the conduct of any such defense, or (C) the Company shall not, in fact, have employed counsel to assume the defense of such proceeding, then the fees and expenses of Indemnatee's counsel shall be at the expense of the Company.

3. ADDITIONAL INDEMNIFICATION RIGHTS; NONEXCLUSIVITY.

(a) Scope. Notwithstanding any other provision of this Agreement, the Company hereby agrees to indemnify the Indemnatee to the fullest extent permitted by law, notwithstanding that such indemnification is not specifically authorized by the other provisions of this Agreement, the Company's Certificate of Incorporation, the Company's By-laws or by statute. In the event of any change, after the date of this Agreement, in any applicable law, statute or rule which expands the right of a Delaware corporation to indemnify a member of its Board of Directors, an officer or other corporate agent, such changes shall be ipso facto, within the purview of Indemnatee's rights and Company's obligations, under this Agreement. In the event of any change in any applicable law, statute or rule which narrows the right of a Delaware corporation to indemnify a member of its Board of Directors, an officer or other corporate agent, such changes, to the extent not otherwise required by such law, statute or rule to be applied to this Agreement shall have no effect on this Agreement or the parties' rights and obligations hereunder.

(b) Nonexclusivity. The indemnification provided by this Agreement shall not be deemed exclusive of any rights to which Indemnatee may be entitled under the Company's Certificate of Incorporation, its By-laws, any agreement, any vote of stockholders or disinterested Directors, the Delaware Corporation Law or otherwise, both as to action in Indemnatee's official capacity and as to action in another capacity while holding such office. The indemnification provided under this Agreement shall continue as to Indemnatee for any action taken or not taken while serving in an indemnified capacity even though he may have ceased to serve in such capacity at the time of any action, suit or other covered proceeding.

4. PARTIAL INDEMNIFICATION. If Indemnatee is entitled under any provision of this Agreement to indemnification by the Company for some or a portion of the expenses, judgments, fines or penalties actually or reasonably incurred by him in the investigation, defense, appeal or settlement of any civil or criminal action or proceeding, but not, however, for the total amount thereof, the Company shall nevertheless indemnify Indemnatee for the portion of such expenses, judgments, fines or penalties to which Indemnatee is entitled.

5. MUTUAL ACKNOWLEDGEMENT. Both the Company and Indemnatee acknowledge that in certain instances, Federal law or applicable public policy may prohibit the Company from

indemnifying its directors and officers under this Agreement or otherwise. Indemnatee understands and acknowledges that the Company has undertaken or may be required in the future to undertake with the Securities and Exchange Commission to submit the question of indemnification to a court in certain circumstances for a determination of the Company's right under public policy to indemnify Indemnatee.

6. OFFICER AND DIRECTOR LIABILITY INSURANCE. The Company shall, from time to time, make the good faith determination whether or not it is practicable for the Company to obtain and maintain a policy or policies of insurance with reputable insurance companies providing the officers and directors of the Company with coverage for losses from wrongful acts, or to ensure the Company's performance of its indemnification obligations under this Agreement. Among other considerations, the Company will weigh the costs of obtaining such insurance coverage against the protection afforded by such coverage. In all policies of director and officer liability insurance, Indemnatee shall be named as an insured in such a manner as to provide Indemnatee the same rights and benefits as are accorded to the most favorably insured of the Company's directors, if Indemnatee is a director; or of the Company's officers, if Indemnatee is not a director of the Company but is an officer; or of the Company's key employees, if Indemnatee is not an officer or director but is a key employee. Notwithstanding the foregoing, the Company shall have no obligation to obtain or maintain such insurance if the Company determines in good faith that such insurance is not reasonably available, if the premium costs for such insurance are disproportionate to the amount of coverage provided, if the coverage provided by such insurance is limited by exclusions so as to provide an insufficient benefit, or if Indemnatee is covered by similar insurance maintained by a subsidiary or parent of the Company.

7. SEVERABILITY. Nothing in this Agreement is intended to require or shall be construed as requiring the Company to do or fail to do any act in violation of applicable law. The Company's inability, pursuant to court order, to perform its obligations under this Agreement shall not constitute a breach of this Agreement. The provisions of this Agreement shall be severable as provided in this Section 7. If this Agreement or any portion hereof shall be invalidated on any ground by any court of competent jurisdiction, then the Company shall nevertheless indemnify Indemnatee to the full extent permitted by any applicable portion of this Agreement that shall not have been invalidated, and the balance of this Agreement not so invalidated shall be enforceable in accordance with its terms.

8. EXCEPTIONS. Any other provision herein to the contrary notwithstanding, the Company shall not be obligated pursuant to the terms of this Agreement:

(a) EXCLUDED ACTS. To indemnify Indemnatee for any acts or omissions or transactions from which a director may not be relieved of liability under the applicable law.

(b) CLAIMS INITIATED BY INDEMNITEE. To indemnify or advance expenses to Indemnatee with respect to proceedings or claims initiated or brought voluntarily by Indemnatee and not by way of defense, except with respect to proceedings brought to establish or enforce a right to

indemnification under this Agreement or any other statute or law or otherwise as required under Section 145 of the Delaware General Corporation Law, but such indemnification or advancement of expenses may be provided by the Company in specific cases if the Board of Directors has approved the initiation or bringing of such suit; or

(c) LACK OF GOOD FAITH. To indemnify Indemnitee for any expenses incurred by the Indemnitee with respect to any proceeding instituted by Indemnitee to enforce or interpret this Agreement, if a court of competent jurisdiction determines that each of the material assertions made by the Indemnitee in such proceeding was not made in good faith or was frivolous; or

(d) INSURED CLAIMS. To indemnify Indemnitee for expenses or liabilities of any type whatsoever (including, but not limited to, judgments, fines, ERISA excise taxes or penalties, and amounts paid in settlement) which have been paid directly to Indemnitee by an insurance carrier under a policy of officers' and directors' liability insurance maintained by the Company.

(e) CLAIMS UNDER SECTION 16(b). To indemnify Indemnitee for expenses and the payment of profits arising from the purchase and sale by Indemnitee of securities in violation of Section 16(b) of the Securities Exchange Act of 1934, as amended, or any similar successor statute.

9. CONSTRUCTION OF CERTAIN PHRASES.

(a) For purposes of this Agreement, references to the "Company" shall include, in addition to the resulting corporation, any constituent corporation (including any constituent of a constituent) absorbed in a consolidation or merger which, if its separate existence had continued, would have had power and authority to indemnify its directors, officers, and employees or agents, so that if Indemnitee is or was a director, officer, employee or agent of such constituent corporation, or is or was serving at the request of such constituent corporation as a director, officer, employee or agent of another corporation, partnership, joint venture, trust or other enterprise, Indemnitee shall stand in the same position under the provisions of this Agreement with respect to the resulting or surviving corporation as Indemnitee would have with respect to such constituent corporation if its separate existence had continued.

(b) For purposes of this Agreement, references to "other enterprises" shall include employee benefit plans; references to "fines" shall include any excise taxes assessed on Indemnitee with respect to an employee benefit plan; and references to "serving at the request of the Company" shall include any service as a director, officer, employee or agent of the Company which imposes duties on, or involves services by, such director, officer, employee or agent with respect to an employee benefit plan, its participants, or beneficiaries; and if Indemnitee acted in good faith and in a manner Indemnitee reasonably believed to be in the interest of the participants and beneficiaries of an employee benefit plan, Indemnitee shall be deemed to have acted in a manner "not opposed to the best interests of the Company" as referred to in this Agreement.

10. COUNTERPARTS. This Agreement may be executed in one or more counterparts, each of which shall constitute an original.

11. SUCCESSORS AND ASSIGNS. This Agreement shall be binding upon the Company and its successors and assigns, and shall inure to the benefit of Indemnatee and Indemnatee's estate, heirs, legal representatives and assigns.

12. ATTORNEYS' FEES. In the event that any action is instituted by Indemnatee under this Agreement to enforce or interpret any of the terms hereof, Indemnatee shall be entitled to be paid all costs and expenses, including reasonable attorneys' fees, incurred by Indemnatee with respect to such action, unless as a part of such action, the court of competent jurisdiction determines that each of the material assertions made by Indemnatee as a basis for such action were not made in good faith or were frivolous. In the event of an action instituted by or in the name of the Company under this Agreement or to enforce or interpret any of the terms of this Agreement, Indemnatee shall be entitled to be paid all costs and expenses, including reasonable attorneys' fees, incurred by Indemnatee in defense of such action (including with respect to Indemnatee's counterclaims and cross-claims made in such action), unless as a part of such action the court determines that each of Indemnatee's material defenses to such action were made in bad faith or were frivolous.

13. NOTICE. All notices, requests, demands and other communications under this Agreement shall be in writing and shall be deemed duly given (i) if delivered by hand and acknowledged in writing as received by the addressee, on the date of such receipt, or (ii) if mailed by domestic certified or registered mail with postage prepaid, on the third business day after the date postmarked. Addresses for notice to either party are as shown on the signature page of this Agreement, or as subsequently modified by written notice.

14. CONSENT TO JURISDICTION. The Company and Indemnatee each hereby irrevocably consent to the jurisdiction of the courts of the State of Delaware for all purposes in connection with any action or proceeding which arises out of or relates to this Agreement and agree that any action instituted under this Agreement shall be brought only in the state courts of the State of Delaware.

15. CHOICE OF LAW. This Agreement shall be governed by and its provisions construed in accordance with the laws of the State of Delaware, as applied to contracts between Delaware residents entered into and to be performed entirely within Delaware.

16. SUBROGATION. In the event of payment under this Agreement, the Company shall be subrogated to the extent of such payment to all of the rights of recovery of Indemnatee, who shall execute all documents required and shall do all acts that may be necessary to secure such rights and to enable to corporation effectively to bring suit to enforce such rights.

17. CONTINUATION OF INDEMNIFICATION. All agreements and obligations of the Company contained herein shall continue during the period that Indemnatee is a director, officer or agent of the Company and shall continue thereafter so long as Indemnatee shall be subject to any possible claim

or threatened, pending or completed action, suit or proceeding, whether civil, criminal, arbitrational, administrative or investigative, by reason of the fact that Indemnatee was serving in the capacity referred to herein.

18. AMENDMENT AND TERMINATION. Subject to Section 17, no amendment, modification, termination or cancellation of this Agreement shall be effective unless in writing signed by both parties hereto.

IN WITNESS WHEREOF, the parties hereto have executed this Agreement as of the date first above written.

PAIN THERAPEUTICS, INC.

By: _____

Title: _____

Address: 250 East Grand Avenue, Suite 70
So. San Francisco, CA 94080

AGREED TO AND ACCEPTED:

INDEMNITEE:

(Signature)

Address: _____

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

TABLE OF CONTENTS

ARTICLE I	
DEFINITIONS	2
1.1 "AFFILIATE"	2
1.2 "AGENCY"	2
1.3 "CALENDAR QUARTER"	2
1.4 "CALENDAR YEAR"	3
1.5 "CONFIDENTIAL INFORMATION"	3
1.6 "DEVELOPMENT SCHEDULE"	3
1.7 "FIRST COMMERCIAL SALE"	3
1.8 "IND"	3
1.9 "KNOW-HOW"	3
1.10 "LICENSED PRODUCT"	4
1.11 "MAJOR COUNTRIES"	4
1.12 "NDA"	4
1.13 "NET SALES"	4
1.14 "NET PROCEEDS"	5
1.15 "PATENT RIGHTS"	5
1.16 "SUBLICENSEE"	6
1.17 "TERRITORY"	6
1.18 "VALID PATENT CLAIM"	6
ARTICLE II	
PATENT RIGHTS AND KNOW-HOW	6
ARTICLE III	
PAYMENTS	8
Table I	10

ARTICLE IV
ROYALTIES AND REPORTS 11

ARTICLE V
DEVELOPMENT AND COMMERCIALIZATION 17

ARTICLE VI
CONFIDENTIALITY AND PUBLICATION 18

ARTICLE VII
PATENTS 21

ARTICLE VIII
TERM AND TERMINATION 24

ARTICLE IX
INDEMNIFICATION 26

ARTICLE X
MISCELLANEOUS 28

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 11

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 right 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 [*] which shall be due within thirty (30) days of

[*] Confidential Treatment Requested

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 [*] as follows:

- (a) FIRST PAYMENT: [*] paid in the first year of this Agreement, which shall be due within thirty (30) days of the Effective Date;
- (b) SECOND PAYMENT: [*] 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: [*], 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: [*], 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.

[*] Confidential Treatment Requested

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.

TABLE 1

MILESTONE EVENT	MILESTONE PAYMENT	MILESTONE DATE
[*]	[*]	4 years from Effective Date
[*]	[*]	8 years from Effective Date
[*]	[*]	10 Years from Effective Date
[*]	[*]	
[*] Confidential Treatment Requested		

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 [*] on the Milestone Date, and achieved this Milestone Event [*] from the Effective Date, then remaining Milestone Dates would be adjusted forward as follows: [*], [*] from Effective Date; [*], [*]. However, if LICENSEE tendered the Milestone Payment associated with the initiation of [*] on the Milestone Date, and achieved this Milestone Event [*] from the Effective Date, then remaining Milestone Dates would be adjusted forward as follows: [*], [*] from Effective Date; [*], [*].

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

[*] Confidential Treatment Requested

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 relief, in addition to any other legal remedies available to it, in any court of competent jurisdiction.
- 6.7 USE OF CONFIDENTIAL 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 [*], 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)

[*] Confidential Treatment Requested

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 from 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 its 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 right 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/ EMANUEL GENN

EMANUEL GENN
ASSOCIATE DEAN FOR BUSINESS AFFAIRS

DATE: 5/5/98

PAIN THERAPEUTICS, INC.

BY: /s/ REMI BARBIER

TITLE: President & CEO

DATE:

35

[*]

[*] Confidential Treatment Requested

[KP PHARMACEUTICALS LETTERHEAD]

CONFIDENTIAL

KP PHARMACEUTICAL TECHNOLOGY, INC.
RESEARCH AGREEMENT

This agreement is entered into by and between KP Pharmaceutical Technology, Inc. hereinafter called "Research Organization", and Pain Therapeutics, Inc., a corporation with its principal office and place of business at 250 East Grand Avenue, Suite 70, South San Francisco, CA 94080, hereinafter called "Sponsor".

WITNESSETH

WHEREAS, The research/development program contemplated by this Agreement is of mutual interest and benefit to the Research Organization and to the Sponsor,

WHEREAS, a Proposal entitled: Development, Manufacture, Testing, Supply and Stability Studies of Naltrexone and Placebo Capsule Formulation for Human Clinical Trials has been written which will guide the performance of this Agreement and the Research Organization agrees it is fully able to perform the research program in a professional, competent manner with strict adherence to its terms, and the Research Organization will utilize its best efforts to do so,

NOW THEREFORE, the parties hereto agree as follows:

1. SCOPE OF WORK

- 1.1. The Research Organization shall exercise its best efforts to carry out the research set forth in the attached Proposal ("Research") and Cost Estimate (and terms). Project Number: KP980012R2 dated May 14, 1999 and consisting of 3 pages.

2. PERFORMANCE PERIOD

- 2.1. Performance of the Research under this Agreement shall start not later than one week of both parties signing this Agreement and shall be completed by August 1, 1999 (except on-going stability studies). Regarding the performance hereunder, time is of the essence. In case of delayed performance, this Agreement may, at Sponsor's option, be extended for subsequent one-month periods until the Research is completed.
- 2.2. This Agreement shall be effective for a period of 3 (three) years from the date of signing. The effective period may be extended by mutual agreement.

3. REGULATORY COMPLIANCE

- 3.1. The Research Organization will be responsible for conducting the research in full compliance with cGMP regulations and in strict accordance with applicable Research Organization policies which Research Organization agrees are not inconsistent with the terms of this Agreement, the Proposal, generally accepted standards of the current Good Manufacturing Practices (cGMPs) and/or Good Laboratory Practices (GLPs), all applicable local, state and federal laws and regulations governing the performance of

research and/or development activities. The Research Organization shall retain all records resulting from the Research for the time required by applicable federal regulations (the Sponsor will notify the Research Organization of the FDA Application filing and approval status), and to allow for sponsor (or sponsor's representative) and FDA unlimited inspection of all such records.

4. RECORDKEEPING, REPORTING AND ACCESS

- 4.1. The Sponsor's authorized representative(s), and regulatory authorities to the extent required by law, may, during regular business hours, arrange in advance with the Research Organization to:
 - 4.1.1 Examine and inspect the Research Organization's facilities required for performance of the Research; and
 - 4.1.2. Inspect and copy all data and work products relating to the Research.
- 4.2. Research Organization shall cooperate with any regulatory authority and allow them access to applicable records and data.
- 4.3. The Research Organization shall perform the following record-keeping and reporting obligations in a timely fashion:
 - 4.3.1. Preparation and maintenance of complete, accurately written records, accounts, notes, reports and data of the Research;
 - 4.3.2. Reports will be delivered to Sponsor by Research Organization in a timely manner throughout the performance of the research/development.
 - 4.3.3. A final written report ("Final Report") including a complete summary of research/development activity will be submitted to the Sponsor.

5. INDEMNIFICATION

- 5.1. During the term of this Agreement, Sponsor shall defend, indemnify and hold harmless the Research Organization and any agents and employees of Research Organization from any and all liabilities, claims, actions or suits (collectively "Claims") for personal injury or death arising out of or in connection with the administration or use of the Research study drug(s) which are manufactured by Research Organization, provided however:
 - 5.1.1. That the Research Organization conducts the Research in strict accordance with and in full compliance with:
 - a) the written Proposal, any other written instructions furnished by Sponsor, and in a manner required of a reasonable and prudent researcher;
 - b) all applicable cGMP/GLP regulations and guidelines related to the performance of this Agreement;

- c) all applicable local, state and federal laws, regulations and ordinances that govern the performance of this Agreement, including those that apply to the research and manufacturing, development, testing, shipping, storage, packaging, distribution, environment disposition and labeling of naltrexone, placebo or other chemical agents related to the performance of this Agreement;

- 5.1.1.1. That the Research Organization notifies the Sponsor immediately of the claim or lawsuit;
- 5.1.1.2. That the Research Organization reasonably cooperates with the Sponsor in its investigation and defense thereof; and
- 5.1.1.3. That the Research Organization not settle or otherwise compromise such claim or lawsuit without the Sponsor's prior written consent.

- 5.1.2. In any event, Sponsor or its agents, employees, or directors shall not be responsible for any compensatory, consequential, special, incidental, punitive or other damages, losses, costs or expenses in excess of the total dollar size of this agreement.

- 5.2. The Sponsor shall provide a diligent defense against any settlement of any claims brought or actions filed with respect to the subject of the indemnity contained herein, whether such claims or actions are rightfully or wrongfully brought or filed. The Sponsor shall not settle any claims without the Research Organization's prior written consent, which consent may not be unreasonably withheld.

- 5.3. Deviations from the terms of the Proposal that may arise out of necessity will be made following written authorization from the Sponsor.

- 5.3.1. Sponsor agrees that it maintains a policy of program of insurance or self-insurance at levels sufficient to support the indemnification obligations assumed herein. Unless the Sponsor is self-insured, upon request the Sponsor will provide evidence of its insurance and will provide to the Research Organization, thirty (30) days prior, written notice of cancellation of its coverage.

6. TERMINATION

- 6.1. This Agreement may be terminated by either party, upon immediate notice, if any of the following conditions occur:
 - 6.1.1. If the authorization and approval to perform the Research in the United States is withdrawn by the U.S. Food and Drug Administration;
 - 6.1.2. If animal, human and/or toxicological test results of the product made by the Research Organization, in the opinion of either the Sponsor or the Research Organization, support termination of the Research.
 - 6.1.3. If either party fails to strictly comply with all terms of the Agreement after receipt of written notice, with a 30 day opportunity to cure, from the other party.
- 6.2. Upon the effective date of termination, there shall be an accounting conducted by the Research Organization, subject to verification by the Sponsor. Within thirty (30) days

after receipt of adequate documentation therefore, the Sponsor will make payment to the Research Organization for:

- 6.2.1. All services properly rendered and moneys properly expended by the Research Organization until the date of termination not yet paid for; and
- 6.2.2. Reasonable non-cancelable obligations properly incurred for the Research by the Research Organization prior to the effective date of termination; unless the Sponsor objects to any charge, in which case, the parties shall use best efforts to resolve expeditiously any disagreement.
- 6.2.3. The Research Organization will credit or return to the Sponsor any funds not expended or obligated by the Research Organization in connection with the Research prior to the effective termination date of the notice of termination.
- 6.2.4. Immediately upon receipt of a notice of termination, the Research Organization shall cease conducting research procedures related to proposal.
- 6.2.5. Termination of this Agreement by either party shall not affect the rights and obligations of the parties accrued prior to the effective date of the termination.

7. DELIVERY OF UNUSED MATERIAL

7.1. Upon termination or completion of the Research, all unused compounds, drugs, equipment, whether or not completed, and other related materials that were furnished to the Research Organization by or on behalf of the Sponsor shall be returned to the Sponsor at the Sponsor's expense.

8. APPLICABLE LAW

8.1. This Agreement shall be governed by the laws of the states of Indiana and California.

9. PUBLICATIONS:

9.1. Research Organization desires to independently publish or publicly release information about any data or techniques arising out of the Research, then, following completion of the Research and at least sixty (60) days prior to submission of any manuscript or abstract for publication, Research Organization will submit a copy of the intended publication to Sponsor for review and comment. Sponsor will review the intended publication to ensure that the nature of Sponsor's support is set forth in the publication; to determine any confidential information should be deleted from the proposed publication; to determine whether there is patentable matter contained in the proposed publication; if the Sponsor request in writing, Research Organization will withhold publication for an additional sixty (60) days to allow for filing a patent application or taking such other measures as Sponsor deems appropriate to establish and preserve its proprietary rights.

10. PATENT RIGHTS:

10.1. Research Organization shall not acquire any rights of any kind whatsoever with respect to Sponsor's intellectual property as a result of performance under this Agreement or

otherwise. All inventions, discoveries and technology relating to the Research, whether patentable or not, conceived by the Research Organization or Sponsor, solely or jointly with others as a result of work done under this Agreement, shall be, and remain, at all times the sole and exclusive property of Sponsor. Any and all acts necessary to assist Sponsor in perfecting its rights to any and all inventions, discoveries and technology shall be performed by the Research Organization or the Research Organization's employees or agents, as appropriate. The Research Organization warrants by the execution of this Agreement that it has not entered or will enter into any contractual agreement or relationship which would in any way conflict with or compromise Sponsor's proprietary interest in, or rights to, any inventions, discoveries or technology existing at the time of the execution of this Agreement or arising out of or related to the performance thereunder.

