AS ETLED WITH THE SECURITIES AND EXCHANGE COMMISSION ON JUNE 20, 200

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AMENDA	MENT NO. 2	
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	APEUTICS, INC. I 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)
SOUTH SAN FRANCIS	D AVENUE, SUITE 70 SCO, CALIFORNIA 94080 ) 624-8200	CODE DE
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MICHAEL J. O'DONNELL, ESQ. MARTIN J. WATERS III, ESQ. WILSON SONSINI GOODRICH & ROSA PROFESSIONAL CORPORATION 650 PAGE MILL ROAD PALO ALTO, CA 94304-1050 (650) 493-9300	O'MELVE ATI EMBARCAD 275 BATTERY SAN FRANCI	T. HEALY, ESQ. ENY & MYERS LLP DERO CENTER WEST  / STREET, SUITE 2600 ESCO, CA 94111-3305 ES) 984-8833
APPROXIMATE DATE OF COMMENCEME As soon as practicable after the effec	ENT OF PROPOSED SALE TO THE PUBL ctive date of this Registration	
If any of the securities being req a delayed or continuous basis pursuant 1933, check the following box. []		
If this Form is filed to register pursuant to Rule 462(b) under the Secu list the Securities Act registration s registration statement for the same of	urities Act, check the following statement number of the earlier	box and
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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.

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 JUNE 20, 2000

**PROSPECTUS** 

LOG0

5,000,000 Shares

Common Stock

. ......

This is an initial public offering of shares of common stock of Pain Therapeutics, Inc. We are offering 5,000,000 shares in this offering. No public market currently exists for our common stock. We anticipate that the initial public offering price will be between \$11 and \$13 per share.

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

.....

	PER SHARE	TOTAL
Public offering price	\$	\$
Underwriting discounts and commissions	\$	\$
Proceeds, before expenses, to us	\$	\$

The underwriters have an option to purchase 750,000 additional shares of common stock from us at the initial public offering price, less underwriting discounts and commissions, to cover any over-allotments of shares at any time until 30 days after the date of this prospectus.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THESE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

THOMAS WEISEL PARTNERS LLC

CIBC WORLD MARKETS

TUCKER ANTHONY CLEARY GULL

The date of this prospectus is

, 2000

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#### PROSPECTUS SUMMARY

This summary highlights information found in greater detail elsewhere in this prospectus. In addition to this summary, we urge you to read the entire prospectus carefully, especially the risks of investing in our common stock discussed under "Risk Factors" and the consolidated financial statements, before you decide to buy our common stock.

### PAIN THERAPEUTICS, INC.

Pain Therapeutics is developing a new generation of opioid painkillers. Opioids are drugs derived from the poppy plant. We use our technology to reformulate opioid drugs, such as morphine, into new 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 reduced 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 are combinations of FDA-approved drugs. For this reason, we believe we will encounter fewer clinical and regulatory hurdles than if we were developing new chemical entities.

#### OPTOTO PATNKTLLERS

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 changing 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 1999, U.S. opioid painkiller sales were approximately \$2.5 billion.

### OUR PRODUCTS

Each of our product candidates consists of two components: an opioid agonist, such as morphine, and a low-dose opioid antagonist, such as naltrexone or naloxone. An opioid agonist is a drug that blocks pain, and an opioid antagonist is a compound that blocks 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;
- minimize adverse side effects; and
- reduce 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. We have 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 relating to our technology.

#### OUR STRATEGY

Our goal is to build a speciality pharmaceutical company focused on 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 may 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.
- Using our technology to develop multiple drugs for both pain and non-pain 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. Pain Therapeutics and our logo are trademarks of Pain Therapeutics, Inc. This prospectus also contains trademarks and tradenames of other parties.

THE OFFERING

Common stock offered by

Pain Therapeutics, Inc. ... 5,000,000 shares

Common stock to be

outstanding after this

offering...... 25,827,142 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 Nasdag National

Market symbol..... PTIE

The number of shares to be outstanding after this offering is based on 20,827,142 shares outstanding as of March 31, 2000. This number excludes:

- 1,757,970 shares of common stock issuable upon exercise of options then outstanding, at a weighted average exercise price of \$0.50 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 \$1.00 per
- 223,800 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 INFORMATION

You should read the following summary financial data together with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the accompanying financial statements and related notes which are included in this prospectus. The following table presents summary financial information for Pain Therapeutics, Inc. The pro forma balance sheet data gives effect to:

- the conversion of all of our convertible preferred and redeemable convertible preferred stock outstanding as of March 31, 2000 into 11,108,912 shares of common stock upon completion of the offering; and
- the sale of 5,000,000 shares of common stock in the offering at an assumed initial offering price of \$12 per share, after deducting estimated underwriting discounts, commissions and offering expenses.

The summary statement of operations data 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 and the summary balance sheet data as of December 31, 1999 are derived from our audited financial statements. The summary statement of operations data for the three months ended March 31, 1999 and 2000 and the period from May 4, 1998 (inception) through March 31, 2000 and the summary balance sheet data as of March 31, 2000 are derived from our unaudited financial statements.

	PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH	98	PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH		NTHS ENDED H 31,
	DECEMBER 31, 1998	DECEMBER 31, 1999	DECEMBER 31, 1999	1999	2000
STATEMENT OF OPERATIONS DATA: Operating expenses					
Licensing fees	\$ 100,000 200,000	\$ 2,092,119	\$ 100,000 2,292,119	\$ 	\$ 1,433,268
administrative	122,168	2,567,355	2,689,523	118,257	4,619,719
Total operating expenses	422,168	4,659,474	5,081,642	118,257	6,052,987
Operating loss Interest income Income tax expense	(422,168) 33,961 800	(4,659,474) 160,689 800	(5,081,642) 194,650 1,600	(118,257)	(6,052,987) 245,050 200
Net loss Return to series C preferred shareholders for beneficial	(389,007)	(4,499,585)	(4,888,592)	(91,050)	(5,808,137)
conversion feature					(14,231,595)
Loss available to common shareholders	\$(389,007) ======	\$(4,499,585) =======	\$(4,888,592) =======	\$ (91,050) ======	\$(20,039,732) =======
Basic and diluted loss per share	\$ (0.06) ======	\$ (0.48) =======		\$ (0.01) ======	\$ (2.10) ======
Weighted average shares used in computing basic and diluted loss per share	6,948,637 ======	9,322,441 =======		9,000,000	9,528,957 ======

PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH MARCH 31, 2000

STATEMENT OF OPERATIONS DATA:	
Operating expenses	ф 100 000
Licensing fees Research and development	\$ 100,000 3,725,387
General and	3, 123, 301
administrative	7,309,242
ddiii_ii_5ci dcivoi i i i i i i i i i i i i i i i i i i	
Total operating	
expenses	11,134,629
Operating loss	(11, 134, 629)
Interest income	439,700
Income tax expense	1,800
Not loss	(40,000,700)
Net loss	(10,696,729)
Return to series C preferred shareholders for beneficial	
conversion feature	(14,231,595)
COUNCI STOIL LEGITALE	(14,231,393)

AT MARCH 31, 2000

	DECEMBER 31, 1999	ACTUAL	PRO FORMA AS ADJUSTED
BALANCE SHEET DATA:			
Cash and cash equivalents	\$ 9,339,669	\$ 22,179,362	\$ 76,879,362
Working capital	9,095,831	21,795,444	76,495,444
Total assets	9,441,173	22,864,799	77,564,799
Series C redeemable convertible preferred			
stock(1)		14,231,595	
Series B redeemable convertible preferred stock	9,703,903	9,703,903	
Series A convertible preferred stock	2,660	2,660	
Common stock	9,445	9,718	25,827
Additional paid-in capital	9,367,750	17,697,759	96,319,808
Deferred compensation	(4,980,180)	(8,448,370)	(8,448,370)
Deficit accumulated during the development stage	(4,888,592)	(10,696,729)	(10,696,729)
Total stockholders' equity (deficit)	(563,317)	(1,558,362)	77,077,136

<sup>(1)</sup> See Note 7 to the Financial Statements

#### RISK FACTORS

An investment in our common stock involves a high degree of risk. You should carefully consider the following information about these risks, together with the other information contained in this prospectus, before you decide whether to buy our common stock. If any of the events described in the following risks actually occurs, the market price of our common stock could decline, and you may lose all or part of the money you paid to buy our common stock.