11. REPRESENTATIONS AND WARRANTIES:

11.1. Research Organization represents and warrants that: (a) it has the technical competence and legal authority to enter into this Agreement; (b) it has no obligation to any other party which is in conflict with its obligations under this Agreement; (c) it will conduct the Research in strict accordance with in full compliance with all applicable local, state and federal laws and regulations for the protection of the rights, safety and welfare for human subjects in clinical trials.

RESEARCH AGREEMENT/PILOT cGMP MANUFACTURING FACILITIES

IN WITNESS WHEREOF, the parties hereto have executed this Agreement in duplicate by proper persons thereunto duly authorized.

RESEARCH ORGANIZATION
KP Pharmaceutical Technology, Inc.
1212 Rappel Dr.,
Bloomington, In 47404-1702

SPONSOR
Pain Therapeutics, Inc
250 East Grand Avenue, Suite 70
South San Francisco, CA 94080

/s/ RS MATHARU

/s/ REMI BARBIER

(Signature)

(Signature)

Rajinder PS Matharu, Ph.D.

Dr. Remi Barbier

(Print or Type Name)

(Print or Type Name)

President & CEO

President & CEO

(Title)

(Title)

5-14-99

5/14/99

(Date)

(Date)

LEASE

Landlord: Britannia Pointe Grand Limited Partnership

Tenant: Pain Therapeutics, Inc.

Date: August 24, 1998,

TABLE OF CONTENTS

1. PREMISES.....	1
1.1. Premises.....	1
1.2. Landlord's Reserved Rights.....	1
2. TERM.....	1
2.1. Term.....	1
2.2. Early Possession.....	2
2.3. Delay In Possession.....	2
2.4. Construction.....	2
2.5. Acknowledgement Of Lease Commencement.....	2
2.6. Holding Over.....	2
3. RENTAL.....	3
3.1. Rental.....	3
3.2. Late Charge.....	3
4. TAXES.....	3
4.1. Personal Property.....	3
5. UTILITIES.....	3
5.1. Payment.....	3
5.2. Interruption.....	4
6. ALTERATIONS.....	4
6.1. Right To Make Alterations.....	4
6.2. Title To Alterations.....	4
6.3. Tenant Fixtures.....	4
6.4. No Liens.....	4
7. MAINTENANCE AND REPAIRS.....	4
7.1. Landlord's Work.....	4
7.2. Tenant's Obligation For Maintenance.....	5
(a) Good Order, Condition And Repair.....	5
(b) Condition Upon Surrender.....	5
8. USE OF PREMISES.....	5
8.1. Permitted Use.....	5
8.2. Requirement Of Continued Use.....	5
8.3. No Nuisance.....	5
8.4. Compliance With Laws.....	5
8.5. Liquidation Sales.....	6
8.6. Environmental Matters.....	6
8. INSURANCE AND INDEMNITY.....	7

9.1.	Liability Insurance.....	7
9.2.	Quality Of Policies and Certificates.....	7
9.3.	Workers' Compensation.....	7
9.4.	Waiver Of Subrogation.....	7
9.5.	Increase In Premiums.....	7
9.6.	Indemnification.....	7
9.7.	Blanket Policy.....	8
10.	SUBLEASE AND ASSIGNMENT.....	8
10.1.	Assignment And Sublease Of Premises.....	8
10.2.	Rights Of Landlord.....	8
11.	RIGHT OF ENTRY AND QUIET ENJOYMENT.....	9
11.1.	Right Of Entry.....	9
11.2.	Quiet Enjoyment.....	9
12.	CASUALTY AND TAKING.....	9
12.1.	Termination Or Reconstruction.....	9
12.2.	Tenant's Rights.....	9
12.3.	Lease To Remain In Effect.....	10
12.4.	Reservation Of Compensation.....	10
12.5.	Restoration Of Fixtures.....	10
13.	DEFAULT.....	10
13.1.	Events Of Default.....	10
	(a) Abandonment.....	10
	(b) Nonpayment.....	10
	(c) Other Obligations.....	10
	(d) General Assignment.....	10
	(e) Bankruptcy.....	10
	(f) Receivership.....	11
	(g) Attachment.....	11
	(h) Insolvency.....	11
13.2.	Remedies Upon Tenant's Default.....	11
13.3.	Remedies Cumulative.....	12
14.	SUBORDINATION, ATTORNMENT AND SALE.....	12
14.1.	Subordination To Mortgage.....	12
14.2.	Sale Of Landlord's Interest.....	12
14.3.	Estoppel Certificates.....	12
14.4.	Subordination to CC&R's.....	13
15.	RESERVED.....	13
16.	MISCELLANEOUS.....	13
16.1.	Notices.....	13
16.2.	Successors And Assigns.....	14
16.3.	No Waiver.....	14
16.4.	Severability.....	14
16.5.	Litigation Between Parties.....	14
16.6.	Surrender.....	14
16.7.	Interpretation.....	14
16.8.	Entire Agreement.....	14
16.9.	Governing Law.....	15
16.10.	No Partnership.....	15
16.11.	Financial Information.....	15
16.12.	Costs.....	15

16.13. Time.....15
16.14. Rules And Regulations.....15
16.15. Brokers.....15
16.16. Memorandum Of Lease.....15
16.17. Corporate Authority.....16
16.18. Execution and Delivery.....16
16.19. Warrants.....16
16.20. Signage.....16
16.21. Parking.....16

EXHIBITS

- A Location of Premises
- B Real Property Description
- C Acknowledgement of Lease Commencement

LEASE

THIS LEASE is made and entered into as of the 25th day of August, 1998, by and between BRITANNIA POINTE GRAND LIMITED PARTNERSHIP, a Delaware limited partnership ("Landlord") and PAIN THERAPEUTICS, INC., a Delaware corporation ("Tenant").

THE PARTIES AGREE AS FOLLOWS:

1. PREMISES

1.1 Premises. Landlord leases to Tenant and Tenant hires and leases from Landlord, on the terms, covenants and conditions hereinafter set forth, the premises (the "Premises") designated in Exhibit A attached hereto and incorporated herein by this reference, consisting of 3,250 square feet of space located within Building D (the "Building") in the Britannia Pointe Grand Business Park (the "Center") in the City of South San Francisco, County of San Mateo, State of California, commonly known as 250 East Grand Avenue, Suite 70, South San Francisco, California 94080, which Premises are located on the real property (the "Property") described in Exhibit B attached hereto and incorporated herein by this reference, together with the nonexclusive right to use any common areas designated from time to time in any Declaration of Covenants, Conditions and Restrictions or similar document affecting the Center.

1.2. Landlord's Reserved Rights. Landlord reserves the right from time to time to (i) install, use, maintain, repair and replace pipes, ducts, conduits, wires and appurtenant meters and equipment for service to other parts of the Building above the ceiling surfaces, below the floor surfaces, within the walls or leading through the Premises in locations which will not materially interfere with Tenant's use thereof, (ii) relocate any pipes, ducts, conduits, wires and appurtenant meters and equipment included in the Premises which are so located or located elsewhere outside the Premises, (iii) make alterations or additions to the Building, (iv) construct, alter or add to other buildings or improvements on the Property, (v) build adjoining to the Property, and (vi) lease any part of the Property for the construction of improvements or building. Landlord may modify or enlarge the common area, alter or relocate accesses to the Premises, or alter or relocate any common facility. Landlord shall not exercise rights reserved to it pursuant to this Section 1.2 in such a manner as to materially impair Tenant's ability to conduct its activities in the normal manner; provided, however, that the foregoing shall not limit or restrict Landlord's right to undertake reasonable construction activity and Tenant's use of the Premises shall be subject to reasonable temporary disruption incidental to such activity diligently prosecuted.

2. TERM

2.1. Term. The term of this Lease shall commence on the earlier to occur of (i) the date Landlord notifies Tenant in writing that Landlord's work pursuant to Section 2.4 is substantially complete, or (ii) the date Tenant takes occupancy of the Premises (except as otherwise provided in Section 2.2), the earlier of such dates being herein called the "Commencement Date," and shall end on the day immediately preceding the second (2nd) anniversary of the Commencement Date, unless sooner terminated as hereinafter provided. To the extent Tenant wishes (and is permitted by Landlord) to take possession of the Premises and begin conducting Tenant's business in portions of the Premises while Landlord is completing Landlord's work under Section 2.4 in the balance of the Premises, such possession shall trigger the occurrence of the Commencement Date under this Section 2.1, regardless of the fact that less than the entire Premises is then ready for occupancy by Tenant. Notwithstanding any other provisions of this Lease, Tenant shall have the right to surrender the Premises and terminate this Lease at any time prior to the termination date specified above in this Section 2.1, but no such early termination or surrender by Tenant shall entitle Tenant to any refund or adjustment with respect to the annual rent prepaid by Tenant on or before the Commencement

Date on or before the first anniversary of the Commencement Date as provided in Section 3.1 hereof. Landlord currently estimates that the Commencement Date will be September 21, 1998.

2.2 Early Possession. If Landlord permits Tenant to occupy, use or take possession of the Premises prior to the Commencement Date determined under Section 2.1, such occupancy, use or possession shall be subject to and upon all of the terms and conditions of this Lease, including the obligation to pay rent and other charges, unless Landlord and Tenant agree otherwise; provided, however, that such early possession shall not advance or otherwise affect the Commencement Date or termination date determined under Section 2.1; provided further, that if Tenant takes early possession solely for the purpose of installing fixtures and equipment and other similar work preparatory to the commencement of business in the Premises, Tenant shall not be required to pay rent and other charges by reason of such possession until the Commencement Date otherwise occurs; and provided further, that Tenant shall not interfere with or delay Landlord's contractors by such early possession and shall indemnify, defend and hold harmless Landlord and its agents and employees from and against any and all claims, demands, liabilities, actions, losses, costs and expenses, including (but not limited to) reasonable attorneys' fees, arising out of or in connection with Tenant's early entry upon the Premises hereunder.

2.3 Delay In Possession. Landlord agrees to use its best reasonable efforts to complete promptly the work described in Section 2.4; provided, however, Landlord shall not be liable for any damages caused by any delay in the completion of such work, nor shall any such delay affect the validity of this Lease or the obligations of Tenant hereunder.

2.4 Construction. The obligation of Landlord to perform work to improve the Premises for occupancy by Tenant is limited to the following, all of which work shall be performed promptly and diligently (subject to delays for causes beyond Landlord's reasonable control), in a neat and workmanlike manner, in compliance with all applicable governmental codes, laws and regulations in force at the time such work is completed, and at no expense to Tenant: Landlord shall repaint the Premises and recarpet the rear portion of the Premises (as designated on Exhibit A) with building-standard materials, colors to be approved by Tenant (which approval shall not be unreasonably withheld or delayed), clean the carpets in the remaining portions of the Premises, and shall replace missing or damaged ceiling tiles. Landlord shall also ensure that the existing improvements in the Premises (including, but not limited to, lighting, windows, doors, partitions, HVAC system, and plumbing, electrical, water, gas (if applicable) and other utility systems) are in clean condition and in good working order, ordinary wear and tear excepted. Except as specifically set forth in this Section 2.4, Landlord shall have no responsibilities or obligations with respect to preparation of the Premises for Tenant's occupancy. Acceptance by Tenant of possession of the Premises after performance of such work by Landlord shall constitute acceptance by Tenant of such work in its then completed condition and Landlord shall have no further responsibility of any kind or character for improvement of the Premises or in connection with such work; provided, however, that within thirty (30) days after the Commencement Date, Tenant may furnish to Landlord a "punch list" identifying any items or matters in the Premises which are not in the condition required under this Section 2.4 and Landlord shall promptly and diligently correct all such matters at its sole cost and expense.

2.5 Acknowledgement Of Lease Commencement. Upon commencement of the term of this Lease, Landlord and Tenant shall execute a written acknowledgement of the Commencement Date, date of termination and related matters (if any), substantially in the form attached hereto as Exhibit C (with appropriate insertions), which acknowledgement shall be deemed to be incorporated herein by this reference. Notwithstanding the foregoing requirement, the failure of one or both parties to execute such a written acknowledgement shall not affect the determination of the Commencement Date, date of termination and related matters (if any) in accordance with the provisions of this Lease.

2.6 Holding Over. If Tenant holds possession of the Premises after the term of this Lease with Landlord's written consent, then except as otherwise specified in such consent, Tenant shall become a tenant from month to month at one and one-half the rental (determined on a monthly rather than an annual basis) and otherwise upon the terms herein specified for a period immediately

prior to such holding over and shall continue in such status until the tenancy is terminated by either party upon not less than thirty (30) days prior written notice. If Tenant holds possession of the Premises after the term of this Lease without Landlord's written consent, then Landlord in its sole discretion may elect (by written notice to Tenant) to have Tenant become a tenant either from month to month or at will, at one and one-half the rental (prorated on a daily basis for an at-will tenancy, if applicable) and otherwise upon the terms herein specified for the period immediately prior to such holding over, or may elect to pursue any and all legal remedies available to Landlord under applicable law with respect to such unconsented holding over by Tenant. Tenant shall indemnify and hold Landlord harmless from any loss, damage, claim, liability, cost or expense (including reasonable attorneys' fees) resulting from any delay by Tenant in surrendering the Premises (except with Landlord's prior written consent), including but not limited to any claims made by a succeeding tenant by reason of such delay. Acceptance of rent by Landlord following expiration or termination of this Lease shall not constitute a renewal of this Lease.

3. RENTAL

3.1. Rental. Tenant shall pay to Landlord as rental for the Premises, in advance, without deduction, offset, notice or demand, (a) in one installment on or before the Commencement Date, the sum of Thirty-Five Thousand and No/100 Dollars (\$35,000.00), being the entire annual rent for first year of the term of this Lease, and (b) in one installment on or before the one-year anniversary of the Commencement Date the sum of Thirty-Five Thousand and No/100 Dollars (\$35,000.00), being the entire annual rent for the second year of the term of this Lease.

3.2. Late Charge. If Tenant fails to pay when due rental or other amounts due Landlord hereunder, such unpaid amounts shall bear interest for the benefit of Landlord at a rate equal to the lesser of fifteen percent (15%) per annum or the maximum rate permitted by law, from the date due to the date of payment. In addition to such interest, Tenant shall pay to Landlord a late charge in an amount equal to ten percent (10%) of any installment of rental and any other amounts due Landlord if not paid in full on or before the fifth (5th) day after such rental or other amount is due. Tenant acknowledges that late payment by Tenant to Landlord of rental or other amounts due hereunder will cause Landlord to incur costs not contemplated by this Lease, including, without limitation, processing and accounting charges and late charges which may be imposed on Landlord by the terms of any loan relating to the Property. Tenant further acknowledges that it is extremely difficult and impractical to fix the exact amount of such costs and that the late charge set forth in this Section 3.2 represents a fair and reasonable estimate thereof. Acceptance of any late charge by Landlord shall not constitute a waiver of Tenant's default with respect to overdue rental or other amounts, nor shall such acceptance prevent Landlord from exercising any other rights and remedies available to it. Acceptance of rent or other payments by Landlord shall not constitute a waiver of late charges or interest accrued with respect to such rent or other payments or any prior installments thereof, nor of any other defaults by Tenant, whether monetary or non-monetary in nature, remaining uncured at the time of such acceptance of rent or other payments.

4. TAXES

4.1. Personal Property. Tenant shall be responsible for and shall pay prior to delinquency all taxes and assessments levied against or by reason of any alterations and additions installed or paid for by Tenant under this Lease, and the personal property, trade fixtures and other property (if any) placed by Tenant in or about the Premises. Upon request by Landlord, Tenant shall furnish Landlord with satisfactory evidence of payment thereof. If at any time during the term of this Lease any of said alterations, additions or personal property, whether or not belong to Tenant, shall be taxed or assessed as part of the Property, then such tax or assessment shall be paid by Tenant to Landlord immediately upon presentation by Landlord of copies of the tax bills in which such taxes and assessments are included and shall, for the purposes of this Lease, be deemed to be personal property taxes or assessments under this Section 4.1. Tenant shall have no liability with respect to

personal property taxes or assessments attributable to the period before the Commencement Date or with respect to personal property of the previous tenant of the Premises.

5. UTILITIES

5.1. Payment. Commencing with the Commencement Date and thereafter throughout the term of this Lease, Tenant shall pay, before delinquency, all charges for water, gas, heat, light, electricity, power, sewer, telephone, alarm system, janitorial and other services or utilities supplied to or consumed in or upon the Premises, including any taxes on such services and utilities. It is the intention of the parties that all such services shall be separately metered to the Premises. In the event that any of such services supplied to the Premises are not separately metered, then Tenant shall pay to Landlord an appropriate proportion of the amounts paid by Landlord for such services, such appropriate proportion to be determined by mutual written agreement of Landlord and Tenant, such agreement not to be unreasonably withheld or delayed by either party.

5.2. Interruption. There shall be no abatement of rent or other charges required to be paid hereunder and Landlord shall not be liable in damages or otherwise for interruption or failure of any service or utility furnished to or used in the Premises because of accident, making of repairs, alterations or improvements, severe weather, difficulty or inability in obtaining services or supplies, labor difficulties or any other cause.

6. ALTERATIONS

6.1. Right To Make Alterations. Tenant shall make no alterations, additions or improvements to the Premises without the prior written consent of Landlord, which consent shall not be unreasonably withheld or delayed, and Landlord shall not charge Tenant an administrative fee to grant such consent. Any such alterations, additions and improvements shall be completed with due diligence in a first-class workmanlike manner and in compliance with plans and specifications approved in writing by Landlord and all applicable laws, ordinances, rules and regulations.

6.2. Title To Alterations. Any and all alterations, additions and improvements installed in, on or about the Premises shall be part of the Building and the property of Landlord, unless Landlord elects to require Tenant to remove the same upon the termination of this Lease; provided however, that the foregoing shall not apply to Tenant's movable furniture, trade fixtures and equipment.

6.3. Tenant Fixtures. Notwithstanding the provisions of Sections 6.1 and 6.2, Tenant may install, remove and reinstall trade fixtures without Landlord's prior written consent, except that any fixtures which are affixed to the Premises or which affect the exterior or structural portions of the Building shall require Landlord's written approval. The foregoing shall apply to Tenant's signs, logos and insignia, all of which Tenant shall have the right to place and remove and replace solely with Landlord's prior written consent as to location, size and composition. Tenant shall immediately repair any damage caused by installation and removal of fixtures under this Section 6.3.

6.4 No Liens. Tenant shall at all times keep the Premises free from all liens and claims of any contractors, subcontractors, materialmen, suppliers or any other parties employed either directly or indirectly by Tenant in construction work on the Premises. Tenant may contest any claim of lien, but only if, prior to such contest, Tenant either (i) posts security in the amount of the claim, plus estimated costs and interest, or (ii) records a bond of a responsible corporate surety in such amount as may be required to release the lien from the Premises. Tenant shall indemnify, defend and hold Landlord harmless against any and all liability, loss, damage, cost and other expenses, including, without limitation, reasonable attorneys' fees, arising out of claims of any lien for work performed or materials or supplies furnished at the request of Tenant or persons claiming under Tenant.

7. MAINTENANCE AND REPAIRS

7.1. Landlord's Work. Landlord shall repair and maintain or cause to be repaired and maintained those portions of the Building outside of the Premises, the common areas of the Property, and the roof, exterior walls and other structural portions of the Building. Landlord shall also maintain and repair in good operating condition the improvements existing in the Premises at the date possession of the Premises is tendered to Tenant, including the ceiling, doors, windows, walls, partitions, signs, lighting, HVAC and other mechanical and utility systems serving the premises, and all other interior improvements, other than routine janitorial service (which shall be Tenant's responsibility as provided in Section 6.1 hereof) and repairs which are expressly made Tenant's responsibility under Section 7.2 hereof. The cost of all work performed by Landlord under this Section 7.1 shall be Landlord's sole expense, except to the extent such work is required due to the negligence or willful misconduct of Tenant or its agents, employees or invitees (in which event Tenant shall bear the full cost of such work pursuant to the indemnification provided in Section 9.6 hereof). Tenant knowingly and voluntarily waives the right to make repairs at Landlord's expense, or to offset the cost thereof against rent, under any law, statute, regulation or ordinance now or hereafter in effect.

7.2. Tenant's Obligation For Maintenance.

(a) Good Order, Condition And Repair. By accepting possession of the Premises, Tenant acknowledges that the Premises are in good sanitary order, condition and repair, subject to completion of any "punch list" items with respect to Landlord's required work under Section 2.4. Tenant at its sole cost and expense shall keep and maintain in good and sanitary order, condition and repair all equipment, trade fixtures and personal property, if any, installed by Tenant in or about the Premises.

(b) Condition Upon Surrender. At the expiration or sooner termination of this Lease, Tenant shall surrender the Premises, including any additions, alterations and improvements thereto, broom clean, in good and sanitary order, condition and repair, ordinary wear and tear excepted, first, however, removing all goods and effects of Tenant and any and all fixtures and items required to be removed or specified to be removed at Landlord's election pursuant to this Lease, and repairing any damage caused by such removal. Tenant shall not have the right to remove fixtures or equipment if Tenant is in default hereunder unless Landlord specifically waives this provision in writing. Tenant expressly waives any and all interest in any personal property and trade fixtures not removed from the Premises by Tenant at the expiration or termination of this Lease, agrees that any such personal property and trade fixtures may, at Landlord's election, be deemed to have been abandoned by Tenant, and authorizes Landlord (at its election and without prejudice to any other remedies under this Lease or under applicable law) to remove and either retain, store or dispose of such property at Tenant's cost and expense, and Tenant waives all claims against Landlord for any damages resulting from any such removal, storage, retention or disposal.

8. USE OF PREMISES

8.1. Permitted Use. Tenant shall use the Premises solely for general office use, biological laboratory research, and related purposes, and for no other purpose.

8.2. Requirement Of Continued Use. Tenant shall not at any time leave the Premises unoccupied or vacant, and shall continuously during the term of this Lease (except during any period when the Premises are unusable by reason of events described in Article 12 hereof) conduct and carry on in the Premises the use permitted hereunder.

8.3. No Nuisance. Tenant shall not use the Premises for or carry on or permit upon the Premises or any part thereof any offensive, noisy or dangerous trade, business, manufacture, occupation, odor or fumes, or any nuisance or anything against public policy, nor interfere with the rights or business of any other tenants or of Landlord in the Building or the Property, nor commit

or allow to be committed any waste in, on or about the Premises, nor make any other unreasonable use of the Premises. Tenant shall not do or permit anything to be done in or about the Premises, nor bring nor keep anything therein, which will in any way cause the Premises to be uninsurable with respect to the insurance required by this Lease or with respect to standard fire and extended coverage insurance with vandalism, malicious mischief and riot endorsements.

8.4. Compliance With Laws. Tenant shall not use the Premises or permit the Premises to be used in whole or in part for any purpose or use that is in violation of any applicable laws, ordinances, regulations or rules of any governmental agency or public authority. Tenant shall keep the Premises equipped with all safety appliances required by law, ordinance or insurance on the Premises, or any order or regulation of any public authority because of Tenant's particular use of the Premises. Tenant shall procure all licenses and permits required for use of the Premises, other than a certificate of occupancy (which Landlord represents has already been obtained and shall be in full force and effect on the Commencement Date). Tenant shall use the Premises in strict accordance with all applicable ordinances, rules, laws and regulations and shall comply with all requirements of all governmental authorities now in force or which may hereafter be in force pertaining to the use of the Premises by Tenant, including, without limitation, regulations applicable to noise, water, soil and air pollution, and making such nonstructural alterations and additions thereto as may be required from time to time by such laws, ordinances, rules, regulations and requirements of governmental authorities or insurers of the Premises (collectively, "Requirements") because of Tenant's construction of improvements in or other particular use of the Premises. Any structural alterations or additions required from time to time by applicable Requirements because of Tenant's construction of improvements in or other particular use of the Premises shall, at Landlord's election, either (i) be made by Tenant, at Tenant's sole cost and expense, in accordance with the procedures and standards set forth in Section 6.1 for alterations by Tenant, or (ii) be made by Landlord at Tenant's sole cost and expense, in which event Tenant shall pay to Landlord as additional rent, within ten (10) days after demand by Landlord, an amount equal to all costs incurred by Landlord in connection with such alterations or additions. The judgment of any court, or the admission by Tenant in any proceeding against Tenant, that Tenant has violated any law, statute, ordinance or governmental rule, regulation or requirement shall be conclusive of such violation as between Landlord and Tenant.

8.5. Liquidation Sales. Tenant shall not conduct or permit to be conducted any auction, bankruptcy sale, liquidation sale, or going out of business sale, in, upon or about the Premises or the Property, whether said auction or sale be voluntary, involuntary or pursuant to any assignment for the benefit of creditors, or pursuant to any bankruptcy or other insolvency proceeding.

8.6. Environmental Matters. Without limiting the generality of Tenant's obligations set forth in Section 8.4. of this Lease:

(a) Tenant shall not cause or permit any hazardous or toxic substance or hazardous waste (as defined in any federal, state or local law, ordinance or regulation applicable to such substances or wastes) to be brought upon, kept, stored or used on or about the Property without the prior written consent of Landlord.

(b) Tenant shall comply with all applicable laws, rules, regulations, orders, permits, licenses and operating plans of any governmental authority with respect to the receipt, use, handling, generation, transportation, storage, treatment, release and/or disposal of hazardous or toxic substances or wastes in the course of or in connection with the conduct of Tenant's business on the Property, and shall provide Landlord with copies of any and all permits, licenses, registrations and other similar documents that authorize Tenant to conduct any such activities in connection with Tenant's use of the Property.

(c) Tenant shall indemnify, defend and hold Landlord harmless from and against any and all claims, losses, damages, liabilities, costs, legal fees and expenses of any sort arising out of or relating to (i) any failure by Tenant to comply with any provisions of subparagraph (a) or (b) above, or (ii) any receipt, use, handling, generation, transportation, storage, treatment, release and/or disposal of any hazardous or toxic substances or wastes on or about the Property in

connection with Tenant's use or occupancy of the Property or as a result of any intentional or negligent acts or omissions of Tenant or of any agent or employee of Tenant.

(d) Landlord shall indemnify, defend and hold Tenant harmless from and against any and all claims, losses, damages, liabilities, costs, legal fees and expenses of any sort arising out of or relating to (i) the presence on the Property of any hazardous or toxic substances or wastes present on the Property as of the Commencement Date (except to the extent their presence is the result of any intentional or negligent acts or omissions of Tenant or of any agent or employee of Tenant), and/or (ii) any unauthorized release into the environment of hazardous or toxic substances or wastes to the extent they result from the negligence of or willful misconduct or omission by Landlord or its agents or employees.

(e) The provisions of this Section 8.6 shall survive the termination of this Lease.

9. INSURANCE AND INDEMNITY

9.1. Liability Insurance. Tenant shall procure and maintain in full force and effect at all times during the term of this Lease, at Tenant's cost and expense, comprehensive public liability and property damage insurance to protect against any liability to the public, or to any invitee of Tenant or Landlord, arising out of or related to the use of or resulting from any accident occurring in, upon or about the Premises, with limits of liability of not less than (i) One Million Dollars (\$1,000,000.00) for injury to or death of one person, (ii) One Million Dollars (\$1,000,000.00) for personal injury or death, per occurrence, and (iii) Five Hundred Thousand Dollars (\$500,000.00) for property damage, or a combined single limit of public liability and property damage insurance of not less than One Million Dollars (\$1,000,000.00). Such insurance shall name Landlord and its general partners, lender(s) and Managing Agent as additional insureds thereunder. The amount of such insurance shall not be construed to limit any liability or obligation of Tenant under this Lease. Tenant's obligation to maintain property damage insurance shall not be deemed to require Tenant to maintain earthquake insurance.

9.2. Quality Of Policies and Certificates. All policies of insurance required hereunder shall be issued by responsible insurers and shall be written as primary policies not contributing with and not in excess of any coverage that Landlord may carry. Tenant shall deliver to Landlord copies of policies or certificates of insurance showing that said policies are in effect. The coverage provided by such policies shall include the clause or endorsement referred to in Section 9.4. If Tenant fails to acquire, maintain or renew any insurance required to be maintained by it under this Article 9 or to pay the premium therefor, then Landlord, at its option and in addition to its other remedies, but without obligation so to do, may procure such insurance, and any sums expended by it to procure any such insurance shall be repaid upon demand, with interest as provided in Section 3.2 hereof. Tenant shall obtain written undertakings from each insurer under policies required to be maintained by it to notify all insureds thereunder at least thirty (30) days prior to cancellation, amendment or revision of coverage.

9.3. Workers' Compensation. Tenant shall maintain in full force and effect during the term of this Lease workers' compensation insurance covering all of Tenant's employees working on the Premises.

9.4. Waiver Of Subrogation. To the extent permitted by the law and without affecting the coverage provided by insurance required to be maintained hereunder, Landlord and Tenant each waive any right to recover against the other (i) damages for injury to or death of persons, (ii) damage to property, (iii) damage to the Premises or any part thereof, or (iv) claims arising by reason of any of the foregoing, but only to the extent that any of the foregoing damages and claims under subparts (i)-(iv) hereof are covered, and only to the extent of such coverage, by casualty insurance actually carried or required to be carried hereunder by either Landlord or Tenant. This provision is intended to waive fully, and for the benefit of each party, any rights and claims which might give rise to a

right of subrogation in any casualty insurance carrier. Each party shall procure a clause or endorsement on any casualty insurance policy required under this Article 9 denying to the insurer rights of subrogation against the other party to the extent rights have been waived by the insured prior to the occurrence of injury or loss. Coverage provided by insurance maintained by Tenant under this Article 9 shall not be limited, reduced or diminished by virtue of the subrogation waiver herein contained.

9.5 Increase in Premiums. Tenant shall do all acts and pay all expenses necessary to insure that the Premises are not used for purposes prohibited by any applicable fire insurance, and that Tenant's use of the Premises complies with all requirements necessary to obtain any such insurance. If Tenant uses or permits the Premises to be used in a manner which increases the existing rate of any insurance on the Premises carried by Landlord, Tenant shall pay the amount of the increase in premium caused thereby, and Landlord's costs of obtaining other replacement insurance policies, including any increase in premium, within ten (10) days after demand therefor by Landlord.

9.6 Indemnification.

(a) Tenant shall indemnify, defend and hold Landlord, its partners, shareholders, officers, directors, affiliates, agents, employees and contractors, harmless from any and all liability for injury to or death of any person, or loss of or damage to the property of any person, and all actions, claims, demands, costs (including, without limitation, reasonable attorneys' fees), damages or expenses of any kind arising therefrom which may be brought or made against Landlord or which Landlord may pay or incur by reason of the use, occupancy and enjoyment of the Premises by Tenant or any invitees, sublessees, licensees, assignees, employees, agents or contractors of Tenant or holding under Tenant from any cause whatsoever other than negligence or willful misconduct or omission by Landlord, its agents or employees. Landlord, its partners, shareholders, officers, directors, affiliates, agents, employees and contractors shall not be liable for, and Tenant hereby waives all claims against such persons for, damages to goods, wares and merchandise in or upon the Premises, or for injuries to Tenant, its agents or third persons in or upon the Premises, from any cause whatsoever other than negligence or willful misconduct or omission by Landlord, its agents or employees. Tenant shall give prompt notice to Landlord of any casualty or accident in, on or about the Premises.

(b) Landlord shall indemnify, defend and hold Tenant, its partners, shareholders, officers, directors, affiliates, agents, employees and contractors, harmless from any and all liability for injury to or death of any person or loss of or damage to the property of any person, and all actions, claims, demands, costs (including, without limitation, reasonable attorneys' fees), damages or expenses of any kind arising therefrom which may be brought or made against Tenant or which Tenant may pay or incur, to the extent such liabilities or other matters arise by reason of any negligence or willful misconduct or omission by Landlord, its agents or employees.

9.7 Blanket Policy. Any policy required to be maintained hereunder may be maintained under a so-called "blanket policy" insuring other parties and other locations so long as the amount of insurance required to be provided hereunder is not thereby diminished.

10. SUBLEASE AND ASSIGNMENT

10.1 Assignment And Sublease Of Premises. Tenant shall not have the right or power to assign its interest in this Lease, or make any sublease, nor shall any interest of Tenant under this Lease be assignable involuntarily or by operation of law, without on each occasion obtaining the prior written consent of Landlord, which consent shall not be unreasonably withheld. Any purported sublease or assignment of Tenant's interest in this Lease requiring but not having received Landlord's consent thereto shall be void. Without limiting the generality of the foregoing, Landlord may withhold consent to any proposed subletting or assignment solely on the ground that the use by the proposed subtenant or assignee is reasonably likely to be incompatible with Landlord's use of the

balance of the Building or Property. Any dissolution, consolidation, merger or other reorganization of Tenant, or any sale or transfer of the stock of or other interest in Tenant, or any series of one or more of such events, involving in the aggregate a change of fifty percent (50%) or more in the beneficial ownership of Tenant or its assets shall be deemed to be an assignment hereunder and shall be void without the prior written consent of Landlord, not to be unreasonably withheld, as required above, provided, however, that a sale of equity interests in the company in a bona fide third party financing (including, without limitation, venture capital financing) shall not be deemed to be an assignment for purposes of this Section 10.1

10.2. Rights Of Landlord. Consent by Landlord to one or more assignments of this Lease, or to one or more sublettings of the Premises, or collection of rent by Landlord from any assignee or sublessee, shall not operate to exhaust Landlord's rights under this Article 10, nor constitute consent to any subsequent assignment or subletting. No assignment of Tenant's interest in this Lease and no sublease shall relieve Tenant of its obligations hereunder, notwithstanding any waiver or extension of time granted by Landlord to any assignee or sublessee, or the failure of Landlord to assert its rights against any assignee or sublessee, and regardless of whether Landlord's consent thereto is given or required to be given hereunder. In the event of a default by any assignee, sublessee or other successor of Tenant in the performance of any of the terms or obligations of Tenant under this Lease, Landlord may proceed directly against Tenant without the necessity of exhausting remedies against any such assignee, sublessee or other successor. In addition, Tenant immediately and irrevocably assigns to Landlord, as security for Tenant's obligations under this Lease, all rent from any subletting of all or a part of the Premises as permitted under this Lease, and Landlord, as Tenant's assignee and as attorney-in-fact for Tenant, or any receiver, for Tenant appointed on Landlord's application, may collect such rent and apply it toward Tenant's obligations under this Lease; except that until the occurrence of an act of default by Tenant, Tenant shall have the right to collect such rent.

11. RIGHT OF ENTRY AND QUIET ENJOYMENT

11.1. Right Of Entry. Landlord and its authorized representatives shall have the right to enter the Premises at any time during the term of this Lease during normal business hours and upon not less than twenty-four (24) hours prior notice, except in the case of emergency (in which event no notice shall be required and entry may be made at any time), for the purpose of inspecting and determining the condition of the Premises or for any other proper purpose including, without limitation, to make repairs, replacements or improvements which Landlord may deem necessary, to show the Premises to prospective purchasers, to show the Premises to prospective tenants, and to post notices of nonresponsibility. Landlord shall not be liable for inconvenience, annoyance, disturbance, loss of business, quiet enjoyment or other damages or loss to Tenant by reason of making any repairs or performing any work upon the Premises, the Building or the Property, and the obligations of Tenant under this Lease shall not thereby be affected in any manner whatsoever, provided, however, Landlord shall use reasonable efforts to minimize the inconvenience to Tenant's normal business operations caused thereby.

11.2. Quiet Enjoyment. Landlord covenants that Tenant, upon paying the rent and performing its obligations hereunder and subject to all the terms and conditions of this Lease, shall peacefully and quietly have, hold and enjoy the Premises throughout the term of this Lease, or until this Lease is terminated as provided by this Lease.

12. CASUALTY AND TAKING

12.1. Termination Or Reconstruction. If during the term of this Lease the Premises or Building, or any substantial part of either, (i) is damaged materially by fire or other casualty or by action of public or other authority in consequence thereof, (ii) is taken by eminent domain or by reason of any public improvement or condemnation proceeding, or in any manner by exercise of the right of eminent domain (including any transfer in avoidance of an exercise of the power of eminent

domain), or (iii) receives irreparable damage by reason of anything lawfully done under color of public or other authority, this Lease shall terminate as to the entire Premises at Landlord's election by written notice given to Tenant within sixty (60) days after the damage or taking has occurred, and Tenant shall be entitled to refund of a prorata portion of the rental paid to Landlord pursuant to Section 3.1 representing the portion of the year for which rental has been paid in advance following the termination. If Landlord does not elect to terminate this Lease as hereinabove provided, Landlord shall, at Landlord's expense, repair any such damage and restore the Premises (to the extent of Landlord's work therein under Section 2.4 and the existing improvements previously constructed by Landlord and located in the Premises on the Commencement Date) and the Building as nearly as reasonably possible to the condition existing before the damage or taking.

12.2 Tenant's Rights. If any portion of the Premises is to be taken by condemnation, Tenant may elect to terminate this Lease if the portion of the Premises taken is of such extent and nature as substantially to handicap, impede or permanently impair Tenant's use of the balance of the Premises. Tenant must exercise its right to terminate by giving notice to Landlord within thirty (30) days after the nature and extent of the taking have been finally determined. If Tenant elects to terminate this Lease, Tenant shall also notify Landlord of the date of termination, which date shall not be earlier than thirty (30) days nor later than ninety (90) days after Tenant has notified Landlord of its election to terminate, except that this Lease shall terminate on the date of taking if the date of taking falls on any date before the date of termination designated by Tenant. If the material damage to the Premises by fire or other casualty or by action of public or other authority in consequence thereof is of such extent and nature as substantially to handicap or impede Tenant's use of the balance of the Premises, and Landlord estimates that the amount of time required to repair any such damage exceeds sixty (60) days, then Tenant may terminate this Lease by giving notice to Landlord within thirty (30) days after Landlord has notified Tenant of Landlord's estimate of the amount of time that will be required to repair such damage; provided, however, that Tenant shall not have such termination rights of the fire or casualty was caused by Tenant or its agents. Following any termination of this Lease pursuant to this Section 12.2, Tenant shall be entitled to a refund of a prorata portion of the rental paid to Landlord pursuant to Section 3.1 representing the portion of the year for which rental has been paid in advance following the termination.

12.3 Lease To Remain In Effect. If neither Landlord nor Tenant terminates this Lease as hereinabove provided, this Lease shall continue in full force and effect, without any abatement or adjustment of the rental paid in advance by Tenant for the term hereof. Each party waives the provisions of Code of Civil Procedure Section 1265.130, allowing either party to petition the Superior Court to terminate this Lease in the event of a partial condemnation of the Premises.

12.4 Reservation Of Compensation. Landlord reserves, and Tenant waives and assigns to Landlord, all rights to any award or compensation for damage to the Premises, Building, Property and the leasehold estate created hereby, accruing by reason of any taking in any public improvement, condemnation or eminent domain proceeding or in any other manner by exercise of the right of eminent domain or of anything lawfully done by public authority, except that Tenant shall be entitled to any and all compensation or damages paid for or on account of Tenant's moving expenses, trade fixtures and equipment. Tenant covenants to deliver such further assignments of the foregoing as Landlord may from time to time request.

12.5 Restoration Of Fixtures. If Landlord repairs or causes repair of the Premises after such damage or taking, Tenant at its sole expense shall repair and replace promptly all trade fixtures, equipment and other property of Tenant located at, in or upon the Premises and all additions, alterations and improvements and all other items installed by Tenant under this Lease that were damaged or taken, so as to restore the same to a condition substantially equal to that which existed immediately prior to the damage or taking.

13. DEFAULT

13.1. Events Of Default. The occurrence of any of the following shall constitute an event of default on the part of Tenant:

(a) Abandonment. Abandonment of the Premises. Tenant waives any right Tenant may have to notice under Section 1951.3 of the California Civil Code, the terms of this subsection (a) being deemed such notice to Tenant as required by said Section 1951.3;

(b) Nonpayment. Failure to pay, when due, any amount payable to Landlord hereunder, such failure continuing for a period of five (5) days after written notice of such failure; provided, however, that any such notice shall be in lieu of, and not in addition to, any notice required under California Code of Civil Procedure Section 1161 et seq., as amended from time to time;

(c) Other Obligations. Failure to perform any obligation, agreement or covenant under this Lease other than those matters specified in subsection (b) hereof, such failure continuing for fifteen (15) days after written notice of such failure, or, if it is not possible to cure such default within fifteen (15) days, failure to commence cure within said fifteen (15) day period and thereafter to proceed diligently to complete cure; provided, however, that any such notice shall be in lieu of, and not in addition to, any notice required under California Code of Civil Procedure Section 1161 et seq., as amended from time to time;

(d) General Assignment. A general assignment by Tenant for the benefit of creditors;

(e) Bankruptcy. The filing of any voluntary petition in bankruptcy by Tenant, or the filing of an involuntary petition by Tenant's creditors, which involuntary petition remains undischarged for a period of thirty (30) days. In the event that under applicable law the trustee in bankruptcy or Tenant has the right to affirm this Lease and continue to perform the obligations of Tenant hereunder, such trustee or Tenant shall, in such time period as may be permitted by the bankruptcy court having jurisdiction, cure all defaults of Tenant hereunder outstanding as of the date of the affirmance of this Lease and provide to Landlord such adequate assurances as may be necessary to ensure Landlord of the continued performance of Tenant's obligations under this Lease. Specifically, but without limiting the generality of the foregoing, such adequate assurances must include assurances that the Premises continue to be operated only for the use permitted hereunder. The provisions hereof are to assure that the basic understandings between Landlord and Tenant with respect to Tenant's use of the Premises and the benefits to Landlord therefrom are preserved, consistent with the purpose and intent of applicable bankruptcy laws;

(f) Receivership. The employment of a receiver appointed by court order to take possession of substantially all of Tenant's assets or the Premises, if such receivership remains undissolved for a period of thirty (30) days;

(g) Attachment. The attachment, execution or other judicial seizure of all or substantially all of Tenant's assets or the Premises, if such attachment or other seizure remains undismissed or undischarged for a period of thirty (30) days after the levy thereof; or

(h) Insolvency. The admission by Tenant in writing of its inability to pay its debts as they become due, the filing by Tenant of a petition seeking any reorganization or arrangement, composition, readjustment, liquidation, dissolution or similar relief under any present or future statute, law or regulation, the filing by Tenant of an answer admitting or failing timely to contest a material allegation of a petition filed against Tenant in any such proceeding or, if within thirty (30) days after the commencement of any proceeding against Tenant seeking any reorganization or arrangement, composition, readjustment, liquidation, dissolution or similar relief under any present or future statute, law or regulation, such proceeding shall not have been dismissed.

13.2. Remedies Upon Tenant's Default.

(a) Upon the occurrence of any event of default described in Section 13.1 hereof, Landlord, in addition to and without prejudice to any other rights or remedies it may have, shall have the immediate right to re-enter the Premises or any part thereof and repossess the same, expelling and removing therefrom all persons and property (which property may be stored in a public warehouse or elsewhere at the cost and risk of and for the account of Tenant), using such force as may be necessary to do so (as which Tenant hereby waives any claim for loss or damage that may thereby occur). In addition to or in lieu of such re-entry, and without prejudice to any other rights or remedies it may have, Landlord shall have the right either (i) to terminate this Lease and recover from Tenant all damages incurred by Landlord as a result of Tenant's default, as hereinafter provided, or (ii) to continue this Lease in effect and recover rent and other charges and amounts as they become due.

(b) Even if Tenant has breached this Lease or abandoned the Premises, this Lease shall continue in effect for so long as Landlord does not terminate Tenant's right to possession under subsection (a) hereof and Landlord may enforce all of its rights and remedies under this Lease, including the right to recover rent as it becomes due, and Landlord, without terminating this Lease, may exercise all of the rights and remedies of a lessor under California Civil Code Section 1951.4 (lessor may continue lease in effect after lessee's breach and abandonment and recover rent as it becomes due, if lessee has right to sublet or assign, subject only to reasonable limitations), or any successor Code section. Acts of maintenance, preservation or efforts to relet the Premises or the appointment of a receiver upon application of Landlord to protect Landlord's interests under this Lease shall not constitute a termination of Tenant's right to possession.