### RISKS RELATED TO OUR BUSINESS

OUR BRIEF OPERATING HISTORY MAY MAKE IT DIFFICULT FOR YOU TO EVALUATE THE SUCCESS OF OUR BUSINESS TO DATE AND TO ASSESS ITS FUTURE VIABILITY.

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

WE HAVE A HISTORY OF LOSSES AND EXPECT TO INCUR SUBSTANTIAL LOSSES AND NEGATIVE OPERATING CASH FLOWS FOR THE FORESEEABLE FUTURE.

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, \$4.5 million in the year ended December 31, 1999 and \$5.8 million in the three months ended March 31, 2000. As a result of ongoing operating losses, we had an accumulated deficit of \$10.7 million as of March 31, 2000. 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. If we cannot successfully develop and commercialize our products, we will not be able to generate such revenues or achieve profitability in the future. Our failure to achieve or maintain profitability could negatively impact the market price of our common stock.

IF WE CANNOT RAISE ADDITIONAL CAPITAL ON ACCEPTABLE TERMS, WE MAY BE UNABLE TO COMPLETE PLANNED CLINICAL TRIALS OF ANY OF OUR PRODUCT CANDIDATES.

Until we receive regulatory approval and commercialize one or more of our products, 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 assumed net proceeds of 54.7 million 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 ABLE TO SUBMIT A NEW DRUG APPLICATION TO THE FDA.

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.

Even if our clinical trials are completed as planned, their results may not support our product claims. Success in pre-clinical testing and early clinical trials does not ensure that later clinical trials will be successful, and the results of later clinical trials may not 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.

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

Satisfaction of all regulatory requirements typically takes many years, is dependent upon the type, complexity and novelty of the product candidate and requires the expenditure of substantial resources for research and development and testing. Our research and clinical approaches may not lead to drugs that the FDA considers safe for humans and effective for 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.

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 OUTSIDE RESEARCHERS FAIL TO DEVOTE SUFFICIENT TIME AND RESOURCES TO OUR DRUG DEVELOPMENT PROGRAMS, OR IF THEIR PERFORMANCE IS SUBSTANDARD, THE SUBMISSION 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. These investigators may not assign as great a priority to our programs or pursue them as diligently as we would if we were undertaking such programs ourselves. If outside collaborators fail to devote sufficient time and resources to our drug development programs, or if their performance is substandard, the approval of our 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 THIRD-PARTY MANUFACTURERS OF OUR PRODUCT CANDIDATES FAIL TO DEVOTE SUFFICIENT TIME AND RESOURCES TO OUR CONCERNS, OR IF THEIR PERFORMANCE IS SUBSTANDARD, OUR CLINICAL TRIALS AND PRODUCT INTRODUCTIONS MAY BE DELAYED AND OUR COSTS MAY 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 product candidates. We currently rely on a single contract manufacturer to supply, store and distribute drug supplies for our clinical trials. Our reliance on a single third-party manufacturer 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 products, result in higher costs or deprive us of potential product revenues:

- Contract manufacturers often encounter difficulties in achieving volume production, quality control and quality assurance, as well as shortages of qualified personnel. Accordingly, our manufacturer might not be able to meet our clinical schedules.
- Switching manufacturers may be difficult because the number of potential manufacturers is limited. It may be difficult or impossible for us to find a replacement manufacturer on acceptable terms quickly, or at all.
- Our 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 WE ARE UNABLE TO PROTECT OUR INTELLECTUAL PROPERTY OUR COMPETITORS COULD DEVELOP AND MARKET PRODUCTS WITH SIMILAR FEATURES THAT MAY REDUCE DEMAND FOR OUR PRODUCTS.

Our success, competitive position and potential future revenues will depend in part on our ability to protect our intellectual property. If either we or Albert Einstein College of Medicine fails to file, prosecute or maintain any of our existing 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 expect that we will rely upon trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position. Others may independently develop substantially equivalent proprietary information or be issued patents that may prevent the sale of our products or know-how or require us to license such information and pay significant fees or royalties in order to produce our products. Moreover, our technology could infringe upon claims of patents owned by others. If we were found to be infringing on a patent held by another, we might have to seek a license to use the patented technology. In that case, we might not be able to obtain such a license on terms acceptable to us, or at all. If a legal action were to be brought against us or our licensors, we could incur substantial defense costs, and any such action might not be resolved in our favor. If such a dispute were to be resolved against us, we could have to pay the other party large sums of money and our use of our technology and the testing, manufacture, marketing or sale of one or more of our proposed products could be restricted or prohibited. Despite the use of confidentiality agreements, which may be of limited effectiveness, we may not be able to protect our trade secrets.

COMPETITION FOR QUALIFIED PERSONNEL IN THE PHARMACEUTICAL INDUSTRY IS INTENSE, AND IF WE ARE NOT SUCCESSFUL IN ATTRACTING AND RETAINING QUALIFIED PERSONNEL, WE COULD EXPERIENCE DELAYS IN COMPLETING NECESSARY CLINICAL TRIALS AND THE REGULATORY APPROVAL PROCESS OR IN FORMULATING, MANUFACTURING, MARKETING AND SELLING OUR POTENTIAL PRODUCTS.

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

THE DEA LIMITS THE AVAILABILITY OF THE ACTIVE INGREDIENTS IN OUR CURRENT PRODUCT CANDIDATES AND, AS A RESULT, OUR QUOTA MAY NOT BE SUFFICIENT TO COMPLETE CLINICAL TRIALS OR MEET COMMERCIAL DEMAND.

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. The active ingredients in our current product candidates, including morphine 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 a high degree of regulation. For example, all Schedule II drug prescriptions must be signed by a physician and may not be refilled without a new prescription. Furthermore, the amount of Schedule II substances we can obtain for clinical trials and commercial distribution is limited by the DEA and our quota may not be sufficient to complete clinical trials or meet commercial demand. There is a risk that DEA regulations

may interfere with the supply of the drugs used in our clinical trials, and in the future, our ability to produce and distribute our products in the volume needed to meet commercial demand.

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.

DEVELOPMENTS BY COMPETITORS MAY RENDER OUR PRODUCTS OR TECHNOLOGIES OBSOLETE OR NON-COMPETITIVE.

Alternative technologies and products are being developed to improve or replace the use of opioids for pain management, several of which are in clinical trials or are awaiting approval from the FDA. Such alternatives include Elan's SNX-111, as well as combination products from Endo Pharmaceuticals. In addition, companies that sell generic opioid drugs represent substantial competition. Many of these organizations competing with us have substantially greater capital resources, larger research and development staffs and facilities, greater experience in drug development and in obtaining regulatory approvals and greater manufacturing and marketing capabilities than we do. These organizations also compete with us to attract qualified personnel, parties for acquisitions, joint ventures or other collaborations.

RISKS RELATED TO THE OFFERING

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. 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 EXECUTIVE 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 executive officers, directors and individuals or entities affiliated with our directors will beneficially own approximately 41% 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 AND DELAWARE LAW 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.

- 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.

In addition, 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, without the approval of our board of directors or a large majority of our stockholders, in certain transactions with any stockholder who controls, alone or together with affiliates, 15% or more of our outstanding common stock for three years following the date on which the stockholder first acquired 15% or more of our outstanding common stock. Although we may opt out of these anti-takeover provisions, we do not intend to do so.

The anti-takeover provisions of our charter documents and of the Delaware General Corporation Law 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.

FUTURE SALES OF COMMON STOCK BY OUR EXISTING STOCKHOLDERS COULD CAUSE OUR STOCK PRICE TO DECLINE.

Sales of a substantial number of shares of our common stock after this offering, or the perception that these sales could occur, could adversely affect the market price of our common stock and impair our ability to raise capital through the sale of additional equity securities. After this offering, based upon the number of shares outstanding at March 31, 2000, we will have 25,827,142 shares of our common stock outstanding. All of the shares sold in the offering will be freely transferable without restriction or further registration, except for any shares purchased by our "affiliates," as defined in Rule 144. 20,969,091 shares of common stock outstanding after this offering will be subject to lock up agreements between our shareholders and Thomas Weisel Partners LLC restricting the sale of these shares for 180 days after the date of this prospectus. In addition, these shares are "restricted securities" as defined in Rule 144 and may be sold in absence of registration in accordance with Rule 144 or Rule 701 under the Securities Act or another exemption from registration.

YOU WILL SUFFER IMMEDIATE AND SUBSTANTIAL DILUTION BECAUSE THE NET TANGIBLE BOOK VALUE OF SHARES PURCHASED IN THIS OFFERING WILL BE SUBSTANTIALLY LOWER THAN THE INITIAL PUBLIC OFFERING PRICE.