(c) If Landlord terminates this Lease pursuant to this Section 13.2, Landlord shall have all of the rights and remedies of a landlord provided by Section 1951.2 of the Civil Code of the State of California, or any successor Code section, which remedies include Landlord's right to recover from Tenant (i) the worth at the time of award of the unpaid rent and additional rent which had been earned at the time of termination, (ii) the worth at the time of award of the amount by which the unpaid rent and additional rent which would have been earned after termination until the time of award exceeds the amount of such rental loss that Tenant proves could have been reasonably avoided, (iii) the worth at the time of award of the amount by which the unpaid rent and addition rent for the balance of the term after the time of award exceeds the amount of such rental loss that Tenant proves could be reasonably avoided, and (iv) any other amount necessary to compensate Landlord for all the detriment proximately caused by Tenant's failure to perform its obligations under this Lease or which in the ordinary course of things would be likely to result therefrom, including, but not limited to, the cost of recovering possession of the Premises, expenses of reletting, including necessary repair, renovation and alteration of the Premises, reasonable attorneys' fees, and other reasonable costs. The "worth at the time of award" of the amounts referred to in clauses (i) and (ii) above shall be computed by allowing interest at ten percent (10%) per annum from the date such amounts accrued to Landlord. The "worth at the time of award" of the amounts referred to in clause (iii) above shall be computed by discounting such amount at one percentage point above the discount rate of the Federal Reserve Bank of San Francisco at the time of award.

13.3. Remedies Cumulative. All rights, privileges and elections or remedies of Landlord contained in this Article 13 are cumulative and not alternative to the extent permitted by law and except as otherwise provided herein.

14. SUBORDINATION, ATTORNMEN AND SALE

14.1. Subordination To Mortgage. This Lease, and any sublease entered into by Tenant under the provisions of this Lease, shall be subject and subordinate to any ground lease, mortgage, deed of trust, sale/leaseback transaction or any other hypothecation for security now or hereafter placed upon the Building, the Property, or both, and the rights of any assignee of Landlord or of any ground lessor, mortgage, trustee, beneficiary or leaseback lessor under any of the foregoing, and

to any and all advances made on the security thereof and to all renewals, modifications, consolidations, replacements and extensions thereof. If any mortgagee, trustee, beneficiary, ground lessor, sale/leaseback lessor or assignee elects to have this Lease be an encumbrance upon the Property prior to the lien of its mortgage, deed of trust, ground lease or leaseback lease or other security arrangement and gives notice thereof to Tenant, this Lease shall be deemed prior thereto, whether this Lease is dated prior or subsequent to the date thereof or the date of recording thereof. Tenant, and any sublessee, shall execute such documents as may reasonably be requested by any mortgagee, trustee, beneficiary, ground lessor, sale/leaseback lessor or assignee to evidence the subordination herein set forth or to make this Lease prior to the lien of any mortgage, deed of trust, ground lease, leaseback lease or other security arrangement, as the case may be, and if Tenant fails to do so within ten (10) days after demand from Landlord, Tenant constitutes and appoints Landlord as Tenant's attorney-in-fact and in Tenant's name, place and stead to do so. Upon any default by Landlord in the performance of its obligations under any mortgage, deed of trust, ground lease, leaseback lease or assignment, Tenant (and any sublessee) shall, notwithstanding any subordination hereunder, attorn to the mortgagee, trustee, beneficiary, ground lessor, leaseback lessor or assignee thereunder upon demand and become the tenant of the successor in interest to Landlord, at the option of such successor in interest, and shall execute and deliver any instrument or instruments confirming the attornment herein provided for.

14.2. Sale Of Landlord's Interest. Upon sale, transfer or assignment of Landlord's entire interest in the Building and Property, Landlord shall be relieved of its obligations hereunder with respect to liabilities accruing from and after the date of such sale, transfer or assignment.

14.3. Estoppel Certificates. Tenant shall at any time and from time to time, within ten (10) days after written request by Landlord, execute, acknowledge and deliver to Landlord a certificate in writing stating: (i) that this Lease is unmodified and in full force and effect, or if there have been any modifications, that this Lease is in full force and effect as modified and stating the date and the nature of each modification; (ii) the date to which rental and all other sums payable hereunder have been paid; (iii) that Landlord is not in default in the performance of any of its obligations under this Lease, that Tenant has given no notice of default to Landlord and that no event has occurred which, but for the expiration of the applicable time period, would constitute an event of default hereunder, or if Tenant alleges that any such default, notice or event has occurred, specifying the same in reasonable detail; and (iv) such other matters as may reasonably be requested by Landlord or any institutional lender, mortgagee, trustee, beneficiary, ground lessor, sale/leaseback lessor or prospective purchaser of the Property. Any such certificate provided under this Section 14.3 may be relied upon by any lender, mortgagee, trustee, beneficiary, assignee or successor in interest to Landlord, by any prospective purchaser, by any purchaser on foreclosure or sale, by any grantee under a deed in lieu of foreclosure of any mortgage or deed of trust on the Property or Premises, or by any other third party. Failure to execute and return within the required time any estoppel certificate requested hereunder shall be deemed to be an admission of the truth of the matters set forth in the form of certificate submitted to Tenant for execution.

14.4. Subordination to CC&R's. This Lease, and any permitted sublease entered into by Tenant under the provisions of this Lease, shall be subject and subordinate (a) to any declarations of covenants, conditions and restrictions affecting the Property from time to time, provided that the terms of such declarations are reasonable and do not discriminate against Tenant relative to other similarly situated tenants occupying portions of the Property, (b) to the Declaration of Covenants, Conditions and Restrictions for Pointe Grand Business Park dated November 4, 1991 and recorded on February 25, 1992 as Instrument No. 92025214, Official Records of San Mateo County, as amended from time to time (the "Master Declaration"), the provisions of which Master Declaration are an integral part of this Lease, (c) to the Declaration of Covenants, Conditions and Restrictions dated November 23, 1987 and recorded on November 24, 1987 as Instrument No. 87177987, Official Records of San Mateo County, which declaration imposes certain covenants, conditions and restrictions on the Property, and (d) to the Environmental Restriction and Covenant (Pointe Grand) dated as of April 16, 1997 and recorded on April 16, 1997 as Instrument No. 97-043682, Official Records of San Mateo County, which declaration imposes certain covenants, conditions and

restrictions on the Center. Tenant agrees to execute, upon request by Landlord, any documents reasonably required from time to time to evidence the subordination provided in this Section 14.4.

15. RESERVED

16. MISCELLANEOUS

16.1. Notices. All notices, consents, waivers and other communications which this Lease requires or permits either party to give to the other shall be in writing and shall be deemed given when delivered personally (including delivery by private courier or express delivery service) or four (4) days after deposit in the United States mail, registered or certified mail, postage prepaid, addressed to the parties at their respective addresses as follows:

To Tenant: (until Commencement Date)

Pain Therapeutics, Inc.
c/o Exelixis
260 Littlefield Avenue
South San Francisco, CA 94080
Attn: Remi Barbier, CEO

(after Commencement Date)

Pain Therapeutics, Inc.
250 East Grand Avenue, Suite 70
South San Francisco, CA 94080
Attn: Remi Barbier, CEO

To Landlord: Britannia Pointe Grand Limited Partnership
1939 Harrison Street, Suite 715
Park Plaza Building
Oakland, CA 94612
Attn: T. J. Bristow

with copy to: Folger Levin & Kahn LLP
Embarcadero Center West
275 Battery Street, 23rd Floor
San Francisco, CA 94111
Attn: Donald E. Kelley, Jr.

or to such other address as may be contained in a notice at least fifteen (15) days prior to the address change from either party to the other given pursuant to this Section. Rental payments and other sums required by this Lease to be paid by Tenant shall be delivered to Landlord at Landlord's address provided in this Section, or to such other address as Landlord may from time to time specify in writing to Tenant, and shall be deemed to be paid only upon actual receipt.

16.2. Successors and Assigns. The obligations of this Lease shall run with the land, and this Lease shall be binding upon and inure to the benefit of the parties hereto and their respective successors and assigns, except that the original Landlord named herein and each successive Landlord under this Lease shall be liable only for obligations accruing during the period of its ownership of the Property, said liability terminating upon termination of such ownership and passing to the successor lessor.

16.3. No Waiver. The failure of Landlord to seek redress for violation, or to insist upon the strict performance, of any covenant or condition of this Lease shall not be deemed a waiver of

such violation, or prevent a subsequent act which would originally have constituted a violation from having all the force and effect of an original violation.

16.4. Severability. If any provision of this Lease or the application thereof is held to be invalid or unenforceable, the remainder of this Lease or the application of such provision to persons or circumstances other than those as to which it is invalid or unenforceable shall not be affected thereby, and each of the provisions of this Lease shall be valid and enforceable, unless enforcement of this Lease as so invalidated would be unreasonable or grossly inequitable under all the circumstances or would materially frustrate the purposes of this Lease.

16.5. Litigation Between Parties. In the event of any litigation or other dispute resolution proceedings between the parties hereto arising out of or in connection with this Lease, the prevailing party shall be reimbursed for all reasonable costs, including, but not limited to, reasonable accountants' fees and attorneys' fees, incurred in connection with such proceedings (including, but not limited to, any appellate proceedings relating thereto) or in connection with the enforcement of any judgment or award rendered in such proceedings. "Prevailing party" within the meaning of this Section shall include, without limitation, a party who dismisses an action for recovery hereunder in exchange for payment of the sums allegedly due, performance of covenants allegedly breached or consideration substantially equal to the relief sought in the action.

16.6. Surrender. A voluntary or other surrender of this Lease by Tenant, or a mutual termination thereof between Landlord and Tenant, shall not result in a merger but shall, at the option of Landlord, operate either as an assignment to Landlord of any and all existing subleases and subtenancies, or a termination of all or any existing subleases and subtenancies. This provision shall be contained in any and all assignments or subleases made pursuant to this Lease.

16.7. Interpretation. The provisions of this Lease shall be construed as a whole, according to their common meaning, and not strictly for or against Landlord or Tenant. The captions preceding the text of each Section and subsection hereof are included only for convenience of reference and shall be disregarded in the construction or interpretation of this Lease.

16.8. Entire Agreement. This written Lease, together with the exhibits hereto, contains all the representations and the entire understanding between the parties hereto with respect to the subject matter hereof. Any prior correspondence, memoranda or agreements are replaced in total by this Lease and the exhibits hereto. This Lease may be modified only by an agreement in writing signed by each of the parties.

16.9. Governing Law. This Lease and all exhibits hereto shall be construed and interpreted in accordance with and be governed by all the provisions of the laws of the State of California.

16.10. No Partnership. The relationship between Landlord and Tenant is solely that of a lessor and lessee. Nothing contained in this Lease shall be construed as creating any type or manner of partnership, joint venture or joint enterprise with or between Landlord and Tenant.

16.11. Financial Information. From time to time Tenant shall promptly provide directly to prospective lenders and purchasers of the Property designated by Landlord such financial information pertaining to the financial status of Tenant as Landlord may reasonably request; provided, Tenant shall be permitted to provide such financial information in a manner which Tenant deems reasonably necessary to protect the confidentiality of such information. In addition, from time to time, Tenant shall provide Landlord with such financial information pertaining to the financial status of Tenant as Landlord may reasonably request. Landlord agrees that all financial information supplied to Landlord by Tenant shall be treated as confidential material, and shall not be disseminated to any person or entity without Tenant's prior written consent, except that Landlord shall be entitled to provide such information, subject to reasonable precautions to protect the confidential nature thereof, (i) to Landlord's partners and professional advisors, solely for use in connection with Landlord's execution and enforcement of this Lease, and (ii) to prospective lenders

and/or purchasers of the Property, solely for use in connection with their bona fide consideration of a proposed financing or purchase of the Property, provided that such prospective lenders and/or purchasers are not engaged in businesses directly competitive with the business then being conducted by Tenant. For purposes of this Section, without limiting the generality of the obligations provided herein, it shall be deemed reasonable for Landlord to request copies of Tenant's most recent audited annual financial statements, or, if audited statements have not been prepared, unaudited financial statements for Tenant's most recent fiscal year, accompanied by a certificate of Tenant's chief financial officer that such financial statements fairly present Tenant's financial condition as of the date(s) indicated.

Landlord and Tenant recognize the need of Tenant to maintain the confidentiality of information regarding its financial and operating status and the need of Landlord to be informed of, and to provide to its partners and to prospective lenders and purchasers of the Property financial information pertaining to, Tenant's financial status. Landlord and Tenant agree to cooperate with each other in achieving these needs within the context of the obligations set forth in this Section.

16.12. Costs. If Tenant requests the consent of Landlord under any provision of this Lease for any act that Tenant proposes to do hereunder, including, without limitation, assignment or subletting of the Premises, Tenant shall, as a condition to doing any such act and the receipt of such consent, reimburse Landlord promptly for any and all reasonable costs and expenses incurred by Landlord in connection therewith, including, without limitation, reasonable attorneys' fees.

16.13. Time. Time is of the essence of this Lease, and of every term and condition hereof.

16.14. Rules and Regulations. Tenant shall observe, comply with and obey, and shall cause its employees, agents and, to the best of Tenant's ability, invitees to observe, comply with and obey such rules and regulations as Landlord may promulgate from time to time for the safety, care, cleanliness, order and use of the Premises, the Building and the Property.

16.15. Brokers. Landlord and Tenant each represents and warrants to the other that no broker participated in the consummation of this Lease and agrees to indemnify, defend and hold the other party harmless against any liability, cost or expense, including, without limitation, reasonable attorney's fees, arising out of any claims for brokerage commissions or other similar compensation in connection with any conversations, prior negotiations or other dealings by the indemnifying party with any broker, finder or other third party claiming such compensation.

16.16. Memorandum Of Lease. At any time during the term of this Lease, either party, at its sole expense, shall be entitled to record a memorandum of this Lease and, if either party so elects, both parties agree to cooperate in the preparation, execution, acknowledgement and recordation of such document in reasonable form.

16.17. Corporate Authority. The person signing this Lease on behalf of Tenant warrants that he or she is fully authorized to do so and, by so doing, to bind Tenant.

16.18. Execution and Delivery. Submission of this Lease for examination or signature by Tenant does not constitute an agreement or reservation of or option for lease of the Premises. This instrument shall not be effective or binding upon either party, as a lease or otherwise, until executed and delivered by both Landlord and Tenant. This Lease may be executed in one or more counterparts and by separate parties on separate counterparts, but each such counterpart shall constitute an original and all such counterparts together shall constitute one and the same instrument.

16.19. Warrants. Within thirty (30) days after execution of this Lease, as a condition to Landlord's obligations hereunder, Tenant shall deliver to Landlord or Landlord's designees (which may be any partners, shareholders or affiliates of Landlord or any affiliates of any such partners, shareholders or affiliates of Landlord) warrants registered in the name of Landlord or Landlord's designees for the acquisition of an aggregate of seventy thousand (70,000) shares of Tenant's common stock, which warrants shall be in form and substance mutually and reasonably satisfactory

to Landlord and Tenant. The warrants shall have an exercise price of One Dollar (\$1.00) per share and shall be exercisable for a period beginning on the Commencement Date and ending on the fifth (5th) anniversary of the closing of the initial public offering (if any) of Tenant's common stock.

16.20. Signage. Tenant shall have the right to install, subject to Section 6.3 hereof and to compliance with applicable laws, with the Master Declaration and with any other covenants, conditions, restrictions and sign criteria applicable to the Center, a sign on the Building bearing Tenant's name and/or logo or other similar identifying information. The costs associated with the approval, design, construction and installation of such sign shall be borne entirely by Tenant.

16.21. Parking. Landlord represents that the Property, in conjunction with the balance of the Center, shall include parking spaces available for use (on a non-exclusive basis) by Tenant and its employees, agents and invitees at the rate of at least 3.5 spaces per 1,000 square feet of building area.

IN WITNESS WHEREOF, the parties hereto have executed this Lease as of the day and year first set forth above.

"Landlord"

"Tenant"

BRITANNIA POINTE GRAND LIMITED
PARTNERSHIP, a Delaware Limited
partnership

PAIN THERAPEUTICS, INC.,
a Delaware corporation

By: Britannia Pointe Grand, LLC, a
California limited liability company,
Its General Partner

By: /s/ REMI BARBIER

Remi Barbier
Chief Executive Officer

By: /s/ T. J. BRISTOW

T.J. Bristow
President, Chief Financial
Officer and Manager

By: Remi Barbier

Its: President & CEO

EXHIBITS

- EXHIBIT A Location of Premises
- EXHIBIT B Real Property Description
- EXHIBIT C Acknowledgement of Lease Commencement

EXHIBIT A
LOCATION OF PREMISES

[DIAGRAM OF PREMISES]

EXHIBIT A

(page 1 of 3)

EXHIBIT A

[DIAGRAM OF FLOOR PLAN]

EXHIBIT A

(page 2 of 3)

REAL PROPERTY DESCRIPTION

Improved real property located in the City of South San Francisco, County of San Mateo, State of California, more particularly described as follows:

Lots 1, 2, 3 and 4, inclusive, as shown on Parcel Map No. 91-284, "Being a resubdivision of the parcels described in the deeds to Metal and Thermit Corporation, recorded in Book 293, at Page 394 of Deeds; in Book 49, at Page 490, Official Records; in Book 77, at Page 415, Official Records; and except that parcel described in Book 1352, at Page 373, Official Records," filed on February 25, 1992, in Book 65 of Parcel Maps, in the Office of the Recorder of the County of San Mateo, California.

EXHIBIT B

ACKNOWLEDGEMENT OF LEASE COMMENCEMENT

This Acknowledgement is executed as of 9/21/, 1998, by BRITANNIA POINT GRAND LIMITED PARTNERSHIP, a Delaware limited partnership ("Landlord"), and PAIN THERAPEUTICS, INC., a Delaware corporation ("Tenant"), pursuant to Section 2.5 of the Lease dated 8/25, 1998 between Landlord and Tenant (the "Lease") covering premises located at 250 East Grand Avenue, Suite 70, South San Francisco, CA 94080 (the "Premises").

Landlord and Tenant hereby acknowledge and agree as follows:

- 1. The Commencement Date under the Lease is 9/21, 1998.
- 2. The termination date under the Lease shall be 9/21, 2000, subject to any applicable provisions of the Lease for early termination thereof.
- 3. Tenant accepts the Premises and acknowledges the satisfactory completion of all improvements therein required to be made by Landlord, subject only to any applicable "punch list" or similar procedures specifically provided under the Lease.

EXECUTED as of the date first set forth above.

"Landlord"

"Tenant"

BRITANNIA POINTE GRAND LIMITED PARTNERSHIP, a Delaware limited partnership

PAIN THERAPEUTICS, INC., a Delaware corporation

By: Britiannia Pointe Grand, LLC, a California limited liability company, Its General Partner

/s/ REMI BARBIER
By: _____
Remi Barbier
Chief Executive Officer

/s/ T. J. BRISTOW
By: _____
T. J. Bristow
President, Chief Financial Officer and Manager

By: _____
Its: _____

PAIN THERAPEUTICS, INC.

1998 STOCK PLAN

1. Purposes of the Plan. The purposes of this Stock Plan are to attract and retain the best available personnel for positions of substantial responsibility, to provide additional incentive to Employees, Directors and Consultants and to promote the success of the Company's business. Options granted under the Plan may be Incentive Stock Options or Nonstatutory Stock Options, as determined by the Administrator at the time of grant. Stock Purchase Rights may also be granted under the Plan.

2. Definitions. As used herein, the following definitions shall apply:

(a) "Administrator" means the Board or any of its Committees as shall be administering the Plan in accordance with Section 4 hereof.

(b) "Applicable Laws" means the requirements relating to the administration of stock option plans under U.S. state corporate laws, U.S. federal and state securities laws, the Code, any stock exchange or quotation system on which the Common Stock is listed or quoted and the applicable laws of any other country or jurisdiction where Options or Stock Purchase Rights are granted under the Plan.

(c) "Board" means the Board of Directors of the Company.

(d) "Code" means the Internal Revenue Code of 1986, as amended.

(e) "Committee" means a committee of Directors appointed by the Board in accordance with Section 4 hereof.

(f) "Common Stock" means the Common Stock of the Company.

(g) "Company" means Pain Therapeutics, Inc., a Delaware corporation.

(h) "Consultant" means any person who is engaged by the Company or any Parent or Subsidiary to render consulting or advisory services to such entity.

(i) "Director" means a member of the Board of Directors of the Company.

(j) "Disability" means total and permanent disability as defined in Section 22(e)(3) of the Code.

(k) "Employee" means any person, including Officers and Directors, employed by the Company or any Parent or Subsidiary of the Company. A Service Provider shall not cease to be an Employee in the case of (i) any leave of absence approved by the Company or (ii) transfers between locations of the Company or between the Company, its Parent, any Subsidiary, or any successor. For purposes of Incentive Stock Options, no such leave may exceed ninety days, unless

reemployment upon expiration of such leave is guaranteed by statute or contract. If reemployment upon expiration of a leave of absence approved by the Company is not so guaranteed, on the 181st day of such leave any Incentive Stock Option held by the Optionee shall cease to be treated as an Incentive Stock Option and shall be treated for tax purposes as a Nonstatutory Stock Option. Neither service as a Director nor payment of a director's fee by the Company shall be sufficient to constitute "employment" by the Company.

(l) "Exchange Act" means the Securities Exchange Act of 1934, as amended.

(m) "Fair Market Value" means, as of any date, the value of Common Stock determined as follows:

(i) If the Common Stock is listed on any established stock exchange or a national market system, including without limitation the Nasdaq National Market or The Nasdaq SmallCap Market of The Nasdaq Stock Market, its Fair Market Value shall be the closing sales price for such stock (or the closing bid, if no sales were reported) as quoted on such exchange or system for the last market trading day prior to the time of determination, as reported in The Wall Street Journal or such other source as the Administrator deems reliable;

(ii) If the Common Stock is regularly quoted by a recognized securities dealer but selling prices are not reported, its Fair Market Value shall be the mean between the high bid and low asked prices for the Common Stock on the last market trading day prior to the day of determination; or

(iii) In the absence of an established market for the Common Stock, the Fair Market Value thereof shall be determined in good faith by the Administrator.