The initial public offering price of the shares of common stock in this offering will significantly exceed the net tangible book value per share of our common stock. Any shares of common stock that investors purchase in this offering will have a post-closing net tangible book value per share of \$9.02 per share less than the initial public offering price paid, assuming an initial public offering price per share of \$12 and based on our pro forma net tangible book value as of March 31, 2000. If outstanding options or warrants are exercised, you will incur additional dilution.

#### CAUTIONARY NOTE ON 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 success of our technology;
- the timing of regulatory processes for our product candidates;
- the future growth of markets for our products;
- our intention to rely on third parties for key functions such as formulation and manufacturing and sales and marketing;
- anticipated increases in our expenses;
- the sufficiency of the net proceeds of this offering, together with our cash on hand, to fund our operations for the next 12 months; and
- the lack of a material impact of the adoption of Statement of Financial Accounting Standards No. 133 and Financial Accounting Standards Board Interpretation No. 44, which is discussed in detail under the caption "Management's Discussion and Analysis of Financial Condition and Results of Operations -- Recent Accounting Pronouncements."

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.

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, and we have not independently verified such data.

#### USE OF PROCEEDS

Our net proceeds from the sale of the shares of common stock we are offering are estimated to be \$54.7 million (\$63.1 million if the underwriters exercise their over-allotment option in full) assuming a public offering price of \$12 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. Pending the use of the net proceeds, we intend to invest the net proceeds in short-term, investment grade, interest bearing instruments in reliance on a non-statutory exemption from the Investment Company Act of 1940. If this exemption were not available, our investments in non-government securities could not constitute more than forty percent of our total assets.

### 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 March 31, 2000. This table should be read in conjunction with the "Selected Financial Data," "Management's Discussion and Analysis of Financial Condition and Results of Operations" and our financial statements and the related notes appearing elsewhere in this prospectus. This information is presented:

- on an actual basis derived from our financial statements;
- on a pro forma basis to give effect to the conversion of all of our convertible preferred and redeemable convertible preferred stock outstanding as of March 31, 2000 into 11,108,912 shares of common stock upon completion of the offering;
- on a pro forma as adjusted basis to give effect to the sale of 5,000,000 shares of common stock in the offering at an assumed initial offering price of \$12 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 MARCH 31, 2000		
	ACTUAL	PRO FORMA	PRO FORMA AS ADJUSTED
Redeemable convertible preferred stock, \$0.001 par value: Series C, 3,200,000 shares authorized and 3,044,018 issued and outstanding actual; none issued and outstanding, pro forma and pro forma as adjusted (See Note 7 to the Financial Statements)	14,231,595		
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	\$	\$
Total redeemable convertible preferred stock	23,935,498		
Stockholders' equity: 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 and pro forma as adjusted  Preferred stock 10,000,000 shares authorized, none issued and outstanding pro forma as adjusted  Common stock, \$0.001 par value; 22,000,000 shares authorized, 9,718,230 shares issued and outstanding actual; 20,827,142 shares issued and outstanding pro forma; 120,000,000 shares authorized, 25,827,142 issued and outstanding pro forma as adjusted  Additional paid-in-capital	(8,448,370) (123,400)	41,624,808 (8,448,370) (123,400)	96,319,808 (8,448,370) (123,400)
Total stockholders' equity (deficit)	(1,558,362)	22,377,136	77,077,136
Total capitalization			\$ 77,077,136

The data in the table above excludes:

- 1,757,970 shares of common stock issuable upon exercise of options outstanding as of March 31, 2000, at a weighted average exercise price of \$0.50 per share;
- 223,800 shares of common stock available for issuance at March 31, 2000, under our 1998 Stock Plan, as amended;
- 70,000 shares of common stock issuable upon exercise of warrants outstanding as of March 31, 2000 at an exercise price of \$1.00 per share;
- 150,000 shares of series A convertible preferred stock issuable upon exercise of warrants outstanding at March 31, 2000 at an exercise price of \$1 per share; and
- 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 Notes 3 and 7 to the Financial Statements.

#### DILUTION

If you invest in our common stock, your interest will be diluted to the extent of the difference between the public offering price per share of our common stock and the pro forma as adjusted net tangible book value per share of our common stock after this offering. Our pro forma net tangible book value as of March 31, 2000 was \$22,377,136, or \$1.07 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 March 31, 2000 and assumes 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 \$12 per share, after deducting underwriting discounts and commissions and estimated offering expenses, our pro forma as adjusted net tangible book value as of March 31, 2000 would have been \$77,077,136, or \$2.98 per share. This represents an immediate increase in pro forma net tangible book value of \$1.91 per share to existing stockholders and an immediate dilution of \$9.02 per share to new investors, or approximately 75% of the assumed offering price of \$12 per share. The following table illustrates this per share dilution:

Assumed offering price per share		\$12.00
2000	\$1.07	
Increase per share attributable to new investors	1.91	
Pro forma as adjusted net tangible book value per share		
after this offering		2.98
Dilution per share to new investors		\$ 9.02 =====

If the underwriters exercise their over-allotment option in full, the pro forma and as adjusted net tangible book value per share to existing stockholders will be \$3.22 per share, the increase in the net tangible book value per share to existing stockholders will be \$2.15 per share and the dilution in net tangible book value to new investors will be \$8.78 per share.

The following table summarizes, on a pro forma basis as of March 31, 2000 after giving effect to 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 \$12 per share:

	SHARES PURCHASED		TOTAL CONSIDERATION		AVERAGE PRICE	
	NUMBER	PERCENT	AMOUNT	PERCENT	PER SHARE	
Existing stockholders	, ,	81% 19	\$26,730,539 60,000,000	32% 68	\$ 1.33 \$12.00	
Total		100.0%	\$87,693,779	100.0%	Ψ12.00	

The foregoing discussion assumes no exercise of any stock options or warrants to purchase common stock outstanding as of March 31, 2000. As of March 31, 2000, there were options and warrants outstanding to purchase 2,097,970 shares of common stock at a weighted average exercise price of \$0.81 per share. To the extent any of these options are exercised, there will be further dilution to investors. In addition, there were 223,800 shares available for issuance upon the exercise of options which may be granted under our 1998 stock plan, as amended after March 31, 2000.

#### SELECTED FINANCIAL DATA

The selected statement of operations 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 selected balance sheet data as of December 31, 1998 and 1999 are derived from our audited financial statements and notes appearing elsewhere in this prospectus. The selected statements of operations data for the three months ended March 31, 1999 and 2000 and for the period from May 4, 1998 (inception) through March 31, 2000, and the selected balance sheet data as of March 31, 2000 are derived from our unaudited financial statements appearing elsewhere in this prospectus which reflect, in the opinion of management, all adjustments, consisting only of normal recurring adjustments, necessary for a fair presentation of the results for these periods and the financial condition as of that date. Historical results are not necessarily indicative of results that may be expected for any future period. 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 20 and the financial statements and related notes beginning on page F-1.

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	PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH YEAR ENDED		PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH	THREE MONTHS ENDED MARCH 31,		
	DECEMBER 31, 1998	DECEMBER 31, 1999	DECEMBER 31, 1999	1999	2000	
STATEMENT OF OPERATIONS DATA: Operating expenses:						
Licensing fees	\$ 100,000 200,000	\$ 2,092,119	\$ 100,000 2,292,119	\$ 		
administrative	122,168	2,567,355	2,689,523	118,257	4,619,719	
Total operating expenses	422,168	4,659,474	5,081,642	118,257	6,052,987	
Operating loss Interest income Income tax expense	(422,168) 33,961 800	(4,659,474) 160,689 800	(5,081,642) 194,650 1,600	(118,257) 27,407 200	(6,052,987) 245,050 200	
Net loss Return to series C preferred	(389,007)	(4,499,585)	(4,888,592)	(91,050)	(5,808,137)	
shareholders for beneficial conversion feature					(14, 231, 595)	
Loss available to common shareholders	\$(389,007) ======	\$(4,499,585) ========	\$(4,888,592) =======	\$ (91,050) ======	\$(20,039,732) ========	
Basic and diluted loss per share	\$ (0.06)	\$ (0.48)		\$ (0.01)	\$ (2.10)	
Weighted average shares used in computing basic and diluted loss per share	6,948,637 ======	9,322,441 =======		9,000,000	9,528,957	
	PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH MARCH 31, 2000					
STATEMENT OF OPERATIONS DATA: Operating expenses:						
Licensing fees	\$ 100,000 3,725,387					
administrative	7,309,242					
Total operating expenses	11,134,629					
Operating loss Interest income	(11,134,629) 439,700					

Shareholders......