(n) "Incentive Stock Option" means an Option intended to qualify as an incentive stock option within the meaning of Section 422 of the Code.

(o) "Nonstatutory Stock Option" means an Option not intended to qualify as an Incentive Stock Option.

(p) "Officer" means a person who is an officer of the Company within the meaning of Section 16 of the Exchange Act and the rules and regulations promulgated thereunder.

(q) "Option" means a stock option granted pursuant to the Plan.

(r) "Option Agreement" means a written or electronic agreement between the Company and an Optionee evidencing the terms and conditions of an individual Option grant. The Option Agreement is subject to the terms and conditions of the Plan.

(s) "Option Exchange Program" means a program whereby outstanding Options are exchanged for Options with a lower exercise price.

(t) "Optioned Stock" means the Common Stock subject to an Option or a Stock Purchase Right.

(u) "Optionee" means the holder of an outstanding Option or Stock Purchase Right granted under the Plan.

(v) "Parent" means a "parent corporation," whether now or hereafter existing, as defined in Section 424(e) of the Code.

(w) "Plan" means this 1998 Stock Plan.

(x) "Restricted Stock" means shares of Common Stock acquired pursuant to a grant of a Stock Purchase Right under Section 11 below.

(y) "Service Provider" means an Employee, Director or Consultant.

(z) "Share" means a share of the Common Stock, as adjusted in accordance with Section 12 below.

(aa) "Stock Purchase Right" means a right to purchase Common Stock pursuant to Section 11 below.

(bb) "Subsidiary" means a "subsidiary corporation," whether now or hereafter existing, as defined in Section 424(f) of the Code.

3. Stock Subject to the Plan. Subject to the provisions of Section 12 of the Plan, the maximum aggregate number of Shares which may be subject to option and sold under the Plan is Three Million Two Hundred Thousand (3,200,000) Shares. The Shares may be authorized but unissued, or reacquired Common Stock.

If an Option or Stock Purchase Right expires or becomes unexercisable without having been exercised in full, or is surrendered pursuant to an Option Exchange Program, the unpurchased Shares which were subject thereto shall become available for future grant or sale under the Plan (unless the Plan has terminated). However, Shares that have actually been issued under the Plan, upon exercise of either an Option or Stock Purchase Right, shall not be returned to the Plan and shall not become available for future distribution under the Plan, except that if Shares of Restricted Stock are repurchased by the Company at their original purchase price, such Shares shall become available for future grant under the Plan.

4. Administration of the Plan.

(a) Administrator. The Plan shall be administered by the Board or a Committee appointed by the Board, which Committee shall be constituted to comply with Applicable Laws.

(b) Powers of the Administrator. Subject to the provisions of the Plan and, in the case of a Committee, the specific duties delegated by the Board to such Committee, and subject to the approval of any relevant authorities, the Administrator shall have the authority in its discretion:

(i) to determine the Fair Market Value;

(ii) to select the Service Providers to whom Options and Stock Purchase Rights may from time to time be granted hereunder;

(iii) to determine the number of Shares to be covered by each such award granted hereunder;

(iv) to approve forms of agreement for use under the Plan;

(v) to determine the terms and conditions, of any Option or Stock Purchase Right granted hereunder. Such terms and conditions include, but are not limited to, the exercise price, the time or times when Options or Stock Purchase Rights may be exercised (which may be based on performance criteria), any vesting acceleration or waiver of forfeiture restrictions, and any restriction or limitation regarding any Option or Stock Purchase Right or the Common Stock relating thereto, based in each case on such factors as the Administrator, in its sole discretion, shall determine;

(vi) to determine whether and under what circumstances an Option may be settled in cash under subsection 9(e) instead of Common Stock;

(vii) to reduce the exercise price of any Option to the then current Fair Market Value if the Fair Market Value of the Common Stock covered by such Option has declined since the date the Option was granted;

(viii) to initiate an Option Exchange Program;

(ix) to prescribe, amend and rescind rules and regulations relating to the Plan, including rules and regulations relating to sub-plans established for the purpose of qualifying for preferred tax treatment under foreign tax laws;

(x) to allow Optionees to satisfy withholding tax obligations by electing to have the Company withhold from the Shares to be issued upon exercise of an Option or Stock Purchase Right that number of Shares having a Fair Market Value equal to the amount required to be withheld. The Fair Market Value of the Shares to be withheld shall be determined on the date that the amount of tax to be withheld is to be determined. All elections by Optionees to have Shares withheld for this purpose shall be made in such form and under such conditions as the Administrator may deem necessary or advisable; and

(xi) to construe and interpret the terms of the Plan and awards granted pursuant to the Plan.

(c) Effect of Administrator's Decision. All decisions, determinations and interpretations of the Administrator shall be final and binding on all Optionees.

5. Eligibility.

(a) Nonstatutory Stock Options and Stock Purchase Rights may be granted to Service Providers. Incentive Stock Options may be granted only to Employees.

(b) Each Option shall be designated in the Option Agreement as either an Incentive Stock Option or a Nonstatutory Stock Option. However, notwithstanding such designation, to the extent that the aggregate Fair Market Value of the Shares with respect to which Incentive Stock Options are exercisable for the first time by the Optionee during any calendar year (under all plans of the Company and any Parent or Subsidiary) exceeds \$100,000, such Options shall be treated as Nonstatutory Stock Options. For purposes of this Section 5(b), Incentive Stock Options shall be taken into account in the order in which they were granted. The Fair Market Value of the Shares shall be determined as of the time the Option with respect to such Shares is granted.

(c) Neither the Plan nor any Option or Stock Purchase Right shall confer upon any Optionee any right with respect to continuing the Optionee's relationship as a Service Provider with the Company, nor shall it interfere in any way with his or her right or the Company's right to terminate such relationship at any time, with or without cause.

6. Term of Plan. The Plan shall become effective upon its adoption by the Board. It shall continue in effect for a term of ten (10) years unless sooner terminated under Section 14 of the Plan.

7. Term of Option. The term of each Option shall be stated in the Option Agreement; provided, however, that the term shall be no more than ten (10) years from the date of grant thereof. In the case of an Incentive Stock Option granted to an Optionee who, at the time the Option is granted, owns stock representing more than ten percent (10%) of the voting power of all classes of stock of the Company or any Parent or Subsidiary, the term of the Option shall be five (5) years from the date of grant or such shorter term as may be provided in the Option Agreement.

8. Option Exercise Price and Consideration.

(a) The per share exercise price for the Shares to be issued upon exercise of an Option shall be such price as is determined by the Administrator, but shall be subject to the following:

(i) In the case of an Incentive Stock Option

(1) granted to an Employee who, at the time of grant of such Option, owns stock representing more than ten percent (10%) of the voting power of all classes of stock of the Company or any Parent or Subsidiary, the exercise price shall be no less than 110% of the Fair Market Value per Share on the date of grant.

(2) granted to any other Employee, the per Share exercise price shall be no less than 100% of the Fair Market Value per Share on the date of grant.

(ii) In the case of a Nonstatutory Stock Option

(1) granted to a Service Provider who, at the time of grant of such Option, owns stock representing more than ten percent (10%) of the voting power of all classes of stock of the Company or any Parent or Subsidiary, the exercise price shall be no less than 110% of the Fair Market Value per Share on the date of grant.

(2) granted to any other Service Provider, the per Share exercise price shall be no less than 85% of the Fair Market Value per Share on the date of grant.

(iii) Notwithstanding the foregoing, Options may be granted with a per Share exercise price other than as required above pursuant to a merger or other corporate transaction.

(b) The consideration to be paid for the Shares to be issued upon exercise of an Option, including the method of payment, shall be determined by the Administrator (and, in the case of an Incentive Stock Option, shall be determined at the time of grant). Such consideration may consist of (1) cash, (2) check, (3) promissory note, (4) other Shares which (x) in the case of Shares acquired upon exercise of an Option, have been owned by the Optionee for more than six months on the date of surrender, and (y) have a Fair Market Value on the date of surrender equal to the aggregate exercise price of the Shares as to which such Option shall be exercised, (5) consideration received by the Company under a cashless exercise program implemented by the Company in connection with the Plan, or (6) any combination of the foregoing methods of payment. In making its determination as to the type of consideration to accept, the Administrator shall consider if acceptance of such consideration may be reasonably expected to benefit the Company.

9. Exercise of Option.

(a) Procedure for Exercise; Rights as a Stockholder. Any Option granted hereunder shall be exercisable according to the terms hereof at such times and under such conditions as determined by the Administrator and set forth in the Option Agreement. Except in the case of Options granted to Officers, Directors and Consultants, Options shall become exercisable at a rate of no less than 20% per year over five (5) years from the date the Options are granted. Unless the Administrator provides otherwise, vesting of Options granted hereunder shall be tolled during any unpaid leave of absence. An Option may not be exercised for a fraction of a Share.

An Option shall be deemed exercised when the Company receives: (i) written or electronic notice of exercise (in accordance with the Option Agreement) from the person entitled to exercise the Option, and (ii) full payment for the Shares with respect to which the Option is exercised. Full payment may consist of any consideration and method of payment authorized by the Administrator and permitted by the Option Agreement and the Plan. Shares issued upon exercise of an Option shall be issued in the name of the Optionee or, if requested by the Optionee, in the name of the Optionee and his or her spouse. Until the Shares are issued (as evidenced by the appropriate entry on the books of the Company or of a duly authorized transfer agent of the Company), no right to vote or receive dividends or any other rights as a stockholder shall exist with respect to the Shares, notwithstanding the exercise of the Option. The Company shall issue (or cause to be issued) such Shares promptly after the Option is exercised. No adjustment will be made for a dividend or other right for which the record date is prior to the date the Shares are issued, except as provided in Section 12 of the Plan.

Exercise of an Option in any manner shall result in a decrease in the number of Shares thereafter available, both for purposes of the Plan and for sale under the Option, by the number of Shares as to which the Option is exercised.

(b) Termination of Relationship as a Service Provider. If an Optionee ceases to be a Service Provider, such Optionee may exercise his or her Option within such period of time as is specified in the Option Agreement (of at least thirty (30) days) to the extent that the Option is vested on the date of termination (but in no event later than the expiration of the term of the Option as set forth in the Option Agreement). In the absence of a specified time in the Option Agreement, the Option shall remain exercisable for three (3) months following the Optionee's termination. If, on the date of termination, the Optionee is not vested as to his or her entire Option, the Shares covered by the unvested portion of the Option shall revert to the Plan. If, after termination, the Optionee does not exercise his or her Option within the time specified by the Administrator, the Option shall terminate, and the Shares covered by such Option shall revert to the Plan.

(c) Disability of Optionee. If an Optionee ceases to be a Service Provider as a result of the Optionee's Disability, the Optionee may exercise his or her Option within such period of time as is specified in the Option Agreement (of at least six (6) months) to the extent the Option is vested on the date of termination (but in no event later than the expiration of the term of such Option as set forth in the Option Agreement). In the absence of a specified time in the Option Agreement, the Option shall remain exercisable for twelve (12) months following the Optionee's termination. If, on the date of termination, the Optionee is not vested as to his or her entire Option, the Shares covered by the unvested portion of the Option shall revert to the Plan. If, after termination, the Optionee does not exercise his or her Option within the time specified herein, the Option shall terminate, and the Shares covered by such Option shall revert to the Plan.

(d) Death of Optionee. If an Optionee dies while a Service Provider, the Option may be exercised within such period of time as is specified in the Option Agreement (of at least six (6) months) to the extent that the Option is vested on the date of death (but in no event later than the expiration of the term of such Option as set forth in the Option Agreement) by the Optionee's estate or by a person who acquires the right to exercise the Option by bequest or inheritance. In the absence of a specified time in the Option Agreement, the Option shall remain exercisable for twelve (12) months following the Optionee's termination. If, at the time of death, the Optionee is not vested as to the entire Option, the Shares covered by the unvested portion of the Option shall immediately revert to the Plan. If the Option is not so exercised within the time specified herein, the Option shall terminate, and the Shares covered by such Option shall revert to the Plan.

(e) Buyout Provisions. The Administrator may at any time offer to buy out for a payment in cash or Shares, an Option previously granted, based on such terms and conditions as the Administrator shall establish and communicate to the Optionee at the time that such offer is made.

10. Non-Transferability of Options and Stock Purchase Rights. The Options and Stock Purchase Rights may not be sold, pledged, assigned, hypothecated, transferred, or disposed of in any manner other than by will or by the laws of descent or distribution and may be exercised, during the lifetime of the Optionee, only by the Optionee.

11. Stock Purchase Rights.

(a) Rights to Purchase. Stock Purchase Rights may be issued either alone, in addition to, or in tandem with other awards granted under the Plan and/or cash awards made outside

of the Plan. After the Administrator determines that it will offer Stock Purchase Rights under the Plan, it shall advise the offeree in writing or electronically of the terms, conditions and restrictions related to the offer, including the number of Shares that such person shall be entitled to purchase, the price to be paid, and the time within which such person must accept such offer. The terms of the offer shall comply in all respects with Section 260.140.42 of Title 10 of the California Code of Regulations. The offer shall be accepted by execution of a Restricted Stock purchase agreement in the form determined by the Administrator.

(b) Repurchase Option. Unless the Administrator determines otherwise, the Restricted Stock purchase agreement shall grant the Company a repurchase option exercisable upon the voluntary or involuntary termination of the purchaser's service with the Company for any reason (including death or disability). The purchase price for Shares repurchased pursuant to the Restricted Stock purchase agreement shall be the original price paid by the purchaser and may be paid by cancellation of any indebtedness of the purchaser to the Company. The repurchase option shall lapse at such rate as the Administrator may determine. Except with respect to Shares purchased by Officers, Directors and Consultants, the repurchase option shall in no case lapse at a rate of less than 20% per year over five (5) years from the date of purchase.

(c) Other Provisions. The Restricted Stock purchase agreement shall contain such other terms, provisions and conditions not inconsistent with the Plan as may be determined by the Administrator in its sole discretion.

(d) Rights as a Stockholder. Once the Stock Purchase Right is exercised, the purchaser shall have rights equivalent to those of a stockholder and shall be a stockholder when his or her purchase is entered upon the records of the duly authorized transfer agent of the Company. No adjustment shall be made for a dividend or other right for which the record date is prior to the date the Stock Purchase Right is exercised, except as provided in Section 12 of the Plan.

12. Adjustments Upon Changes in Capitalization, Merger or Asset Sale.

(a) Changes in Capitalization. Subject to any required action by the stockholders of the Company, the number of shares of Common Stock covered by each outstanding Option or Stock Purchase Right, and the number of shares of Common Stock which have been authorized for issuance under the Plan but as to which no Options or Stock Purchase Rights have yet been granted or which have been returned to the Plan upon cancellation or expiration of an Option or Stock Purchase Right, as well as the price per share of Common Stock covered by each such outstanding Option or Stock Purchase Right, shall be proportionately adjusted for any increase or decrease in the number of issued shares of Common Stock resulting from a stock split, reverse stock split, stock dividend, combination or reclassification of the Common Stock, or any other increase or decrease in the number of issued shares of Common Stock effected without receipt of consideration by the Company. The conversion of any convertible securities of the Company shall not be deemed to have been "effected without receipt of consideration." Such adjustment shall be made by the Board, whose determination in that respect shall be final, binding and conclusive. Except as expressly provided herein, no issuance by the Company of shares of stock of any class, or securities convertible into shares of stock of any class, shall affect, and no adjustment by reason thereof shall be made with

respect to, the number or price of shares of Common Stock subject to an Option or Stock Purchase Right.

(b) Dissolution or Liquidation. In the event of the proposed dissolution or liquidation of the Company, the Administrator shall notify each Optionee as soon as practicable prior to the effective date of such proposed transaction. The Administrator in its discretion may provide for an Optionee to have the right to exercise his or her Option or Stock Purchase Right until fifteen (15) days prior to such transaction as to all of the Optioned Stock covered thereby, including Shares as to which the Option or Stock Purchase Right would not otherwise be exercisable. In addition, the Administrator may provide that any Company repurchase option applicable to any Shares purchased upon exercise of an Option or Stock Purchase Right shall lapse as to all such Shares, provided the proposed dissolution or liquidation takes place at the time and in the manner contemplated. To the extent it has not been previously exercised, an Option or Stock Purchase Right will terminate immediately prior to the consummation of such proposed action.

(c) Merger or Asset Sale. In the event of a merger of the Company with or into another corporation, or the sale of substantially all of the assets of the Company, each outstanding Option and Stock Purchase Right shall be assumed or an equivalent option or right substituted by the successor corporation or a Parent or Subsidiary of the successor corporation. In the event that the successor corporation refuses to assume or substitute for the Option or Stock Purchase Right, the Optionee shall fully vest in and have the right to exercise the Option or Stock Purchase Right as to all of the Optioned Stock, including Shares as to which it would not otherwise be vested or exercisable. If an Option or Stock Purchase Right becomes fully vested and exercisable in lieu of assumption or substitution in the event of a merger or sale of assets, the Administrator shall notify the Optionee in writing or electronically that the Option or Stock Purchase Right shall be fully exercisable for a period of fifteen (15) days from the date of such notice, and the Option or Stock Purchase Right shall terminate upon the expiration of such period. For the purposes of this paragraph, the Option or Stock Purchase Right shall be considered assumed if, following the merger or sale of assets, the option or right confers the right to purchase or receive, for each Share of Optioned Stock subject to the Option or Stock Purchase Right immediately prior to the merger or sale of assets, the consideration (whether stock, cash, or other securities or property) received in the merger or sale of assets by holders of Common Stock for each Share held on the effective date of the transaction (and if holders were offered a choice of consideration, the type of consideration chosen by the holders of a majority of the outstanding Shares); provided, however, that if such consideration received in the merger or sale of assets is not solely common stock of the successor corporation or its Parent, the Administrator may, with the consent of the successor corporation, provide for the consideration to be received upon the exercise of the Option or Stock Purchase Right, for each Share of Optioned Stock subject to the Option or Stock Purchase Right, to be solely common stock of the successor corporation or its Parent equal in fair market value to the per share consideration received by holders of Common Stock in the merger or sale of assets.

13. Time of Granting Options and Stock Purchase Rights. The date of grant of an Option or Stock Purchase Right shall, for all purposes, be the date on which the Administrator makes the determination granting such Option or Stock Purchase Right, or such other date as is determined by the Administrator. Notice of the determination shall be given to each Service Provider to whom an Option or Stock Purchase Right is so granted within a reasonable time after the date of such grant.

14. Amendment and Termination of the Plan.

(a) Amendment and Termination. The Board may at any time amend, alter, suspend or terminate the Plan.

(b) Stockholder Approval. The Board shall obtain stockholder approval of any Plan amendment to the extent necessary and desirable to comply with Applicable Laws.

(c) Effect of Amendment or Termination. No amendment, alteration, suspension or termination of the Plan shall impair the rights of any Optionee, unless mutually agreed otherwise between the Optionee and the Administrator, which agreement must be in writing and signed by the Optionee and the Company. Termination of the Plan shall not affect the Administrator's ability to exercise the powers granted to it hereunder with respect to Options granted under the Plan prior to the date of such termination.

15. Conditions Upon Issuance of Shares.

(a) Legal Compliance. Shares shall not be issued pursuant to the exercise of an Option unless the exercise of such Option and the issuance and delivery of such Shares shall comply with Applicable Laws and shall be further subject to the approval of counsel for the Company with respect to such compliance.

(b) Investment Representations. As a condition to the exercise of an Option, the Administrator may require the person exercising such Option to represent and warrant at the time of any such exercise that the Shares are being purchased only for investment and without any present intention to sell or distribute such Shares if, in the opinion of counsel for the Company, such a representation is required.

16. Inability to Obtain Authority. The inability of the Company to obtain authority from any regulatory body having jurisdiction, which authority is deemed by the Company's counsel to be necessary to the lawful issuance and sale of any Shares hereunder, shall relieve the Company of any liability in respect of the failure to issue or sell such Shares as to which such requisite authority shall not have been obtained.

17. Reservation of Shares. The Company, during the term of this Plan, shall at all times reserve and keep available such number of Shares as shall be sufficient to satisfy the requirements of the Plan.

18. Stockholder Approval. The Plan shall be subject to approval by the stockholders of the Company within twelve (12) months after the date the Plan is adopted. Such stockholder approval shall be obtained in the degree and manner required under Applicable Laws.

19. Information to Optionees and Purchasers. The Company shall provide to each Optionee and to each individual who acquires Shares pursuant to the Plan, not less frequently than annually during the period such Optionee or purchaser has one or more Options or Stock Purchase Rights outstanding, and, in the case of an individual who acquires Shares pursuant to the Plan, during the period such individual owns such Shares, copies of annual financial statements. The

Company shall not be required to provide such statements to key employees whose duties in connection with the Company assure their access to equivalent information

PAIN THERAPEUTICS, INC.

SECOND AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT

This Second Amended and Restated Investors' Rights Agreement is made as of February 1, 2000 by and among Pain Therapeutics, Inc., a Delaware corporation (the "Company") and the investors listed on Exhibit A hereto, each of which is herein referred to as an "Investor."

RECITALS

WHEREAS, certain Investors are holders of shares of the Company's Series A Preferred Stock, Series B Preferred Stock and/or shares of Common Stock issued upon conversion thereof (the "Prior Parties") and possess registration rights, information rights, rights of first refusal, and other rights pursuant to that certain First Amended and Restated Investor Rights Agreement dated as of October 15, 1999 between the Company and such Prior Parties (the "Prior Agreement"); and

WHEREAS, the undersigned Prior Parties desire to amend and restate in its entirety the Prior Agreement and to accept the rights created pursuant hereto in lieu of the rights granted to them under the Prior Agreement; and

WHEREAS, certain other Investors are parties to the Series C Preferred Stock Purchase Agreement dated as of February 1, 2000 between the Company and such Investors (the "Purchase Agreement"), such Investors' obligations under which are conditioned upon, among other things, the execution and delivery of this Agreement by such Investors, holders of in excess of fifty percent (50%) of the shares held by the Prior Parties and the Company:

NOW, THEREFORE, in consideration of the mutual promises and covenants set forth herein, the parties to the Prior Agreement hereby agree that the Prior Agreement shall be superseded and replaced in its entirety by this Agreement, and the parties hereto further agree as follows:

1. Information Rights.

1.1 Financial Information.

(a) The Company shall deliver to each Investor who continues to hold at least 100,000 shares of Series A Preferred Stock ("Series A Preferred Stock") of the Company (or the Common Stock into which the shares of Series A Preferred Stock have been converted) or any shares of Series B Preferred Stock ("Series B Preferred Stock") of the Company (or the Common Stock into which shares of Series B Preferred Stock have been converted) or any shares of Series C Preferred Stock ("Series C Preferred Stock") of the Company (or the Common Stock into which shares of Series C Preferred Stock have been converted) (in each case as adjusted for any stock split, stock dividends, combinations, recapitalizations and the like with respect to such shares), and as long as such Investor or a principal, partner or manager of such Investor, is not employed by or an officer or director of a competitor of the Company, and the Company remains private, unaudited financial

statements, prepared in accordance with generally accepted accounting principles, of the Company within 90 days after the close of each fiscal year, and audited financial statements, prepared in accordance with generally accepted accounting principles, of the Company within 120 days after the close of each fiscal year.