Basic and diluted loss per share......

Weighted average shares used in computing basic and diluted loss per share.....

Loss available to common

Income tax expense.....

 1,800 (10,696,729)

(14, 231, 595)

\$(24,928,324)

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.

	DECEMB			
			MARCH 31,	
	1998	1999	2000	
SELECTED BALANCE SHEET DATA:				
Cash and cash equivalents	\$ 2,333,512	\$ 9,339,669	\$22,179,362	
Working capital	2,264,038	9,095,831	21,795,444	
Total assets	2,382,600	9,441,173	22,864,799	
Series C redeemable convertible preferred stock(1)			14,231,595	
Series B redeemable convertible preferred stock		9,703,903	9,703,903	
Series A convertible preferred stock	2,660	2,660	2,660	
Common stock	9,000	9,445	9,718	
Additional paid-in-capital	2,686,839	9,367,750	17,697,759	
Deferred compensation		(4,980,180)	(8,448,370)	
Deficit accumulated during the development stage	(389,007)	(4,888,592)	(10,696,729)	
Total stockholders' equity (deficit)	2,274,492	(563,317)	(1,558,362)	

(1) See Note 7 to the Financial Statements

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

You should read the following discussion and analysis in conjunction with "Selected Financial Data" and the financial statements and related notes included elsewhere in this prospectus. This discussion contains forward-looking statements. Please see "Risk Factors" and "Cautionary Note on Forward-Looking Statements."

### OVERVIEW

Pain Therapeutics is a clinical stage specialty pharmaceutical company engaged in the development of a new generation of opioid painkillers. We use our technology to reformulate opioid drugs, such as morphine, into new 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 reduced tolerance and addiction compared to existing opioid painkillers.

We have yet to generate any revenues from product sales. We have not been profitable and, since our inception, we have incurred a cumulative deficit of approximately \$10.7 million through March 31, 2000. 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.

## Deferred Non-Cash Compensation

During the three month period ended March 31, 2000 and the year ended December 31, 1999 we granted stock options to employees and non-employee consultants for which we recorded deferred compensation of approximately \$4.7 million and \$6.5 million, respectively. No options were granted in 1998.

For employees, deferred compensation represents the difference between the exercise price of the option and the 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 as that methodology most closely approximates the way in which our options are earned by the option holder. For the three month period ended March 31, 2000 and the year ended December 31, 1999, amounts amortized to the statement of operations as compensation expense for both employees and non-employees totalled \$1.2 million and \$1.5 million, respectively.

### RESULTS OF OPERATIONS

THREE MONTHS ENDED MARCH 31, 2000 AND 1999

#### 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 generally reduced by one-half of the amount of such additional royalty. The licensing fee payments made through March 31, 2000 have been charged to licensing fees in accordance with Statement of Financial Accounting Standards No. 2, Accounting for Research and Development Costs, as this technology has no alternative future use. No such payments were made during the three month periods ended March 31, 2000 and 1999.

### Research and Development

Research and development expense consists of drug development work associated with product candidates, including costs of clinical trials and clinical supplies, and research payments to the Albert Einstein College of Medicine. Research and development expenses were \$1.4 million for the three months ended March 31, 2000. For the three months ended March 31, 1999 no research and development was incurred as clinical trial activity was initiated during the second quarter of 1999.

### General and Administrative

General and administrative expense consists primarily of amortization of deferred compensation for options granted to employees and consultants, charges resulting from stock issuances pursuant to restricted stock purchase agreements, salaries and related benefit costs, facilities expenses, consulting and professional services expenses, travel and other general corporate expenses. General and administrative expenses increased to \$4.6 million for the three months ended March 31, 2000 from \$118,000 for the three months ended March 31, 1999. This increase was primarily attributable to the hiring of additional personnel and related expenses, the amortization of deferred compensation, charges resulting from stock issuances pursuant to restricted stock purchase agreements and increased consulting and professional services expenses. There will be future non-cash charges for options granted to employees and consultants.

#### Interest Income

Interest income increased to approximately \$245,000 for the three months ended March 31, 2000 from \$27,000 for the period ended March 31, 1999. This increase resulted from higher average balances of cash and cash equivalents following the sale of our series B and series C redeemable convertible preferred stock

Return to Series C Preferred Stockholders for Beneficial Conversion Feature

We determined that our series C preferred stock was issued with a beneficial conversion feature. The beneficial conversion feature has been recognized by allocating a portion of the preferred stock proceeds equal to the intrinsic value of that feature, limited to the net proceeds received (approximately \$14.2 million), to additional paid-in capital. The intrinsic value is calculated at the date of issue as the difference between the conversion price of the preferred stock and the fair value of our common stock, into which the preferred stock is convertible, multiplied by the number of common shares into which the preferred stock is convertible, limited to the net proceeds received. As our series C preferred stock is convertible into common stock at the option of the holder, at the issuance date of the preferred stock the entire \$14.2 million discount resulting from the allocation of proceeds to the beneficial conversion feature has been treated as a dividend and recognized as a return to the preferred stockholders for purposes of computing basic and diluted loss per share in the three months ended March 31, 2000.

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

### Licensing Fees

The licensing fee payments made pursuant to the terms of the license agreement with the Albert Einstein College of Medicine have been charged to licensing fees 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 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 expenses increased to \$2.6 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 \$3.3 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 carry forwards 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. We have allocated approximately \$14.2 million of these proceeds to a beneficial conversion feature which we have treated as a dividend to the preferred shareholders.

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 March 31, 2000, cash and cash equivalents were \$22.2 million, up from \$9.3 million at the end of 1999 and \$2.3 million at the end of 1998.

For the three months ended March 31, 2000 we used approximately \$1.8 million of cash for operations principally as a result of the net loss of \$5.8 million offset by non-cash compensation of approximately \$1.2 million, non-cash charges resulting from stock issuances pursuant to restricted stock purchase agreements of \$2.6 million and the increase in accounts payable of \$187,000. In the year ended December 31, 1999 we used approximately \$2.7 million of cash for operations principally as a result of the net loss of \$4.5 million offset by non-cash compensation of approximately \$1.5 million and the increase in accounts payable of \$162,000. We used approximately \$300,000 of cash for operations in the 1998 period.

Our investing activities used cash of approximately \$83,000 in the three months ended March 31, 2000. For the year ended December 31, 1999 our investing activities used cash of approximately \$39,000 compared to approximately \$11,000 in the 1998 period. These activities 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.

Financing activities provided cash of \$14.7 million in the three months ended March 31, 2000. Our financing activities in the year ended December 31, 1999 and for the period ended December 31, 1998 generated approximately \$9.7 million and \$2.7 million, respectively. These amounts are primarily from the private sales of preferred stock. The 2000 period also includes approximately \$460,000 of deferred charges related to our initial public offering. 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 PRONOUNCEMENTS

In June 1998 the Financial Accounting Standards Board issued Statement of Financial Accounting Standards No. 133, or SFAS No. 133, Accounting for Derivative Instruments and Hedging Activities. 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 our financial position, results of operations or cash flows.

In March 2000, the Financial Accounting Standards Board issued FASB Interpretation No. 44, or FIN No. 44, Accounting for Certain Transactions Involving Stock Compensation. This Interpretation clarifies the application of APB Opinion No. 25, Accounting for Stock Issued to Employees and is generally effective July 1, 2000, with certain conclusions in this Interpretation covering specific events that occur after either December 15, 1998, or January 12, 2000. To the extent that this Interpretation covers events occurring during the period after December 15, 1998, or January 12, 2000, but before the effective date of July 1, 2000, the effects of applying this Interpretation are recognized on a prospective basis from July 1, 2000. Management believes the adoption of FIN No. 44 will not have a material impact on our financial position, results of operations or cash flows.

# 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 March 31, 2000, 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 technology to reformulate existing opioid painkillers into new drugs, which we believe offer enhanced pain relief, fewer adverse side effects and reduced 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 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 knee 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 an opioid painkiller will be prescribed to treat the pain. The following diagram illustrates the types of pain which physicians typically treat with opioid painkillers:

### [GRAPHIC]

### Pain Management Market

The medical effort to treat pain, known as pain management, addresses 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, Monsanto, which is now part of Pharmacia, and Merck, all of which are large pharmaceutical companies, launched non-opioid prescription pain relievers 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 the price of aspirin. The success of COX-2 inhibitors demonstrates the potential for rapid market acceptance and premium pricing of pain products that offer reduced side effects.