(b) The Company shall deliver to each Investor who continues to hold at least 100,000 shares of Series B or Series C Preferred Stock (or the Common Stock into which shares of Series B Preferred Stock have been converted) (as adjusted for any stock split, stock dividends, combinations, recapitalizations and the like with respect to such shares), and as long as such Investor or a principal, partner or manager or such Investor, is not employed by or an officer or director of a competitor of the Company; and the Company remains private, unaudited monthly and quarterly financial statements, with comparisons to prior year periods and budgets prepared in accordance with generally accepted accounting principles, and progress reports on major clinical programs within 30 days after each month or fiscal quarter, as applicable.

1.2 Inspection Rights. Each Investor shall have the right to visit and inspect any of the properties of the Company or any of its subsidiaries, and to discuss the affairs, finances and accounts of the Company or any of its subsidiaries with its officers, and to review such information as is reasonably requested all at such reasonable times and as often as may be reasonably requested; provided, however, that the Company shall not be obligated under this Section 1.2 with respect to a competitor of the Company or with respect to information which the Board of Directors determines in good faith is confidential and should not, therefore, be disclosed, unless Investor first executes and delivers a confidentiality agreement with the Company in form and substance reasonably satisfactory to the Board of Directors; provided further that, whenever requested, the Investor shall sign an agreement satisfactory to the Company stating that the Investor shall hold all such information in confidence.

1.3 Termination of Covenants. Except as required by law, the rights set forth in Sections 1.1 and 1.2 shall terminate and be of no further force or effect upon the closing of a public offering of the Company's securities pursuant to an effective registration statement filed by the Company under the Securities Act of 1933, as amended, or on the date the Company otherwise becomes subject to the reporting requirements under Section 13 or 15(d) of the Securities Exchange Act, as amended, whichever first occurs.

2. Registration Rights. The Company and the Investors covenant and agree as follows:

2.1 Definitions. For purposes of this Section 2:

(a) The terms "register," "registered," and "registration" refer to a registration effected by preparing and filing a registration statement or similar document in compliance with the Securities Act of 1933, as amended (the "Securities Act"), and the declaration or ordering of effectiveness of such registration statement or document.

(b) The term "Registrable Securities" means (i) the shares of Common Stock issuable or issued upon conversion of the Series A Preferred Stock, Series B Preferred Stock and Series C Preferred Stock and (ii) any other shares of Common Stock of the Company issued as (or issuable upon the conversion or exercise of any warrant, right or other security which is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of, the shares listed in (i); or (iii) other shares of Common Stock acquired by a holder of registrable Securities; provided, however, that the foregoing definition shall exclude in all cases any Registrable Securities sold by a person in a transaction in which his or her rights under this Agreement are not assigned. Notwithstanding the foregoing, Common Stock or other securities shall only be treated as Registrable Securities if and so long as they have not been (A) sold to or through a broker or dealer or underwriter in a public distribution or a public securities transaction, or (B) sold in a transaction exempt from the registration and prospectus delivery requirements of the Securities Act under Section 4(1) thereof so that all transfer restrictions, and restrictive legends with respect thereto, if any, are removed upon the consummation of such sale.

(c) The number of shares of "Registrable Securities then outstanding" shall be determined by the number of shares of Common Stock outstanding which are, and the number of shares of Common Stock issuable pursuant to then exercisable or convertible securities which are, Registrable Securities; provided, however, that the foregoing definition shall exclude in all cases any securities sold by a person in a transaction in which his or her rights under this Agreement are not assigned, and any securities that have been sold to or through a broker or dealer or underwriter in a public distribution or a public securities transaction, or sold in a transaction exempt from the registration and prospectus delivery requirements of the Securities Act under Section 4(1) thereof so that all transfer restrictions, and restrictive legends with respect thereto, if any, are removed upon the consummation of such sale.

(d) [Intentionally Omitted].

(e) The term "Series B Holder" means any person owning or having the right to acquire (i) the shares of Common Stock issuable or issued upon conversion of the Series B Preferred Stock and (ii) any other shares of Common Stock of the Company issued as (or issuable upon the conversion or exercise of any warrant, right or other security which is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of, the shares listed in (i).

(f) The term "Series C Holder" means any person owning or having the right to acquire (i) the shares of Common Stock issuable or issued upon conversion of the Series C Preferred Stock and (ii) any other shares of Common Stock of the Company issued as (or issuable upon the conversion or exercise of any warrant, right or other security which is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of, the shares listed in (i).

(g) The term "Form S-3" means such form under the Securities Act as in effect on the date hereof or any successor form under the Securities Act.

(h) The term "SEC" means the Securities and Exchange Commission.

(i) The term "Series B Qualified IPO" means a firm commitment underwritten public offering by the Company of shares of its Common Stock pursuant to a registration statement on Form S-1 under the Securities Act, in which the public offering price per share of Common Stock is at least \$5.00 (as adjusted for stock splits, stock dividends, combinations, recapitalizations and the like) and the gross proceeds to the Company are not less than \$15,000,000 (net of underwriting discounts and commissions)

(j) The term "Series C Qualified IPO" means a firm commitment underwritten public offering by the Company of shares of its Common Stock pursuant to a registration statement on Form S-1 under the Securities Act, in which the public offering price per share of Common Stock is at least \$7.00 (as adjusted for stock splits, stock dividends, combinations, recapitalizations and the like) and the gross proceeds to the Company are not less than \$15,000,000 (net of underwriting discounts and commissions).

2.2 Request for Registration.

(a) If the Company shall receive at any time at least six (6) months after the effective date of the first registration statement for a public offering of securities of the Company (other than a registration statement relating either to the sale of securities to employees of the Company pursuant to a stock option, stock purchase or similar plan or an SEC Rule 145 transaction), a written request from the holders of a majority of the Registrable Securities held by the Series B Holders or the Series C Holders, that the Company file a registration statement under the Securities Act covering Registrable Securities, then the Company shall, within ten (10) days of the receipt thereof, give written notice of such request to all Series B Holders or Series C Holders (as applicable) and shall, subject to the limitations of subsection 2.2(b), use commercially reasonable efforts to effect as soon as practicable, and in any event within 90 days of the receipt of such request, the registration under the Securities Act of all Registrable Securities which the Series B Holders or Series C Holders (as applicable) request to be registered within twenty (20) days of the mailing of such notice by the Company in accordance with the terms hereof; provided, however, that the Company shall not be obligated to effect such registration if the Series B Holders or Series C Holders (as applicable), together with the holders of any other securities of the Company entitled to inclusion in such registration, propose to sell Registrable Securities and such other securities (if any) at an aggregate price to the public (net of any underwriter's discounts and commissions) of less than \$7,500,000.

(b) If the Series B Holders or Series C Holders initiating the registration request hereunder ("Initiating Holders") intend to distribute the Registrable Securities covered by their request by means of an underwriting, they shall so advise the Company as a part of their request made pursuant to this Section 2.2 and the Company shall include such information in the written notice referred to in subsection 2.2(a). The underwriter will be selected by the Company subject to the prior written consent of Ohio Valley Venture Fund LP, if participating (in the case of the Series B Holders) or Cascade Investment L.L.C. if participating (in the case of the Series C Holders), which consent shall not be unreasonably withheld; provided, however, that no such

consent shall be required if the Company selects a nationally recognized underwriter with demonstrable, pharmaceutical and/or biotechnology industry-specific expertise and experience. In such event, the right of any Series B Holder or Series C Holder (as applicable) to include Registrable Securities in such registration shall be conditioned upon such Series B Holder's or Series C Holder's participation in such underwriting and the inclusion of such Series B Holder's or Series C Holder's Registrable Securities in the underwriting (unless otherwise mutually agreed by a majority in interest of the Initiating Holders and such Series B Holder or Series C Holder (as applicable)) to the extent provided herein. All Series B Holders or Series C Holders proposing to distribute their securities through such underwriting shall (together with the Company as provided in subsection 2.5(e)) enter into an underwriting agreement in customary form with the underwriter or underwriters selected for such underwriting. Notwithstanding any other provision of this Section 2.2, if the underwriter advises the Initiating Holders in writing that marketing factors require a limitation or the exclusion of the number of shares to be underwritten, then the Initiating Holders shall so advise all Series B Holders or Series C Holders (as applicable) of Registrable Securities which would otherwise be underwritten pursuant hereto, and, in the case of a limitation, of the number of shares of Registrable Securities that may be included in the underwriting shall be allocated among all Series B Holders or Series C Holders (as applicable), including the Initiating Holders, in proportion (as nearly as practicable) to the amount of Registrable Securities of the Company owned by each Series B Holder or Series C Holder (as applicable); provided, however, that the shares of Registrable Securities to be included in such underwriting shall not be reduced in number or completely excluded unless all other securities, are first entirely excluded from the underwriting. If the Series B Holders or Series C Holders (as applicable) cannot sell at least 85% of the Registrable Securities proposed to be sold, then the transaction shall be deemed not to be a registration with respect to them for purposes of Section 2.2(d)(i) hereof.

(c) Notwithstanding the foregoing, if the Company shall furnish to Holders requesting a registration statement pursuant to this Section 2.2, a certificate signed by the President of the Company stating that in the good faith judgment of the Board of Directors of the Company, it would be seriously detrimental to the Company and its stockholders for such registration statement to be filed and it is therefore essential to defer the filing of such registration statement, the Company shall have the right to defer such filing for a period of not more than 60 days after receipt of the request of the Initiating Holders; provided, however, that the Company may not utilize this right more than once in any twelve-month period.

(d) In addition, the Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to this Section 2.2:

(i) After the Company has effected two (2) registrations pursuant to this Section 2.2 and such registrations have been declared or ordered effective or within six (6) months of the effective date of another registration;

(ii) During the period starting with the date ninety (90) days prior to the Company's good faith estimate of the date of filing of, and ending on a date one hundred

eighty (180) days after the effective date of, a registration subject to Section 2.3 hereof; provided that the Company is actively employing in good faith all reasonable efforts to cause such registration statement to become effective; or

(iii) If the Initiating Holders propose to dispose of shares of Registrable Securities that may be immediately registered on Form S-3 pursuant to a request made pursuant to Section 2.4 below; provided, however, that if the Company so refuses to effect a registration by the Series B Holders or Series C Holders (as applicable) pursuant to this Section 2.2(d)(iii), they shall be entitled to an additional registration pursuant to Section 2.4 for each such registration so refused until such time as they shall have had the benefit a total of four (4) registrations pursuant to Section 2.2 and/or Section 2.4.

2.3 Company Registration. If (but without any obligation to do so) the Company proposes to register (including for this purpose a registration effected by the Company for stockholders other than the Series B Holders or Series C Holders) any of its stock under the Securities Act in connection with the public offering of such securities solely for cash (other than a registration relating solely to the sale of securities to participants in a Company stock plan or a transaction covered by Rule 145 under the Securities Act, a registration in which the only stock being registered is Common Stock issuable upon conversion of debt securities which are also being registered, or any registration on any form which does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Registrable Securities), the Company shall, at such time, promptly give each Series B Holder and Series C Holder written notice of such registration. Upon the written request of each Holder given within twenty (20) days after mailing of such notice by the Company in accordance with the terms hereof, the Company shall, subject to the provisions of Section 2.8, cause to be registered under the Securities Act all of the Registrable Securities that each such holder has requested to be registered.

2.4 Form S-3 Registration. In case the Company shall receive from Series B Holders or Series C Holders of the Registrable Securities then outstanding a written request or requests that the Company effect a registration on Form S-3 and any related qualification or compliance with respect to all or a part of the Registrable Securities owned by such holder or holders, the Company will:

(a) promptly give written notice of the proposed registration, and any related qualification or compliance, to all other Series B Holders or Series C Holders; and

(b) as soon as practicable, effect such registration and all such qualifications and compliances as may be so requested and as would permit or facilitate the sale and distribution of all or such portion of such Series B or Series C Holder's or Holders' Registrable Securities as are specified in such request, together with all or such portion of the Registrable Securities of any other Series B or Series C (as the case may be) Holder or Holders joining in such request as are specified in a written request given within 15 days after receipt of such written notice from the Company; provided, however, that the Company shall not be obligated to effect any such registration, qualification or compliance, pursuant to this Section 2.4: (i) if Form S-3 is not available

for such offering by the Series B or Series C Holders; (ii) if the Series B or Series C Holders, together with the holders of any other securities of the Company entitled to inclusion in such registration, propose to sell Registrable Securities and such other securities (if any) at an aggregate price to the public (net of any underwriters' discounts or commissions) of less than \$5,000,000; (iii) if the Company shall furnish to the Series B or Series C Holders a certificate signed by the President of the Company stating that in the good faith judgment of the Board of Directors of the Company, it would be seriously detrimental to the Company and its stockholders for such Form S-3 Registration to be effected at such time, in which event the Company shall have the right to defer the filing of the Form S-3 registration statement for a period of not more than 90 days after receipt of the request of the Series B or Series C Holder or Holders under this Section 2.4; provided, however, that the Company shall not utilize this right more than once in any twelve month period; (iv) if the Company has, within the six (6) month period preceding the date of such request, already effected one registration on Form S-3 for such holders pursuant to this Section 2.4 or within six (6) months of the effective date of another registration; (v) in any particular jurisdiction in which the Company would be required to qualify to do business or to execute a general consent to service of process in effecting such registration, qualification or compliance; or (vi) during the period ending one hundred eighty (180) days after the effective date of a registration statement subject to Section 2.3.

(c) Subject to the foregoing, the Company shall file a registration statement covering the Registrable Securities and other securities so requested to be registered as soon as practicable after receipt of the request or requests of the Series B or Series C Holders. Registrations effected pursuant to this Section 2.4 shall not be counted as demands for registration or registrations effected pursuant to Sections 2.2 or 2.3, respectively.

(d) Subject to the proviso in Section 2.2(d)(iii), the Company shall not be obligated to effect, or to take any action to effect, any registration pursuant to this Section 2.4 after the Company has effected two (2) registrations initiated by the holders of a majority of the Registrable Securities held by the Series B Holders and two (2) registrations initiated by the holders of a majority of the Registrable Securities held by the Series C Holders pursuant to this Section 2.4.

If the registration is to be underwritten, the underwriter will be selected by the Company subject to the prior written consent of Ohio Valley Venture Fund LP, if participating (in the case of the Series B Holders) and Cascade Investment L.L.C., if participating (in the case of the Series C Holders), which consent shall not be unreasonably withheld; provided, however, that no such consent shall be required if the Company selects a nationally recognized underwriter with demonstrable, pharmaceutical and/or biotechnology industry-specific expertise and experience. If Series B Holders or Series C Holders (as applicable) are not able to sell at least 85% of their Registrable Securities proposed to be sold, then the transaction shall not be deemed a registration for purposes of Section 2.4(d) hereof.

2.5 Obligations of the Company. Whenever required under this Section 2 to effect the registration of any Registrable Securities, the Company shall, as expeditiously as reasonably possible:

(a) Prepare and file with the SEC a registration statement with respect to such Registrable Securities and use its best efforts to cause such registration statement to become effective, and, upon the request of the Holders of a majority of the Registrable Securities registered thereunder, keep such registration statement effective for up to one hundred twenty (120) days.

(b) Prepare and file with the SEC such amendments and supplements to such registration statement and the prospectus used in connection with such registration statement as may be necessary to comply with the provisions of the Securities Act with respect to the disposition of all securities covered by such registration statement for up to one hundred twenty (120) days.

(c) Furnish to the Series B Holders and/or Series C Holders (as the case may be) such numbers of copies of a prospectus, including a preliminary prospectus, in conformity with the requirements of the Securities Act, and such other documents as they may reasonably request in order to facilitate the disposition of Registrable Securities owned by them.

(d) Use its best efforts to register and qualify the securities covered by such registration statement under such other securities or Blue Sky laws of such jurisdictions as shall be reasonably requested by the Series B Holders and/or Series C Holders (as the case may be), provided that the Company shall not be required in connection therewith or as a condition thereto to qualify to do business or to file a general consent to service of process in any such states or jurisdictions.

(e) In the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the managing underwriter of such offering. Each Series B Holder or Series C Holder participating in such underwriting shall also enter into and perform its obligations under such an agreement.

(f) Notify each Series B Holder or Series C Holder of Registrable Securities covered by such registration statement at any time when a prospectus relating thereto is required to be delivered under the Securities Act of the happening of any event as a result of which the prospectus included in such registration statement, as then in effect, includes an untrue statement of a material fact or omits to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances then existing. In such event, the Company shall use all reasonable efforts to amend promptly the registration statement to conform the prospectus to the requirement of the 1933 Act and applicable regulations.

(g) Cause all such Registrable Securities registered pursuant hereunder to be listed on each securities exchange on which similar securities issued by the Company are then listed.

(h) Provide a transfer agent and registrar for all Registrable Securities registered pursuant hereunder and a CUSIP number for all such Registrable Securities, in each case not later than the effective date of such registration.

(i) Use its best efforts to furnish, at the request of any Series B Holder and/or Series C Holder (as the case may be) requesting registration of Registrable Securities pursuant to this Section 2, on the date that such Registrable Securities are delivered to the underwriters for sale in connection with a registration pursuant to this Section 2, if such securities are being sold through underwriters, or, if such securities are not being sold through underwriters, on the date that the registration statement with respect to such securities becomes effective, (i) an opinion, dated such date, of the counsel representing the Company for the purposes of such registration, in form and substance as is customarily given to underwriters in an underwritten public offering, addressed to the underwriters, if any, and to the Series B Holders and/or Series C Holders (as the case may be) requesting registration of Registrable Securities and (ii) a letter dated such date, from the independent certified public accountants of the Company, in form and substance as is customarily given by independent certified public accountants to underwriters in an underwritten public offering, addressed to the underwriters, if any, and to the Series B Holders and/or Series C Holders (as the case may be) requesting registration of Registrable Securities.

2.6 Furnish Information. It shall be a condition precedent to the obligations of the Company to take any action pursuant to this Section 2 with respect to the Registrable Securities of any selling Series B Holder or Series C Holder that such holder shall furnish to the Company such information regarding itself, the Registrable Securities held by it, and the intended method of disposition of such securities as shall be required to effect the registration of such holder's Registrable Securities. The Company shall have no obligation with respect to any registration requested pursuant to Section 2.2 or Section 2.4 of this Agreement if, as a result of the application of the preceding sentence, the number of shares or the anticipated aggregate offering price of the Registrable Securities to be included in the registration does not equal or exceed the number of shares or the anticipated aggregate offering price required to originally trigger the Company's obligation to initiate such registration as specified in subsection 2.2(a) or subsection 2.4(b)(2), whichever is applicable.

2.7 Expenses of Registration.

(a) Demand Registration. All expenses other than underwriting discounts and commissions incurred in connection with one (1) demand registration, pursuant to Section 2.2, including (without limitation) all registration, filing and qualification fees, printers' and accounting fees, fees and disbursements of counsel for the Company, and the reasonable fees and disbursements of one counsel for the selling Series B Holders or Series C Holders (as applicable) selected by them (collectively "Registration Expenses") shall be borne by the Company it being understood that all such expenses shall be borne by the Company in connection with at least one (1) such registration in which Series B Holders are able to sell Registrable Securities and at least one (1) such registration in which Series C Holders are able to sell Registrable Securities; provided, however, that if the Series B Holders or Series C Holders (as applicable) bear the Registration Expenses for any registration proceeding begun pursuant to Section 2.2 and subsequently withdrawn by them registering shares therein, such registration proceeding shall not be counted as a requested registration pursuant to Section 2.2 hereof; in the event that such withdrawal is based upon material adverse information

relating to the Company that is different from the information known or available (upon request from the Company or otherwise) to the Series B Holders or Series C Holders requesting registration at the time of their request for registration under Section 2.2, such registration shall not be treated as a counted registration for purposes of Section 2.2 hereof, even though the Series B Holders or Series C Holders (as applicable) do not bear the Registration Expenses for such registration.

(b) Company Registration. All expenses other than underwriting discounts and commissions incurred in connection with registrations, filings or qualifications of Registrable Securities pursuant to Section 2.3 for each Series B or Series C Holder (which right may be assigned as provided in Section 2.12), including (without limitation) all registration, filing, and qualification fees, printers' and accounting fees, fees and disbursements of counsel for the Company and the reasonable fees and disbursements of one counsel for the selling Series B Holders and one counsel for the Series C Holders selected by them shall be borne by the Company.

(c) Registration on Form S-3. All expenses other than underwriting discounts and commissions incurred in connection with one (1) registration requested pursuant to Section 2.4, including (without limitation) all registration, filing, qualification, printers' and accounting fees and the reasonable fees and disbursements of one counsel for the selling Series B Holders and of one counsel for the selling Series C Holders selected by them shall be borne by the Company, it being understood that all such expenses shall be borne by the Company in connection with at least one (1) such registration in which Series B Holders are able to sell Registrable Securities and at least one (1) such registration in which Series C Holders are able to sell Registrable Securities.