There has been little innovation in the area of opioid painkillers. 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 were approximately \$2.5 billion in 1999.

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	1999 U.S. SALES (IN MILLIONS)
Strong Opioids Weak Opioids	Cancer pain Outpatient surgery	Morphine Hydrocodone and oxycodone	MS Contin and others Vicodin and others	\$ 700 \$1,300
Synthetic Opioids	Back pain	Tramadol	Ultram	\$ 450
			Total	\$2,450 ======

Source: IMS HEALTH, Retail & Provider Perspectives 1999

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 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 under-treated 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 drugs that address the shortcomings of existing opioid painkillers. We believe our drugs will:

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

If approved by the FDA, we believe our 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 may encounter fewer clinical and regulatory hurdles than if we were developing new chemical entities because the safety and therapeutic profiles of these individual 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 drugs that we believe may 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 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.

Using Our Technology to Develop Multiple Drugs for Both Pain and Non-Pain 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 pl0.001, 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 receive final clinical 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 1999, U.S. sales of tramadol exceeded \$450 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 patents for Ultram expire 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.

- 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, oxycodone and similar weak opioids. In 1999, U.S. sales of such drugs exceeded \$1.3 billion. 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 within and outside the field of pain management. In particular, 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.

Upon our formation in May 1998, we licensed our technology from Albert Einstein College of Medicine. We have worldwide exclusive rights to the technology. Our rights terminate upon the expiration of the patents used to protect the technology between 2013 and 2015. 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.

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

We seek to protect our technology by, among other methods, filing and prosecuting U.S. and foreign patents and patent applications with respect to our technology and products and their uses. The issued patents expire between 2013 and 2015. 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 drug has been separately approved for human use by the FDA, we believe that we may encounter fewer regulatory hurdles than if we were developing new chemical entities.

#### The Drug Approval Process

- 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  ${\rm drug}\,.$

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 pain relief 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 supension 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 31, 2000, we had approximately 18 employees and seven executive consultants, including five 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.

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#### 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	59	Executive Vice President and Chief Medical Officer
Edmon R. Jennings	54	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, Esq	42	Director and Secretary
Sanford R. Robertson(1)(2)	68	Director

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. From April 1996 to February 1999, 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. From November 1998 to December 1999, Mr. Johnson was an independent financial consultant, and acted as Chief Financial Officer at Aradigm, a drug delivery technology company. From October 1997 to November 1998, Mr. Johnson held

<sup>(1)</sup> Member of Audit Committee.

<sup>(2)</sup> Member of Compensation Committee.

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 January 1995 to September 1996, Mr. Johnson was an independent financial consultant and provided accounting services to Chiron, a biotechnology company. From June 1993 to December 1994, Mr. Johnson was Director of Financial Planning and Operational Analysis at Chiron. 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 by 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. Friedmann was President and Chief Executive Officer of Daiichi Pharmaceutical Corporation, a pharmaceutical company, from 1997 to April 2000 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 has been a private investor since retiring as Vice President of the radio pharmaceuticals division of Mallinckrodt, Inc., a healthcare company, in 1973. He served as a director of Mallinckrodt from 1966 to 1975. 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, Esq. has served as a director since June 1998. Mr. O'Donnell has been a member of the law firm of Wilson Sonsini Goodrich & Rosati, Professional Corporation, our corporate counsel, since 1993. 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 has been a general partner of Francisco Partners, a technology investment fund since January 2000. From October 1998 to December 1999 he was President of Robertson and Co. Mr. Robertson is the founder and former chairman of Robertson, Stephens & Company, an investment banking firm founded in October 1978, with which Mr. Robertson was associated through September 1998. 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 So University of California, San Fra	
Stanley Crain, Ph.D Professor of Neurosciences, Emeri Einstein College of Medicine	
Nadav Friedmann, M.D., Ph.D Independent Consultant, former Pr Chief Executive Officer, Daiichi	resident &
Pharmaceuticals Corp.	
Scott R. Hamann, M.D., Ph.D Department of Anesthesiology, Uni Kentucky College of Medicine	iversity of
, ,	am Cadman
Don R. Mehlisch, M.D., D.D.S Independent Consultant, Co-founder Corporation	er, Scirex
Fredrick L. Minn, M.D., Ph.D Independent Consultant, formerly Johnson/Ortho-McNeil Pharmaceutic	
Robert B. Raffa, Ph.D Associate Professor of Pharmacolo University	ogy, Temple
Patrick Scannon, M.D., Ph.D Chief Medical and Scientific Offi Corporation	icer, Xoma
Ke-Fei Shen, M.D., Ph.D Principal Associate, Albert Einst of Medicine	cein College
Barry M. Sherman, M.D Executive Vice President & Chief Officer, Pain Therapeutics, Inc.	Medical
Eric J. Simon, Ph.D Professor of Psychiatry and Pharm York University School of Medicin	
Frank Porreca, Ph.D	esthesiology,

# 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

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

		INDIVID	JAL GRANTS			
	NUMBER OF SECURITIES	PERCENT OF TOTAL OPTIONS GRANTED TO			VALUE AT ANNUAL R STOCK APP	REALIZABLE ASSUMED RATES OF PRECIATION ON TERM(\$)
NAME	UNDERLYING OPTIONS GRANTED	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	4,861,683	7,756,227
	250,000	25.9	0.10	9/10/09	4,861,683	7,756,227
	100,000	10.4	0.20	12/10/09	1,934,673	3,092,490

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 \$12 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.

	SHARES ACOUIRED VALUE	VALUE	NUMBER OF SECURITIES UNDERLYING UNEXERCISED OPTIONS AT DECEMBER 31, 1999(#)		VALUE OF UNEXERCISED IN-THE-MONEY OPTIONS AT DECEMBER 31, 1999(\$)(1)	
NAME	ON EXERCISE	REALIZED(\$)	EXERCISABLE	UNEXERCISABLE	EXERCISABLE	UNEXERCISABLE
Remi Barbier						
Barry M. Sherman, M.D			52,083	547,917	619,787	6,510,212

<sup>(1)</sup> Value is determined by subtracting the exercise price of an option from an assumed \$12 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 31, 2000, 223,800 shares were available for issuance under the 1998 Stock Plan.

The purpose of the 1998 Stock Plan is to provide us with an opportunity to retain and attract employees, directors and consultants who are essential to our future growth and success by providing such individuals with an opportunity to acquire shares of our common stock. Our 1998 Stock Plan provides for the grant of nonstatutory stock options to our (and our parent and subsidiary corporations) employees, directors and consultants, and for the grant of incentive stock options, within the meaning of Section 422 of the Internal Revenue Code, to our employees and employees of our parent and subsidiary corporations.

A total of 3,200,000 shares of our common stock are authorized for issuance under the 1998 Stock Plan. On the effective date of our initial public offering a total of 1,500,000 shares will be added to reserve of shares available for issuance under the 1998 Stock Plan. In addition, on the first day of each fiscal year during the term of the 1998 Stock Plan, beginning with our fiscal year 2001, the number of shares available for issuance under our 1998 Stock Plan will increase by an amount of shares equal to the lesser of 5% of the outstanding shares of our common stock on the last day of our immediately preceding fiscal year, 2,000,000 shares or a lesser amount as our board may determine.

Our board of directors or a committee of our board administers the 1998 Stock Plan. In the case of options intended to qualify as performance-based compensation within the meaning of Section 162(m) of the Internal Revenue Code, the committee will consist of two or more outside directors within the meaning of Section 162(m) of the Internal Revenue Code. The administrator has the power to determine the terms of the options granted, including the exercise price, the number of shares subject to each option, the exercisability of the options and the form of consideration payable upon exercise.

The administrator determines the exercise price of options granted under the 1998 Stock Plan, but with respect to nonstatutory stock options intended to qualify as performance-based compensation within

the meaning of Section 162(m) of the Internal Revenue Code and all incentive stock options, the exercise price must at least be equal to the fair market value of our common stock on the date of grant. The term of an incentive stock option may not exceed 10 years, except that with respect to any participant who owns 10% of the voting power of all classes of our outstanding capital stock, the term must not exceed five years and the exercise price must equal at least 110% of the fair market value on the grant date. The administrator determines the term of all other options.

No optionee may be granted an option to purchase more than 1,000,000 shares in any fiscal year. In connection with his or her initial service, an optionee may be granted options to purchase up to an additional 1,000,000 shares.