2.8 Underwriting Requirements. In connection with any offering involving an underwriting of shares of the Company's capital stock, the Company shall not be required under Section 2.3 to include any of the Series B Holders' or Series C Holders' securities in such underwriting unless they accept the terms of the underwriting as agreed upon between the Company and the underwriters selected by it (or by other persons entitled to select the underwriters), provided that such agreement does not require indemnification by any of them except to the extent contemplated by Section 2.10 hereof; and then only in such quantity as the underwriters determine in their sole discretion will not jeopardize the success of the offering by the Company. If the total amount of securities, including Registrable Securities, requested by stockholders to be included in such offering exceeds the amount of securities sold other than by the Company that the underwriters determine in their sole discretion is compatible with the success of the offering, then the Company shall be required to include in the offering only that number of such securities, including Registrable Securities, which the underwriters determine in their sole discretion will not jeopardize the success of the offering. The Company will include in such registration (i) first, the securities the Company proposes to sell for its own account; (ii) second, to the extent that the number of securities the Company proposes to sell is less than the number of securities which the Company has been advised can be sold in such offering that is compatible with the success of the offering, such number of Registrable Securities which the Series B Holders and/or Series C Holders have requested to be included in such registration pursuant to Section 2.3 hereof; provided, however, in no event will

shares of any other selling stockholder be included in such registration which would reduce the number of shares which have been requested to be included by the Series B Holder and/or Series C Holders (or completely exclude the Shares) without the written consent of a majority of the then outstanding Registrable Securities proposed to be sold in the offering; and (iii) third, to the extent that the number of securities which are to be included in such registration pursuant to clauses (i) and (ii) is, in the aggregate, less than the number of securities which the Company has been advised can be sold in such offering that is compatible with the success of the offering, such number of other securities requested to be included in the offering for the account of any holders not contractually entitled to registration which, in the opinion of the underwriters, is compatible with the success of the offering. The number of Registrable Securities included in such registration statement shall be allocated pro rata among the holders of Registrable Securities based on the number of Registrable Securities held by each of them or in such other proportions as shall mutually be agreed to by them, but in no event shall any shares being sold by such a holder exercising a demand registration right similar to that granted in Section 2.2 or 2.4 be excluded from such offering. For purposes of the preceding sentence concerning apportionment, for any selling stockholder which is a holder of Registrable Securities and which is a partnership or corporation, the partners, retired partners and stockholders of such holder, or the estates and family members of any such partners and retired partners and any trusts for the benefit of any of the foregoing persons shall be deemed to be a single "selling stockholder" and any pro-rata reduction with respect to such "selling stockholder" shall be based upon the aggregate amount of shares carrying registration rights owned by all entities and individuals included in such "selling stockholder," as defined in this sentence.

2.9 Delay of Registration. No Holder shall have any right to obtain or seek an injunction restraining or otherwise delaying any such registration as the result of any controversy that might arise with respect to the interpretation or implementation of this Section 2.

2.10 Indemnification. In the event any Registrable Securities are included in a registration statement under this Section 2:

(a) To the extent permitted by law, the Company will indemnify and hold harmless each Series B and Series C Holder, its legal counsel, its accountants, any underwriter (as defined in the Securities Act) for such holder and each person, if any, who controls such holder or underwriter within the meaning of the Securities Act or the Securities Exchange Act of 1934, as amended (the "Exchange Act"), against any losses, claims, damages, or liabilities (joint or several) to which they may become subject under the Securities Act, the Exchange Act or other federal or state law, insofar as such losses, claims, damages, or liabilities (or actions in respect thereof) arise out of or are based upon any of the following statements, omissions or violations (collectively a "Violation"): (i) any untrue statement or alleged untrue statement of a material fact contained in such registration statement, including any preliminary prospectus or final prospectus contained therein or any amendments or supplements thereto, (ii) 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, or (iii) any violation or alleged violation by the Company of the Securities Act, the Exchange Act, any state securities law or any rule or regulation promulgated under the Securities

Act, the Exchange Act or any state securities law; and the Company will pay to each such holder, underwriter or controlling person, as incurred, 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 indemnity agreement contained in this subsection 2.10(a) shall not apply to amounts paid in settlement of any such loss, claim, damage, liability, or action if such settlement is effected without the consent of the Company (which consent shall not be unreasonably withheld), nor shall the Company be liable to any holder, underwriter or controlling person for any such loss, claim, damage, liability, or action to the extent that it arises out of or is based upon a Violation which occurs in reliance upon and in conformity with written information furnished expressly for use in connection with such registration by any such holder, underwriter or controlling person.

(b) To the extent permitted by law, each selling Series B and Series C Holder will indemnify and hold harmless the Company, each of its directors, each of its officers who has signed the registration statement, each person, if any, who controls the Company within the meaning of the Securities Act, its legal counsel, its accountants, any underwriter, any other holder selling securities in such registration statement and any controlling person of any such underwriter or other holder, against any losses, claims, damages, or liabilities (joint or several) to which any of the foregoing persons may become subject, under the Securities Act, the Exchange Act or other federal or state law, insofar as such losses, claims, damages, or liabilities (or actions in respect thereto) arise out of or are based upon any Violation, in each case to the extent (and only to the extent) that such Violation occurs in reliance upon and in conformity with written information furnished by such holder expressly for use in connection with such registration; and each such holder will pay, as incurred, any legal or other expenses reasonably incurred by any person intended to be indemnified pursuant to this subsection 2.10(b), in connection with investigating or defending any such loss, claim, damage, liability, or action; provided, however, that the indemnity agreement contained in this subsection 2.10(b) shall not apply to amounts paid in settlement of any such loss, claim, damage, liability or action if such settlement is effected without the consent of the holder, which consent shall not be unreasonably withheld; provided, that in no event shall any indemnity under this subsection 2.10(b) exceed the net proceeds from the offering received by such holder, except in the case of willful fraud by such holder.

(c) Promptly after receipt by an indemnified party under this Section 2.10 of notice of the commencement of any action (including any governmental action), such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this Section 2.10, deliver to the indemnifying party a written notice of the commencement thereof and the indemnifying party shall have the right to participate in, and, to the extent the indemnifying party so desires, jointly with any other indemnifying party similarly noticed, to assume the defense thereof with counsel mutually satisfactory to the parties; provided, however, that an indemnified party (together with all other indemnified parties which may be represented without conflict by one counsel) shall have the right to retain one separate counsel, with the reasonable fees and expenses to be paid by the indemnifying party, if representation of such indemnified party by the counsel retained by the indemnifying party would be inappropriate due to actual or potential differing interests between such indemnified party and any other party represented by such counsel in such

proceeding. The failure to deliver written notice to the indemnifying party within a reasonable time of the commencement of any such action, if prejudicial to its ability to defend such action, shall relieve such indemnifying party of any liability to the indemnified party under this Section 2.10, but the omission so to deliver written notice to the indemnifying party will not relieve it of any liability that it may have to any indemnified party otherwise than under this Section 2.10.

(d) If the indemnification provided for in this Section 2.10 is held by a court of competent jurisdiction to be unavailable to an indemnified party with respect to any loss, liability, claim, damage or expense referred to therein, then the indemnifying party, in lieu of indemnifying such indemnified party hereunder, shall contribute to the amount paid or payable by such indemnified party as a result of such loss, liability, claim, damage, or expense in such proportion as is appropriate to reflect the relative fault of the indemnifying party on the one hand and of the indemnified party on the other in connection with the statements or omissions that resulted in such loss, liability, claim, damage or expense as well as any other relevant equitable considerations; provided, that in no event shall any contribution by a holder under this Subsection 2.10(d) exceed the net proceeds from the offering received by such holder, except in the case of willful fraud by such holder. The relative fault of the indemnifying party and of the indemnified party shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission to state a material fact relates to information supplied by the indemnifying party or by the indemnified party and the parties' relative intent, knowledge, access to information, and opportunity to correct or prevent such statement or omission.

(e) Notwithstanding the foregoing, to the extent that the provisions on indemnification and contribution contained in the underwriting agreement entered into in connection with the underwritten public offering are in conflict with the foregoing provisions, the provisions in the underwriting agreement shall control.

(f) The obligations of the Company and Series B and Series C Holders under this Section 2.10 shall survive the completion of any offering of Registrable Securities in a registration statement under this Section 2, and otherwise.

2.11 Reports Under Securities Exchange Act of 1934. With a view to making available to the Series B and Series C Holders the benefits of Rule 144 promulgated under the Securities Act and any other rule or regulation of the SEC that may at any time permit a holder to sell securities of the Company to the public without registration or pursuant to a registration on Form S-3, the Company agrees to:

(a) make and keep public information available, as those terms are understood and defined in SEC Rule 144, at all times after ninety (90) days after the effective date of the first registration statement filed by the Company for the offering of its securities to the general public so long as the Company remain subject to the periodic reporting requirements under Sections 13 or 15(d) of the Exchange Act;

(b) take such action, including the voluntary registration of its Common Stock under Section 12 of the Exchange Act, as is necessary to enable the Series B and Series C Holders to utilize Form S-3 for the sale of their Registrable Securities;

(c) file with the SEC in a timely manner all reports and other documents required of the Company under the Securities Act and the Exchange Act; and

(d) furnish to any Series B or Series C Holder, so long as the holder owns any Registrable Securities, forthwith upon request (i) a written statement by the Company that it has complied with the reporting requirements of SEC Rule 144 (at any time after ninety (90) days after the effective date of the first registration statement filed by the Company), the Securities Act and the Exchange Act (at any time after it has become subject to such reporting requirements), or that it qualifies as a registrant whose securities may be resold pursuant to Form S-3 (at any time after it so qualifies), (ii) a copy of the most recent annual or quarterly report of the Company and such other reports and documents so filed by the Company, and (iii) such other information as may be reasonably requested in availing any Series B or Series C Holder of any rule or regulation of the SEC which permits the selling of any such securities without registration or pursuant to such form.

2.12 Assignment of Registration Rights. The rights to cause the Company to register Registrable Securities pursuant to this Section 2.12 may be assigned (but only with all related obligations) by a Series B or Series C Holder to (i) a transferee or assignee of at least 100,000 shares of such securities, (ii) a transferee or assignee of all of such Registrable Securities held by such transferring holder, if less than 100,000 shares, or (iii) a general partner, limited partner, retired partner, member or retired member, affiliate, parent or majority-owned subsidiary of the transferee, provided the Company is, within a reasonable time after such transfer, furnished with written notice of the name and address of such transferee or assignee and the securities with respect to which such registration rights are being assigned; and provided, further, that such assignment shall be effective only if immediately following such transfer the further disposition of such securities by the transferee or assignee is restricted under the Securities Act. For the purposes of determining the number of shares of Registrable Securities held by a transferee or assignee, the holdings of transferees and assignees of a partnership who are partners or retired partners of such partnership (including spouses and ancestors, lineal descendants and siblings of such partners or spouses who acquire Registrable Securities by gift, will or intestate succession) shall be aggregated together and with the partnership; provided that all assignees and transferees who would not qualify individually for assignment of registration rights shall have a single attorney-in-fact for the purpose of exercising any rights, receiving notices or taking any action under Section 2.

2.13 Limitations on Subsequent Registration Rights. From and after the date of this Agreement, the Company shall not, without the prior written consent of the holders of a majority of the then outstanding Registrable Securities, enter into any agreement with any holder or prospective holder of any securities of the Company which would allow such holder or prospective holder to include such securities in any registration filed under Section 2.2 hereof, unless under the terms of such agreement, such holder or prospective holder may include such securities in any such

registration only to the extent that the inclusion of his securities will not reduce the amount of the Registrable Securities of the Series B or Series C Holders which is included.

2.14 "Market Stand-Off" Agreement. Each holder of Registrable Securities hereby agrees that, during the period of duration (up to, but not exceeding, 180 days) specified by the Company and an underwriter of Common Stock or other securities of the Company, following the effective date of a registration statement of the Company filed under the Securities Act, it shall not, to the extent requested by the Company and such underwriter, directly or indirectly sell, offer to sell, contract to sell (including, without limitation, any short sale), grant any option to purchase or otherwise transfer or dispose of (other than to donees who agree to be similarly bound) any securities of the Company held by it at any time during such period except Common Stock included in such registration; provided, however, that:

(a) such agreement shall be applicable only to the first such registration statement of the Company which covers Common Stock (or other securities) to be sold on its behalf to the public in an underwritten offering; and

(b) all officers, directors, and key employees of the Company, all five-percent security holders, and all other persons with registration rights (whether or not pursuant to this Agreement) enter into similar agreements.

In order to enforce the foregoing covenant, the Company may impose stop-transfer instructions with respect to the Registrable Securities of each holder (and the shares or securities of every other person subject to the foregoing restriction) until the end of such period, and each holder agrees that, if so requested, such holder will execute an agreement in the form provided by the underwriter containing terms which are essentially consistent with the provisions of this Section 2.14.

Notwithstanding the foregoing, the obligations described in this Section 2.14 shall not apply to a registration relating solely to employee benefit plans on Form S-1 or Form S-8 or similar forms which may be promulgated in the future, or a registration relating solely to an SEC Rule 145 transaction on Form S-4 or similar forms which may be promulgated in the future.

2.15 Termination of Registration Rights. No holder of registrable securities shall be entitled to exercise any right provided for in this Section 2 after five (5) years following the consummation of a Qualified IPO.

3. Right of First Offer.

3.1 General. Except for (i) conversion rights applicable to the Company's Preferred Stock, (ii) securities issued pursuant to an underwritten public offering pursuant to an effective registration statement under the Securities Act, (iii) securities issued pursuant to the Company's acquisition of another corporation by merger, purchase of substantially all the assets or other corporate reorganization, (iv) securities issued in connection with any stock split or stock dividend

of the Company, (v) securities issued after the date hereof to employees, officers, directors or consultants of the Company pursuant to stock purchase or stock option plans, stock bonuses or awards, contracts or other arrangements that are approved by the Company's board of directors, (vi) warrants or other securities issued to financial institutions or commercial lenders in connection with equipment financing transactions approved by the Company's board of directors or to Williams Trading, L.L.C. in connection with the Company's Series C Preferred Stock Financing and (vii) securities issued in connection with strategic corporate partner agreements approved by the Company's board of directors, the Company will not, nor will it permit any subsidiary to, authorize or issue any shares of stock of the Company of any class and will not authorize, issue or grant any options, warrants, conversion rights or other rights to purchase or acquire any shares of stock of the Company of any class without offering the Investors the right of first refusal described below. In the event the Company grants subsequent purchasers any rights of first refusal or registration rights which are, in the good faith judgment of the Board of Directors, superior to those granted to the Series B Holders or Series C Holders pursuant to this Agreement, then the Series B Holders and Series C Holders, respectively, shall receive such rights.

3.2 Right of First Offer.

(a) Each holder of Series B and/or Series C Preferred Stock shall have a right of first refusal to purchase an amount of equity securities of the Company of any class or kind which the Company proposes to sell (other than the issuance of shares contemplated by Section 3.1 above) sufficient to maintain such holder's proportionate beneficial ownership interest in the Company. If the Company wishes to make any such sale of its securities, it shall give the holders of Series B and Series C Preferred Stock written notice of the proposed sale. The notice shall set forth (i) the Company's bona fide intention to offer such shares and (ii) the material terms and conditions of the proposed sale (including the number of shares to be offered and the price, if any, for which the Company proposes to offer such shares), and shall constitute an offer to sell such securities to the holders of Series B and Series C Preferred Stock on such terms and conditions. Any holder of Series B or Series C Preferred Stock may accept such offer by delivering a written notice of acceptance to the Company within ten (10) days after receipt of the Company's notice of the proposed sale. Any holder of Series B or Series C Preferred Stock exercising its right of first refusal shall be entitled to participate in the purchase of such securities on a pro rata basis to the extent necessary to maintain such holder's proportionate beneficial ownership interest in the Company (for purposes of determining the pro rata interest of the holder, any holder shall be treated as owning that number of shares of Common Stock into which any outstanding convertible securities may be converted and for which any outstanding options or warrants may be exercised). The Company shall promptly, in writing, inform each holder which elects to purchase its pro rata portion of such shares of any other holder's failure to do so, in which case the holders electing to purchase such shares shall have the right to purchase all or a portion of such shares on a pro rata basis, on terms no less favorable to the holder, for a period of ten (10) days. Such holder shall be entitled to apportion the right of first refusal hereby granted among itself and its partners, affiliates and related parties in such proportions it deems appropriate. If the Investor does not accept such offer within ten (10) days, then that

portion of the shares which is not purchased may be offered to other parties on terms no less favorable to the Company for a period of ten (10) days.

(b) In lieu of delivering Notice to the holders of Series B and/or Series C Preferred Stock prior to the sale of Company offered securities to third parties, as provided in Section 3, above, the Company may elect first to sell Company offered securities to third parties and then, within thirty (30) days thereafter, offer such holders the opportunity to purchase their pro rata portions of the Company offered securities. Such offer shall remain in effect for twenty (20) days after notice to the Investors and, if accepted, the closing of the sale of Company offered securities shall occur within thirty (30) days after the date of the acceptance notice.

3.3 Expiration of Right of First Refusal. The right of first refusal granted under this Agreement shall expire when a sale of securities pursuant to a registration statement filed by the Company under the Securities Act in connection with a firm commitment underwritten offering of its securities to the general public is consummated.

3.4 Assignment. The right of first refusal granted under this Section 3 may be assigned (i) to a transferee or assignee in connection with any transfer or assignment of Registrable Securities by a holder of not less than 100,000 shares of Registrable Securities, or such lesser number if such shares constitute all of the registrable securities then held by such holder, or (ii) to any transferee or assignee who is a constituent, member or partner or retired partner of a holder of the estate of such partner, or to any transferee or assignee who is a family member of the holder or a trust for the benefit of the holder or any family member of the holder or any parent corporation or subsidiary corporation of the holder, provided that, with respect to each such transfer or assignment, the Company be given prior written notice of the transfer, the transferee or assignee agree writing to all provisions contained in this Section 3 and that such transfer otherwise be effected in accordance with applicable laws.

4. Miscellaneous.

4.1 Waivers and Amendments. With the written consent of the Company and the holders of more than 50% of the Registrable Securities, including at least 50% of the Series B Holders and 50% of the Series C Holders, the obligations of the Company and the rights of the holders of registrable securities under this Agreement may be waived (either generally or in a particular instance, either retroactively or prospectively and either for a specified period of time or indefinitely), and with the same consent, the Company, when authorized by resolution of its Board of Directors, may amend this Agreement or enter into a supplementary agreement for the purpose of adding any provisions of this Agreement; provided however that no consent or amendment shall be necessary to add Investors to this Agreement in connection with their purchase of Series B Preferred Stock from the Company. Neither this Agreement nor any provisions hereof may be changed, waived, discharged or terminated orally, but only by a signed statement in writing. Any amendment, waiver or supplementary agreement effected in accordance with this paragraph shall be binding upon each holder or any Registrable Securities then outstanding, each future holder of all such Registrable Securities and the Company.

4.2 Notices. All notices and other communications required or permitted hereunder shall be in writing and, except as otherwise noted herein, shall be deemed effectively given upon personal delivery, delivery by nationally recognized courier or upon deposit with the United States Post Office, (by first class mail, postage prepaid) addressed: (a) if to the Company, at 250 East Grand Avenue, Suite 70, South San Francisco, California 94080 (or at such other address as the Company shall have furnished to the holders of Registrable Securities in writing) attention of the Chief Executive Officer and (b) if to a holder of Registrable Securities, at the latest address of such person shown on the Company's records.

4.3 Descriptive Headings. The descriptive headings herein have been inserted for convenience only and shall not be deemed to limit or otherwise affect the construction of any provisions hereof.

4.4 Governing Law. This Agreement shall be governed by and interpreted under the laws of the State of California as applied to agreements among California residents, made and to be performed entirely within the State of California.

4.5 Counterparts. This Agreement may be executed in one or more counterparts, each of which shall for all purposes be deemed to be an original and all of which shall constitute the same instrument, but only one of which need be produced.

4.6 Expenses. If any action at law or in equity is necessary to enforce or interpret the terms of this Agreement, the prevailing party shall be entitled to reasonable attorney's fees, costs and necessary disbursements in addition to any other relief to which such party may be entitled.

4.7 Successors and Assigns. Except as otherwise expressly provided in this Agreement, this Agreement shall benefit and bind the successors, assigns, heirs, executors and administrators of the parties to this Agreement.

4.8 Entire Agreement. This Agreement constitutes the full and entire understanding and agreement between the parties with regard to the subject matter of this Agreement.

4.9 Separability; Severability. Unless expressly provided in this Agreement, the rights of each Investor under this Agreement are several rights, not rights jointly held with any other Investors. Any invalidity, illegality or limitation on the enforceability of this Agreement with respect to any Investor shall not affect the validity, legality or enforceability of this Agreement with respect to the other Investors. If any provision of this Agreement is judicially determined to be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not be affected or impaired.

4.10 Stock Splits. All references to numbers of shares in this Agreement shall be appropriately adjusted to reflect any stock dividend, split, combination or other recapitalization of shares by the Company occurring after the date of this Agreement.

IN WITNESS WHEREOF, the parties have executed this Second Amended and Restated Investors' Rights Agreement on the day and year first set forth above.

PAIN THERAPEUTICS, INC.

By: _____

Title: _____

INVESTORS:

[Print Name]

[Signature]

[Title, if applicable]

[SIGNATURE PAGE TO SECOND AMENDED AND RESTATED INVESTORS' RIGHTS AGREEMENT]

PAIN THERAPEUTICS, INC.

EMPLOYMENT AGREEMENT

This Employment Agreement (the "Agreement") is made by and between Pain Therapeutics, Inc., a Delaware corporation (the "Company") and Remi Barbier ("Executive") as of July 1, 1998.

RECITALS

A. The Company desires to have Executive's active services as President, Chief Executive Officer and Chairman of the Board of the Company for the period set forth in this Agreement.

B. The Company and Executive desire to enter into this Agreement on the terms and conditions set forth in this Agreement.

AGREEMENT

NOW, THEREFORE, in consideration of the mutual covenants herein contained, and in consideration of Executive's continued employment by the Company, the parties hereto agree as follows:

1. Duties and Scope of Employment

(a) Duties. The Company shall employ Executive to render services to the Company. Executive agrees that he will devote his full business time and efforts to the business of the Company, excluding up to four (4) weeks paid vacation per year, and, in addition, sick leave in accordance with the Company's policies. In the course of Executive's employment, Executive shall perform the duties of President and Chief Executive Officer of the Company under the direction of the Board of Directors.

(b) Term of Employment. Executive's employment with the Company pursuant to this Agreement shall commence on the date hereof and shall continue until thirty-six (36) months thereafter (the "Employment Period"), provided that such term shall automatically renew for an additional 12 months at the end of such initial term and each subsequent renewal, unless ninety (90) days prior to the date of such renewal either party shall give written notice to the other party of cancellation, and in such event the Executive's employment hereunder shall terminate. Subject to Executive's right to severance compensation under certain circumstances as set forth herein, the employment relation of Executive with the Company shall be terminable upon sixty (60) days prior written notice by either party.

(c) Director. As long as Executive serves as President and Chief Executive Officer, Executive shall be nominated to serve on the Company's Board of Directors. Executive

agrees to submit his resignation immediately as a director if Executive ceases to be President and Chief Executive Officer, unless removed as President and Chief Executive Officer without Cause as defined below.

2. Compensation

(a) Base Compensation. The Company shall pay the Executive as compensation for his service a base salary at the annualized rate of Two Hundred Fifty Thousand Dollars (\$250,000) ("Salary"). Such Salary shall increase each anniversary date by the greater of the Company's Consumer Price Index or five percent (5%), whichever is greater, and shall be reviewed at least annually and may be increased from time to time subject to accomplishment of such performance and contribution goals and objectives as may be established and agreed upon from time to time by the Board of Directors and the Executive. Such Salary shall be paid periodically in accordance with normal Company payroll. The annual compensation (including bonus and benefit amounts pursuant to Section 2(b) and (c) below) specified in this Section 2(a), together with any increases in such compensation that the Board of Directors may grant from time to time, is referred to in this Agreement as "Base Compensation."

(b) Deferment of Salary. One Hundred Thousand Dollars (\$100,000) of the Executive's annual Salary shall be deferred until such time as the Company raises a total of Four Million Dollars (\$4,000,000) or more in any combination of debt or equity capital from outside investors, corporate partners, alliances, mergers, etc, The Executive shall automatically forgive the Company any deferred compensation in month 36 of this Employment Agreement, provided Executive is still an employee in good standing at such time. Any deferred compensation shall be immediately due upon termination of the Executive's employment without Cause (as defined below).

(c) Bonuses. Beginning with the Company's 1998 fiscal year and for each fiscal year thereafter during the Employment Period, the Executive will be eligible to receive an annual bonus based upon certain criteria to be agreed upon by Executive and the Board of Directors to be paid on January 15 of each calendar year hereafter, provided that Executive is employed by the Company on such dates.

(d) Executive Benefits. The Executive shall be eligible to participate in the employee benefit plans and executive compensation programs maintained by the Company applicable to other key executives of the Company, including (without limitation) retirement plans, savings or profit-sharing plans, deferred compensation plans, supplemental retirement or excess benefit plans, life, disability, health, accident and other insurance programs, paid vacations, and similar plans or programs, subject in each case to the generally applicable terms and conditions of the plan or program in question and to the determination of any committee administering such plan or program.

(e) Expenses During Employment. The Company shall reimburse the Executive for all reasonable business, entertainment and travel expenses actually incurred or paid by the

Executive in the performance of his services on behalf of the Company, in accordance with the Company's expense reimbursement policy as from time to time in effect.

3. Termination of Employment

(a) By Death. The Employment Period shall terminate automatically upon the death of the Executive. In such event, the Company shall pay to Executive's beneficiaries or his estate, as the case may be, any accrued Salary, the pro rata amount of the guaranteed annual bonus, any vested deferred compensation (other than pension plan or profit-sharing plan benefits which will be paid in accordance with the applicable plan), any benefits under any plan of the Company in which Executive is a participant to the full extent of Executive's rights under such plan, any accrued vacation pay and any appropriate business expenses incurred by Executive in connection with his duties hereunder, all to the date of termination (collectively "Accrued Compensation"), but no other compensation or reimbursement of any kind, including, without limitation, severance compensation, and thereafter, the Company's obligations hereunder shall terminate. Nothing in this Section shall affect any entitlement of the Executive's heirs to the benefits of any life insurance provided by the Company as set forth above.

(b) By Disability. If the Executive is prevented from properly performing his duties hereunder by reason of any physical or mental incapacity for a period of more than sixty (60) days in the aggregate in any 365-day period, then, to the extent permitted by law, the Company may terminate the Employment Period on the 60th day of such incapacity. In such event, the Company shall pay to Executive all Accrued Compensation, and shall continue to pay to Executive the Salary and the pro rata amount of the guaranteed annual bonus until such time as Executive shall become entitled to receive disability insurance payments under the disability insurance policy maintained by the Company (but not more than ninety (90) days following termination), but no other compensation or reimbursement of any kind, including without limitation, severance compensation, and thereafter the Company's obligations hereunder shall terminate. Nothing in this Section shall affect Executive's rights under any disability plan in which he is a participant.

(c) By Resignation or By Company for Cause. If Executive's employment with the Company terminates due to his voluntary resignation or if the Company terminates Executive's employment due to Cause (as defined below), the Company shall pay Executive all Accrued Compensation less the pro rata, amount of the annual guaranteed bonus (which shall not be paid to Executive), but no other compensation or reimbursement of any kind, including without limitation, severance compensation, and thereafter the Company's obligations hereunder shall terminate. Termination shall be for "Cause" in the event of the occurrence of any of the following: (i) any intentional action or intentional failure to act that was performed in bad faith and to the detriment of the Company; (ii) any intentional refusal or intentional failure to act in accordance with any lawful and proper direction or order of the Board; (iii) any willful and habitual neglect of the duties of full or part-time employment as assigned by the Board from time to time; or (iv) any conviction of a felony crime under the state or federal laws of the United States of America; provided that, in the event that any of the foregoing events is capable of being cured, the Company shall provide written

notice to the Purchaser describing the nature of such event, and the Purchaser shall thereafter have five (5) business days to cure such event.

(d) By Company for Other Than Cause. If the Company terminates Executive's employment with the Company for any reason other than Cause, Executive shall be entitled to receive: (i) Accrued Compensation to the date of termination; (ii) severance compensation equal to Executive's Base Compensation, immediately prior to the termination, for twelve (12) months after the date of termination (the "Termination Date"); (iii) continued participation in the Company medical and disability plans, at the Company's expense, for twelve (12) months after the date of termination; and (iv) all insurance coverages, at the Company's expense, in effect immediately prior to the termination. "Other Than Cause" shall include, but not be limited to the following: (i) without the Executive's express written consent, the assignment to the Executive of any duties or the reduction of the Executive's duties, either of which results in a significant diminution in the Executive's position or responsibilities with the Company in effect immediately prior to such assignments or the removal of the Executive from such position and responsibilities; (ii) without the Executive's express written consent, a substantial reduction, without good business reasons, of the facilities and perquisites (including office space and location) available to the Executive immediately prior to such reduction; (iii) a reduction by the Company in the Base Compensation of the Executive as in effect immediately prior to such reduction, other than a bonus reduction resulting from application of a bonus formula or plan on a basis that is consistent with prior practice; (iv) a material reduction by the Company in the kind or level of employee benefits to which the Executive is entitled immediately prior to such reduction with the result that the Executive's overall benefits package is significantly reduced; (v) the relocation of the Executive to a facility or a location more than twenty-five (25) miles from the Executive's then present location, without the Executive's express written consent; (vi) any purported termination of the Executive by the Company which is not effected for Cause, for valid grounds, or due to the Executive's death or Disability; or (vii) any purported termination of the Executive's employment by the Company which is not effected pursuant to a notice of termination satisfying the requirements of Section I (b) above, and for purposes of this, Agreement, no such purported termination shall be effective. If Executive resigns due to one of the above enumerated factors, such resignation shall be deemed a termination by the Company for Other Than Cause and shall be governed by this Section 3(d).

(e) Insurance, If the Executive is entitled to severance compensation under Section 3(d), in addition to such severance benefits, the Executive shall receive health insurance coverage as provided to the Executive immediately prior to the Termination Date to the extent the cost of such health insurance coverage does not exceed the cost of such health insurance coverage prior to Executive's termination. The health insurance coverage shall continue for a period of twelve (12) months following the Termination Date; provided, however, that to the extent Executive becomes covered under another employer's group health insurance plan, the Company shall not be obligated to provide such health insurance coverage.

(f) No Duty to Mitigate. The Executive shall not be required to mitigate the amount of any payment contemplated by Section 3(d) (whether by seeking new employment or in any other manner).

4. Equity In the event Executive resigns due to one of the enumerated factors in Section 3(d), all of the unvested portion of the shares of Common Stock of the Company owned by the Executive pursuant to the Restricted Stock Purchase Agreement between the Company and the Executive dated June 22, 1998 shall immediately vest and be released from the Company's repurchase option as of the Termination Date.

5. Confidential Information

(a) Company Information. Executive agrees at all times during the term of Executive's employment and thereafter to hold in strictest confidence and not to use, except for the benefit of the Company, or to disclose to any person, firm or corporation without written authorization of the Board of Directors of the Company, any Confidential Information of the Company. Executive understands that "Confidential Information" means any Company proprietary information, technical data, trade secrets or know-how, including, but not limited to, research product plans, products, services, customer lists and customers (including, but not limited to, customers of the Company on whom Executive called or with whom Executive became acquainted during the term of Executive's employment), markets, software, developments, inventions, processes, formulas, technology, designs, drawings, engineering, hardware configuration information, marketing, finances or other business information disclosed to Executive by the Company either directly or indirectly in writing, orally or by drawings or observation of parts or equipment. Executive further understands that Confidential Information does not include any of the foregoing item which has become publicly known and made generally available through no wrongful act of Executive's or of others who were under confidentiality obligations as to the item or items involved,

(b) Former Employer Information. Executive agrees that Executive will not, during Executive's employment with the Company, improperly use or disclose any proprietary information or trade secrets of any former or concurrent employer or other person or entity and that Executive will not bring onto the premises of the Company any unpublished document or proprietary information belonging to any such employer, person or entity unless consented to in writing by such employer, person or entity.

(c) Third Party Information. Executive recognizes that the Company has received and in the future will receive from third parties their confidential or proprietary information subject to a duty on the Company's part to maintain the confidentiality of such information and to use it only for certain limited purposes. Executive agrees to hold all such confidential or proprietary information in the strictest confidence and not to disclose it to any person, firm or corporation or to use it except as necessary in carrying out his work for the Company consistent with the Company's agreement with such third party.

6. Representations. Executive has not entered into, and will not enter into, any oral or written agreement in conflict herewith.

7. Arbitration. Executive and Company agree that any dispute or controversy arising out of or relating to any interpretation, construction, performance or breach of this Agreement shall be settled by arbitration of a single arbitrator to be held in South San Francisco, California, in accordance with the rules then in effect of the American Arbitration Association. The arbitrator may grant injunctions or other relief in such dispute or controversy. The decision of the arbitrator shall be final, conclusive and binding on the parties to the arbitration. Judgment may be entered on the arbitrator's decision in any court having jurisdiction. The Company and Executive shall each pay one-half of the costs and expenses of such arbitration, and each party shall separately pay counsel fees and expenses.

8. General Provisions

(a) Governing Law; Consent to Personal Jurisdiction. This Agreement will be governed by the laws of the State of California. Executive and Company hereby expressly consent to the personal jurisdiction of the state and federal courts located in California for any lawsuit filed relating to this Agreement.-

(b) Entire Agreement. This Agreement sets forth the entire agreement and understanding between the Company and Executive relating to the subject matter herein and merges all prior discussions between the parties. No modification of or amendment to this Agreement, nor any waiver of any rights under this Agreement, will be effective unless in writing signed by both parties hereto. Any subsequent change or changes in Executive's duties, Salary or compensation will not affect the validity or scope of this Agreement

(c) Severability. If one or more of the provisions in this Agreement are deemed void by law, then the remaining provisions will continue in full force and effect.

(d) Successors and Assigns. This Agreement shall be binding upon and shall inure to the benefit of the parties and their respective heirs, legal representatives, successors, and permitted assigns.

(e) Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed an original, but all of which together will constitute one and the same instruments.

IN WITNESS WHEREOF, each of the parties has executed this Agreement of the Company by its duly authorized OFFICER, as of the day and year first written above.

REMI BARBIER, AN INDIVIDUAL

Date: July 1

/s/ REMI BARBIER

PAIN THERAPEUTICS, INC.

Date: _____

By: REMI BARBIER

Title: President & CEO

[PAIN THERAPEUTICS, INC. LETTERHEAD]

Edmon R. Jennings
P.O. Box 2102
South San Francisco, CA 94083-2102

Dear Ed,

I believe PTI could benefit tremendously from your years of experience commercializing life science products. In this spirit, I am pleased to offer you the position of Chief Commercialization Officer. The terms of your employment, outlined below, reflect our previous discussions:

1. As Chief Commercialization Officer and an officer of the Company, you will report to the President & CEO.
2. Your primary responsibilities will include advising the Company on its commercialization strategy, advising the Company on its business development strategy, assessing outside product and late-stage technology opportunities and other responsibilities as these may arise from time-to-time.
3. Your cash compensation will be \$195,000 per year will be reviewed annually. You will be eligible to receive a discretionary year end cash and/or equity bonus.
4. You will receive an option to buy 225,000 shares of PTI common stock within 30 days of your full-time start date. This option will be priced at the fair market value of PTI's common stock at the date of grant, which is currently \$0.20 per share. Your option will vest monthly and equally over 48 months, starting on the date of your full-time employment with PTI.
5. We agree that your full-time start date will be February 1, 2000.
6. You will be eligible to receive medical, life insurance, disability or other health, insurance or other benefits provided to PTI's full-time employees as these become defined and available to other employees. Until these benefits are defined, you will be reimbursed in full and at cost for all COBRA associated expenses.
7. You will be entitled to earn and to take up to three (3) weeks paid vacation at times mutually agreeable to you and PTI. Vacation time is accrued at the rate of 1.25 days per month. Unused vacation may not be reimbursed or carried forward from year to year without prior written consent of the CEO.

8. You acknowledge and agree that in accordance with California law, your employment at PTI is "at will". You understand that PTI or you may terminate your employment at any time, for any reason or no reason, with or without cause and with and without notice. PTI also reserves the right to make personnel decisions regarding your employment, including but not limited to, promotions, salary adjustment, scope of responsibilities, transfer and termination consistent with PTI's needs.

In the event PTI terminates your employment without cause after your one year anniversary with the Company, PTI will continue to provide you with your regular base salary and health benefits until the earlier of a) three months from the date of termination, or b) your date of new employment or other compensated position elsewhere. You will not receive severance or other termination benefits or any other benefits (including vesting of unvested stock) in the event either a) you terminate this employment arrangement for any reason or no reason, or b) PTI terminates this employment arrangement for any reason or no reason in the first 12 months of your full-time employment, or c) PTI terminates this employment arrangement with cause.

You and PTI further agree that all disputes, claims or causes of action arising out of your employment or its termination shall be submitted to binding arbitration before a neutral arbitrator, except where the law specifically forbids the use of arbitration as a final and binding remedy.

9. You warrant and represent that you have no commitments or obligations inconsistent with PTI's offer of employment. You further understand and agree that this is a full-time and exclusive position in the services of PTI. Notwithstanding the foregoing, PTI is aware and agrees that you continue to serve as director or trustee of Asilomar Software, Inc. and San Francisco performances.

10. PTI will reimburse you for all reasonable business and travel expenses incurred on behalf of PTI.

11. You agree to sign a "CONFIDENTIAL INFORMATION AND INVENTION ASSIGNMENT AGREEMENT" (attached).

12. This offer expires December 31, 1999 unless mutually signed and received by PTI before then.

Ed, I believe these terms reflect our discussions. If acceptable to you, please sign, date and return one original copy.

I truly look forward to working with you!

/s/ REMI BARBIER

Remi Barbier
President & CEO

I agree to the terms and conditions of employment set forth in this letter,

/s/ EDMON R. JENNINGS

Date: 29 December 1999

[PAIN THERAPEUTICS LETTERHEAD]

November 23, 1999

David L. Johnson, CPA
46 Mott Place
Oakland, CA 94619

Dear Dave,

I am pleased to offer you the position of Chief Financial Officer of Pain Therapeutics, Inc. I believe the terms of your proposed employment, outlined below, reflect both the spirit and the letter of our previous discussions:

1. As Chief Financial Officer and an officer of PTI, you will report to the President & CEO.
2. Your primary responsibilities will include advising and directing PTI on its finance and accounting functions, internal/external reporting requirements, administrative functions, budget forecasting and monitoring, and contributing to PTI long term strategic planning efforts and other responsibilities as they may arise from time-to-time.
3. Your cash compensation will be \$155,000 per year and will be reviewed annually. You will be eligible to receive a discretionary year end cash and or equity bonus.
4. You will receive an option to buy 190,000 shares of PTI common stock. This option will be priced at the fair market value of PTI's common stock at the date of grant, which is currently \$0.185 per share. Your option will vest monthly and equally over 48 months, starting on your first day at PTI.
5. We agree that your full-time start date will be no later than Monday, January 3, 2000.
6. You will be eligible to receive medical, life insurance, disability or other health, insurance or other benefits provided to PTI's full-time employees as these become defined and available to other employees. Until these benefits are defined (3-4 months), you will be reimbursed in full and at cost for your COBRA associated expenses.
7. You will be entitled to earn and to take up to three (3) weeks paid vacation at times mutually agreeable to you and PTI. Unused vacation may not be reimbursed or carried forward from year to year.

8. You acknowledge and agree that in accordance with California law, your employment at PTI is "at will". You understand that PTI or you may terminate your employment at any time, for any reason or no reason, with or without cause and with and without notice. PTI also reserves the right to make personnel decisions regarding your employment, including but not limited to, promotions, salary adjustment, scope of responsibilities, transfer and termination consistent with PTI's needs.

In the event PTI terminates your employment without cause after your one year anniversary with the Company, PTI will continue to provide you with your regular base salary and health benefits until the earlier of a) three months from date of termination, or b) your date of new employment or other compensated position elsewhere. You will not receive severance or other termination benefits or any other benefits (including vesting of unvested stock) in the event either a) you terminate this employment arrangement for any reason or no reason, or b) PTI terminates this employment arrangement for any reason or no reason in the first 12 months of your full-time employment, or c) PTI terminates this employment arrangement with cause at any time.

You and PTI further agree that all disputes, claims or causes of action arising out of your employment or its termination shall be submitted to binding arbitration before a neutral arbitrator, except where the law specifically forbids the use of arbitration as a final and binding remedy.

9. You warrant and represent that you have no commitments or obligations inconsistent with PTI's offer of employment. You further understand and agree that this is a full-time and exclusive position in the services of PTI.

10. PTI will reimburse you for all reasonable business and travel expenses incurred on behalf of PTI.

11. You agree to sign a "CONFIDENTIAL INFORMATION AND INVENTION ASSIGNMENT AGREEMENT" (attached).

12. This offer expires on Friday, December 3, 1999 unless mutually signed before then.

Dave, I believe these terms reflect our discussions. If acceptable to you, please sign, date and return one original copy. Over the course of the next 12 months, PTI will be building a world class organization and I see you and others as an integral member of that team.

I look forward to working with you!

/s/ REMI BARBIER

Remi Barbier
President & CEO

I agree to all the terms and conditions of employment set forth in this letter,

/s/ DAVID L. JOHNSON

David L. Johnson, CPA

Date: 11/29/99

[PAIN THERAPEUTICS LETTERHEAD]

March 29, 1999

Barry M. Sherman, M.D.
2830 Churchill Drive
Hillsborough, CA 94010

Dear Barry,

As an entrepreneurial enterprise, I believe PTI could tremendously benefit from your experience in providing leadership to fast growing bio-medical organizations. In this spirit, I am pleased to offer you the position of Executive Vice President and Chief Medical Officer of PTI. The terms of your employment reflect both the letter and the spirit of our previous discussions and are outlined below:

1. As Executive Vice President and Chief Medical Officer, you will report to PTI's President & CEO.
2. Your primary responsibilities will include helping:
 - a) to grow the Company from an entrepreneurial outfit to a structured organization
 - b) to generally advise the Company in your area of expertise from
 - c) to assess the reasonableness of PTI's clinical development strategy
 - d) to execute its clinical trials
3. You will be a member of PTI's Management Committee.
4. Your cash compensation will be \$12,500 per month (\$150,000 per year) and will be reviewed annually.
5. You will receive an option to buy 250,000 (two hundred and fifty thousand) shares of PTI common stock. This option will be priced at the fair market value of PTI's common stock at the date of grant, which is currently \$0.10 per share. Your option will vest monthly over 48 months, starting on a mutually agreed upon vesting commencement date.

- 6. Your start date will be April 5, 1999, as we've mutually agreed upon.
- 7. You be eligible to receive medical, life insurance, disability or other health, insurance or other benefits provided to regular PTI employees as these become defined and available to other employees.
- 8. You will be entitled to earn and to take three (3) weeks paid vacation at times mutually agreeable to you and PTI. Unused vacation may not be reimbursed or carried forward from year to year.
- 9. You or PTI may terminate this employment agreement with 1 month notice for any or no reason. You will not receive severance or other termination benefits or any other benefits (including vesting of unvested stock) in the event either you or PTI terminates this employment arrangement for any reason or no reason.
- 10. You warrant and represent that you have no commitments or obligations inconsistent with PTI's offer of employment.
- 11. PTI will reimburse you for all reasonable business and travel expenses incurred on behalf of PTI.
- 12. You agree to sign a Confidentiality Agreement (attached).
- 13. This offer expires March 31, 1999 unless mutually signed before then.
- 14. In the event of termination of this agreement, you agree to facilitate the transfer to PTI of all clinical data and intellectual property that, in PTI's opinion, is relevant to the conduct of its business.

Barry, I believe these terms reflect our discussions. If acceptable to you, please sign and return one original copy. Over the course of the next 12 months, we will be building a world management team and I see you as an integral member of that team.

I truly look forward to working with you!

/s/ REMI BARBIER

 Remi Barbier
 President & CEO

I accept,

/s/ BARRY M. SHERMAN

 Barry M. Sherman, M.D.

Date: 4/2/99

The Board of Directors
Pain Therapeutics, Inc.

We consent to the use of our report included herein and to the reference to our firm under the heading "Experts" in the Prospectus.

/s/ KPMG LLP

San Francisco, California
March 13, 2000

YEAR
DEC-31-1999
JAN-01-1999
DEC-31-1999
9,339,669
0
0
0
9,396,418
44,755
4,762
9,441,173
300,587
9,703,903
2,660
9,445
575,422
9,441,173
0
0
0
3,433,300
0
0
(3,272,611)
800
0
0
0
(3,273,411)
(0.35)
(0.35)