After termination of one of our employees, directors or consultants, he or she may exercise his or her option for the period of time stated in the option agreement. Generally, if termination is due to death or disability, the option will remain exercisable for 12 months. In all other cases, the option will generally remain exercisable for three months. However, an option may never be exercised later than the expiration of its term.

Our 1998 Stock Plan provides for the periodic automatic grant of options to our nonemployee directors. Each option granted under this automatic grant provision will have an exercise price per share equal to 100% of the fair market value per share of our common stock on the date of grant, and will have a term of 10 years, unless terminated earlier upon the optionee's termination of service as a director.

Our 1998 Stock Plan generally does not allow for the transfer of options and only the optionee may exercise an option during his or her lifetime. The administrator may, however, allow options to be transferable.

Our 1998 Stock Plan provides that in the event of our merger with or into another corporation or a sale of substantially all of our assets, the successor corporation will assume or substitute each option. If the outstanding options are not assumed or substituted, the administrator will provide notice to the optionee that he or she has the right to exercise the options as to all of the shares subject to the option, including shares which would not otherwise be exercisable, for a period of 15 days from the date of the notice. The option will terminate upon the expiration of the 15-day period.

Our 1998 Stock Plan will automatically terminate in 2008, unless we terminate it sooner. In addition, our board of directors has the authority to amend, suspend or terminate the 1998 Stock Plan provided it does not adversely affect any option previously granted under our 1998 Stock Plan.

2000 Employee Stock Purchase Plan.

Our board of directors adopted the 2000 Employee Stock Purchase Plan in April 2000 and our stockholders subsequently approved it. Our 2000 Employee Stock Purchase Plan provides eligible employees the opportunity to purchase shares of our common stock at a discount through payroll deductions.

A total of 500,000 shares of our common stock are authorized for issuance under the 2000 Employee Stock Purchase Plan. In addition, the number of shares authorized for issuance under the 2000 Employee Stock Purchase Plan will increase annually on the first day of each fiscal year, beginning with our fiscal year 2001, equal to the lesser of 1% of the outstanding shares of our common stock on the last day of the immediately preceding fiscal year, 500,000 shares, or such other amount as may be determined by our board of directors.

Our board of directors or a committee of our board administers the 2000 Employee Stock Purchase Plan. Our board of directors or its committee has full and exclusive authority to interpret the terms of the 2000 Employee Stock Purchase Plan.

All of our 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, an employee may not be granted an option to purchase stock under the 2000 Employee Stock Purchase Plan if such employee:

- 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 accrue at a rate that exceeds \$25,000 worth of stock for each calendar year.

Our 2000 Employee Stock Purchase Plan is intended to qualify under Section 423 of the Internal Revenue Code and contains consecutive, overlapping 24-month offering periods. Each offering period includes four 6-month purchase periods. The offering periods generally start on the first trading day on or after May 1st and November 1st of each year, except for the first such offering period which will commence on the first trading day on or after the effective date of this offering and will end on the last trading day on or after May 1, 2002.

Our 2000 Employee Stock Purchase Plan permits participants to purchase common stock through payroll deductions of up to 15% of their eligible compensation which includes a participant's base straight time gross earnings. A participant may purchase a maximum of 7,500 shares during a 6-month purchase period.

Amounts deducted from a participant's eligible compensation and accumulated during a six month purchase period are used to purchase shares of our common stock at the end of the six-month purchase period. The price is 85% of the lower of the fair market value of our common stock at the beginning of an offering period or at the end of a purchase period. If the fair market value at the end of a purchase period is less than the fair market value at the beginning of the offering period, participants will be withdrawn from the current offering period following their purchase of shares on the purchase date and will be automatically re-enrolled in a new offering period. Participants may end their participation at any time during an offering period, and will be paid their payroll deductions to date. Participation ends automatically upon termination of employment with us.

A participant may not transfer rights granted under the 2000 Employee Stock Purchase Plan other than by will, the laws of descent and distribution or as otherwise provided under the 2000 Employee Stock Purchase Plan.

In the event of our merger with or into another corporation or a sale of all or substantially all of our assets, a successor corporation may assume or substitute each outstanding option. 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.

Our 2000 Employee Stock Purchase Plan will terminate in 2010. However, our board of directors has the authority to amend or terminate our 2000 Employee Stock Purchase Plan, except that, subject to certain exceptions described in the 2000 Employee Stock Purchase Plan, no such action may adversely affect any outstanding rights to purchase stock under our 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 31, 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 31, 2000, there would have been 20,827,142 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 31, 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.

	SHARES BENEFICIALLY	PERCENT OF SHARES OUTSTANDING(2)	
NAME OR GROUP OF BENEFICIAL OWNERS	OWNED PRIOR TO OFFERING(1)	PRIOR TO OFFERING	AFTER OFFERING
William H. Gates, III(3)2365 Carillon Point Kirkland, WA 98033	2,000,000	9.6%	7.7%
TVM-Techno Venture Management III GmbH(4)	1,644,104	7.9	6.4
John Griffin(5) Blue Ridge Limited Partnership 660 Madison Avenue New York, NY 10021	1,710,270	8.2	6.6
GMS Capital Partners, L.P.(6)	1,146,070	5.5	4.4
Remi Barbier(7)	8,180,000	39.3	31.7
Gert Caspritz, Ph.D.(8)	1,644,104	7.9	6.4
Sanford R. Robertson(9) One Maritime Plaza, Suite 2500 San Francisco, CA 94111	258,333	1.2	1.0
David L. Johnson(10)	190,000	*	*
Barry M. Sherman, M.D.(11)	114,584	*	*

	SHARES BENEFICIALLY	PERCENT OF SHARES OUTSTANDING(2)		
NAME OR GROUP OF BENEFICIAL OWNERS	OWNED PRIOR TO OFFERING(1)	PRIOR TO OFFERING	AFTER OFFERING	
Nadav Friedmann, M.D., Ph.D.(12) 91 Bacon Court Lafayette, CA 94549	128,333	*	*	
Michael J. O'Donnell(13)	65,756	*	*	
Edmon R. Jennings(14)	14,063	*	*	
Wilfred R. Konneker, Ph.D				
(9 persons)(15)	10,595,173	50.9%	41.0%	

- \* 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 20,827,142 shares of Common Stock outstanding prior to this offering.
- (3) Includes 2,000,000 shares held by Cascade Investment, LLC, which is controlled by William H. Gates, III.
- (4) TVM Techno Venture Management III GmbH is controlled by its two Managing Directors, Helmut Schuhsler and Friedrich Bornikee.
- (5) 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.
- (6) GMS Capital Investments, L.L.C. is the general partner of GMS Capital Partners, L.P. Joachim Gfeeller, David Meek and Andrew Stallman are the managing members of GMS Capital Investments, L.L.C.
- (7) All of these shares are subject to our right of repurchase which lapses over time.
- (8) 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.

- (9) Includes 8,333 shares issuable pursuant to options exercisable within 60 days of March 31, 2000.
- (10) All of these shares are subject to our right of repurchase which lapses over time.
- (11) Includes 114,584 shares issuable pursuant to options exercisable within 60 days of March 31, 2000.
- (12) Includes 8,333 shares issuable pursuant to options exercisable within 60 days of March 31, 2000.
- (13) 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 1,042 shares issuable to Mr. O'Donnell pursuant to options exercisable within 60 days of March 31, 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.
- (14) Includes 14,063 shares issuable pursuant to options exercisable within 60 days of March 31, 2000.
- (15) Includes 146,355 shares issuable pursuant to options exercisable within 60 days of March 31, 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 31, 2000, assuming the conversion of all outstanding shares of preferred stock into common stock, there were 20,827,142 shares of common stock outstanding which were held by approximately 85 stockholders. There will be 25,827,142 shares of common stock outstanding (assuming no exercise of the underwriters' over-allotment option and no exercise of outstanding options after March 31, 2000) after giving effect to the sale of our common stock in this offering. In addition to 1,757,970 shares issuable upon exercise of outstanding options, and 223,800 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 31, 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 or 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 Action 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 ChaseMellon Shareholder Services, LLC.

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 31, 2000, there will be 25,827,142 shares of our common stock outstanding. Of these outstanding shares, the 5,000,000 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

20,967,091 shares of our common stock outstanding after this offering will be 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. In the lock-up agreements, our 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 Thomas Weisel Partners LLC.

#### SALES OF RESTRICTED SHARES

In addition to being subject to the lock-up agreements 20,967,091 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 258,000 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 5,200,000 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.

#### UNITED STATES TAX CONSEQUENCES TO NON-U.S. HOLDERS

The following is a general discussion of the principal United States federal income and estate tax consequences of the acquisition, ownership and disposition of our common stock by a Non-U.S. Holder. As used in this prospectus, the term "Non-U.S. Holder" is a person who holds our common stock other than:

- a citizen or resident of the United States,
- a corporation or other entity taxable as a corporation created or organized in or under the laws of the United States or of any political subdivision of the United States,
- an estate the income of which is includable in gross income for United States federal income tax purposes regardless of its source, or
- a trust subject to the primary supervision of a United States court and the control of one or more United States persons, or a trust (other than a wholly-owned grantor trust) that was treated as a domestic trust despite not meeting the requirements described above.

This discussion does not consider:

- state, local or foreign tax consequences,
- specific facts and circumstances that may be relevant to a particular Non-U.S. Holder's tax position in light of their particular circumstances.
- the tax consequences for the stockholders or beneficiaries of a Non-U.S. holder.
- special tax rules that may apply to certain Non-U.S. Holders, including without limitation, partnerships, banks, insurance companies, dealers in securities and traders in securities, or
- special tax rules that may apply to a Non-U.S. Holder that holds our common stock as part of a "straddle," "hedge" or "conversion transaction"

The following discussion is based on provisions of the United States Internal Revenue Code of 1986, as amended, also known as the Code, applicable Treasury regulations and administrative and judicial interpretations, all as of the date of this prospectus, and all of which are subject to change, retroactively or prospectively. The following discussion assumes that our common stock is held as a capital asset. The following summary is for general information. Accordingly, each Non-U.S. Holder should consult a tax advisor regarding the United States federal, state, local and foreign income and other tax consequences of acquiring, holding and disposing of shares of our common stock.

## DIVIDENDS

We do not anticipate paying cash dividends on our common stock in the foreseeable future. See "Dividend Policy." In the event, however, that dividends are paid on shares of our common stock, dividends paid to a Non-U.S. Holder of our common stock generally will be subject to withholding of United States federal income tax at a 30% rate, or such lower rate as may be provided by an applicable income tax treaty. Non-U.S. Holders should consult their tax advisors regarding their entitlement to benefits under a relevant income tax treaty.

Dividends that are effectively connected with a Non-U.S. Holder's conduct of a trade or business in the United States or, if an income tax treaty applies, attributable to a permanent establishment in the United States, known as United States trade or business income, are generally subject to United States federal income tax on a net income basis at regular graduated rates, but are not generally subject to the

30% withholding tax if the Non-U.S. Holder files the appropriate United States Internal Revenue Service form with the payor. Any United States trade or business income received by a Non-U.S. Holder that is a corporation may also, under certain circumstances, be subject to an additional "branch profits tax" at a 30% rate or such lower rate as specified by an applicable income tax treaty.

Dividends paid prior to 2001 to an address in a foreign country are presumed, absent actual knowledge to the contrary, to be paid to a resident of such country for purposes of the withholding discussed above and for purposes of determining the applicability of a tax treat rate. For dividends paid after 2000, a Non-U.S. Holder of our common stock who clams the benefit of an applicable income tax treaty rate generally will be required to satisfy applicable certification and other requirements.

A Non-U.S. Holder of our common stock that is eligible for a reduced rate of United States withholding tax under an income tax treaty may obtain a refund or credit of any excess amounts withheld by filing an appropriate claim for a refund with the United States Internal Revenue Services.

#### GAIN ON DISPOSITION OF COMMON STOCK

A Non-U.S. Holder generally will not be subject to United States federal income tax in respect of gain recognized on a disposition of our common stock unless:

- the gain is United States trade or business income, in which case the branch profits tax described above may apply to a corporate Non-U.S. Holder,
- the Non-U.S. Holder is an individual who holds our common stock as a capital asset within the meaning of Section 1221 of the Code, is present in the United States for more than 182 days in the taxable year of the disposition and meets certain other requirements, the Non-U.S. Holder is subject to tax pursuant to the provisions of the United States tax law applicable to certain United States expatriates, or
- we are or have been a United States real property holding corporation for United States federal income tax purposes at any time during the shorter of the five-year period ending on the date of disposition of the period that the Non-U.S. Holder held our common stock.

Generally, a corporation is a United States real property holding corporation if the fair market value of its United States real property interest, such as interest in real property located in the United States or the Virgin islands, and certain interests in other United States real property holding corporations, equals or exceeds 50% of the sum of the fair market value of its worldwide real property interests plus its other assets used or held for use in a trade or business. We believe we have never been, are not currently and are not likely to become a United States real property holding corporation for United States federal income tax purposes.

## FEDERAL ESTATE TAX

Common stock owned or treated as owned by an individual who is a Non-U.S. Holder at the time of death will be included in the individual's gross estate for United States federal estate tax purposes, unless an applicable estate tax or other treaty provides otherwise.

## INFORMATION REPORTING AND BACKUP WITHHOLDING TAX

We must report annually to the United States Internal Revenue Service and to each Non-U.S. Holder the amount of dividends paid to that holder and the tax withheld with respect to those dividends. Copies of the information returns reporting those dividends and withholding may also be made available

to the tax authorities in the country in which the Non-U.S. Holder is a resident under the provisions of an applicable income tax treaty or agreement.

Under certain circumstances, United States Treasury Regulations require information reporting and backup withholding at a rate of 31% on certain payments on our common stock. Under currently applicable law, Non-U.S. Holders of our common stock, generally will be exempt from these information reporting requirements and from backup withholding on dividends paid prior to 2001 to an address outside the United States. For dividends paid after 2000, however, a Non-U.S. Holder of our common stock that fails to certify its Non-U.S. holder status in accordance with applicable United States Treasury Regulations may be subject to backup withholding at a rate of 31% of dividends.

The payment of the proceeds of the disposition of our common stock by a holder to or through the United States office of a broker generally will be subject to information reporting and backup withholding at a rate of 31% unless the holder either certifies its status as a Non-U.S. Holder under penalties of perjury or otherwise establishes an exemption. The payment of the proceeds of the disposition by a Non-U.S. Holder of our common stock to or through a foreign office of a foreign broker will not be subject to backup withholding or information reporting unless the foreign broker will not be subject to backup withholding or information reporting unless the foreign broker is a United States related person. In the case of the payment of proceeds from the disposition of our common stock by or through a foreign office of a broker that is a United States person or a "United States related person," information reporting, but currently not backup withholding, on the payment applies unless the broker receives a statement from the owner, signed under penalty of perjury, certifying its foreign status or the broker has documentary evidence in its files that the holder is a Non-U.S. Holder and the broker has no actual knowledge to the contrary. For this purpose, a United States related person is:

- a "controlled foreign corporation" for United States federal income tax purposes,
- a foreign person 50% or more of whose gross income from all sources for the three-year period ending with the close of its taxable year preceding the payment, or for such part of the period that the broker has been in existence, is derived from activities that are effectively connected with the conduct of a United State trade or business,
- effective after 2000, a foreign partnership if, at any time during the taxable year, (A) at least 50% of the capital or profits interest in the partnership is owned by United States persons, or (B) the partnership is engaged in a United States trade or business, or
- certain U.S. branches of foreign banks or insurance companies.

Effective after 2000, backup withholding may apply to the payment of disposition proceeds by or through a foreign office or a broker that is a United States person or a United States related person unless certain certification requirements are satisfied or an exemption is otherwise established and the broker has no actual knowledge that the holder is a United States person. Non-U.S. Holders should consult their own tax advisors regarding the application of the information reporting and backup withholding rules to them, including changes to these rules that will become effective after 2000.

Any amounts withheld under the backup withholding rules from a payment to a Non-U.S. Holder will be refunded, or credited against the holder's United States federal income tax liability, if any, provided that the required information is furnished to the United States Internal Revenue Service.

#### UNDERWRITING

**GENERAL** 

Subject to the terms and conditions set forth in an agreement among the underwriters and us, each of the underwriters named below, through their representatives, Thomas Weisel Partners LLC, CIBC World Markets Corp. and Tucker Anthony Incorporated, has severally agreed to purchase from us the aggregate number of shares of common stock set forth opposite its name below:

UNDERWRITERS	NUMBER OF SHARES
Thomas Weisel Partners LLC	
Total	5,000,000

The underwriting agreement provides that the obligations of the several underwriters are subject to various conditions. The nature of the underwriters' obligations commits them to purchase and pay for all of the shares of common stock listed above if any are purchased.

The underwriting agreement provides that we will indemnify the underwriters against liabilities specified in the underwriting agreement under the Securities Act or will contribute to payments that the underwriters may be required to make relating to these liabilities.

Thomas Weisel Partners LLC expects to deliver the shares of common stock to purchasers on  $\,$  , 2000.

## OVER-ALLOTMENT OPTION

We have granted a 30-day over-allotment option to the underwriters to purchase up to a total of 750,000 additional shares of our common stock from us at the initial public offering price, less the underwriting discounts and commissions, as set forth on the cover page of this prospectus. If the underwriters exercise this option in whole or in part, then each of the underwriters will be separately committed, subject to conditions described in the underwriting agreement, to purchase the additional shares of our common stock in proportion to their respective commitments set forth in the table above.

## 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.

#### COMMISSIONS AND DISCOUNTS

The underwriters propose to offer the shares of common stock directly to the public at the public offering price set forth on the cover page of this prospectus, and at this price less a concession not in excess of \$ per share of common stock to other dealers specified in a master agreement among underwriters who are members of the National Association of Securities Dealers, Inc. The underwriters may allow, and the other dealers specified may reallow, concessions, not in excess of \$0.10 per share of common stock to these other dealers. After this offering, the offering price, concessions and other selling terms may be changed by the underwriters. Our common stock is offered subject to receipt and acceptance by the underwriters and to other conditions, including the right to reject orders in whole or in part.

		TOTAL			
	PER SHARE	WITHOUT OVER-ALLOTMENT	WITH OVER-ALLOTMENT		
Underwriting discounts and commissions paid by us	\$ \$	\$ \$	\$ \$		

# 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.

## RESERVED SHARES

The underwriters, at our request, have reserved for sale at the initial public offering price up to 250,000 shares of common stock to be sold in this offering for sale to our employees and other persons designated by us. The number of shares available for sale to the general public will be reduced to the extent that any reserved shares are purchased. Any reserved shares not purchased in this manner will be offered by the underwriters on the same basis as the other shares offered in this offering.

Our directors, officers and securityholders holding a total of 20,967,091 shares of common stock have agreed or have a contractual obligation to agree, subject to specified exceptions, not to offer, sell,

agree to sell, directly or indirectly, or otherwise dispose of any shares of common stock or any securities convertible into or exchangeable for shares of common stock without the prior written consent of Thomas Weisel Partners LLC for a period of 180 days after the date of this prospectus.

We have agreed that for a period of 180 days after the date of this prospectus we will not, without the prior written consent of Thomas Weisel Partners LLC, offer, sell, or otherwise dispose of any shares of common stock, except for the shares of common stock offered in the offering and the shares of common stock issuable upon exercise of outstanding options and warrants on the date of this prospectus.

## INFORMATION REGARDING THOMAS WEISEL PARTNERS LLC

Thomas Weisel Partners LLC, one of the representatives of the underwriters, was organized and registered as a broker-dealer in December 1998. Thomas Weisel Partners LLC has been named as a lead or co-manager on 164 filed public offerings of equity securities, of which 120 have been completed, and has acted as a syndicate member in an additional 95 public offerings of equity securities. Thomas Weisel Partners LLC does not have any material relationship with us or any of our officers, directors or controlling persons, except with respect to its contractual relationship with us under the underwriting agreement entered into in connection with this offering.

## NASDAQ NATIONAL MARKET LISTING

Prior to this offering, there has been no public market for our common stock. Consequently, the initial public offering price for our common stock was determined through negotiations between us and representatives of the underwriters. Some of the factors considered in these negotiations included our results of operations in recent periods, estimates of our prospects and the industry in which we compete, an assessment of our management, the general state of the securities markets at the time of this offering and the prices of similar securities of generally comparable companies. We have applied to have our common stock quoted on the Nasdaq National Market under the symbol "PTIE". We cannot assure you that an active or orderly trading market will develop for our common stock or that our common stock will trade in the public markets subsequent to this offering at or above the initial offering price.

## DISCRETIONARY ACCOUNTS

The underwriters do not expect sales of shares of common stock offered by this prospectus to any accounts over which they exercise discretionary authority to exceed five percent of the shares offered.

# MARKET STABILIZATION, SHORT POSITIONS AND PENALTY BIDS

In order to facilitate this offering, persons participating in this offering may engage in transactions that stabilize, maintain or otherwise affect the price of our common stock during and after this offering. Specifically, the underwriters may over-allot or otherwise create a short position in our common stock for their own account by selling more shares of common stock than we have sold to them. The underwriters may elect to cover any short position by purchasing shares of common stock in the open market or by exercising the over-allotment option granted to the underwriters. In addition, the underwriters may stabilize or maintain the price of the common stock by bidding for or purchasing shares of common stock in the open market and may impose penalty bids. Under these penalty bids, selling concessions that are allowed to syndicate members or other broker-dealers participating in this offering are reclaimed if shares of common stock previously distributed in this offering are repurchased, usually in order to stabilize the market. The effect of these transactions may be to stabilize or maintain the market price at a level above that which might otherwise prevail in the open market. No representation is made as to the magnitude or

effect of any stabilization or other transaction. These transactions may be effected on the Nasdaq National Market or otherwise and may be discontinued at any time after they are commenced.

#### 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

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#### 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.

/s/ KPMG LLP

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

## BALANCE SHEETS

				1, 2000
	DECEMBER 31, 1998	DECEMBER 31, 1999	ACTUAL	PRO FORMA STOCKHOLDERS' EQUITY
			(UNAUDITED)	
ASSETS Current assets:				
Cash and cash equivalentsInterest receivablePrepaid expenses	\$2,333,512 3,138 35,496	41,387	\$ 22,179,362 32,095 71,650	
Total current assets  Property and equipment, net  Deferred financing costs	10,434	9,396,418	22,283,107	
Total assets		\$ 9,441,173	\$ 22,864,799	
LIABILITIES AND STOCKHOLDERS' EQUITY (DEFICIT) Liabilities:				
Accounts payable	\$ 108,108	\$ 300,587	\$ 487,663	
Total liabilities		300,587	487,663	
Commitments and contingencies Redeemable convertible preferred stock Series C \$.001 par value; 3,044,018 shares authorized; 3,200,000 shares designated, issued and outstanding at March 31, 2000; none pro forma; liquidation preference and redemption value of \$5 per share Series B \$.001 par value; 5,405,405 shares authorized; 5,405,405 shares designated, issued and outstanding in 1999 and 2000; none pro forma; liquidation preference and			14,231,595	
redemption value of \$1.85 per share		9,703,903	9,703,903	
		9,703,903	23,935,498	
Stockholders' equity (deficit): Convertible preferred stock Series A \$.001 par value; 3,500,000 shares authorized; 2,659,489 shares issued and outstanding in 1998, 1999 and 2000; none pro forma; liquidation preference of \$1.00 per share Common stock, \$.001 par value; 20,000,000 shares authorized and 9,000,000 and 9,445,000 issued and outstanding as of December 31, 1998 and 1999, respectively; 22,000,000 shares authorized and 9,718,230 shares issued and outstanding as of March 31, 2000, 20,827,142 shares issued and		2,660		
outstanding pro formaAdditional paid-in-capitalDeferred compensationNotes receivable	9,000 2,686,839  (35,000)	9,445 9,367,750 (4,980,180) (74,400)	9,718 17,697,759 (8,448,370) (123,400)	20,827 41,624,808 (8,448,370) (123,400)
Deficit accumulated during the development stage	(389,007)	(4,888,592)	(10,696,729)	(10,696,729)
Total stockholders' equity (deficit)	2,274,492	(563,317)	(1,558,362)	22,377,136
Total liabilities and stockholders' equity (deficit)	\$2,382,600	\$ 9,441,173 =======	\$ 22,864,799	========

See accompanying notes to financial statements.

## STATEMENTS OF OPERATIONS

	PERIOD FROM MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1998		MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1999	MARC	THREE MONTHS ENDED MARCH 31,		MARCH 31, (INCE	
				(UNAUDITED)	 (UNAUDITED)	(UNAUDITED)		
				(UNAUDITED)	(UNAUDITED)	(UNAUDITED)		
Operating expenses: Licensing fees Research and development General and	\$ 100,000 200,000	\$ 2,092,119	\$ 100,000 2,292,119	\$	\$ 1,433,268			
administrative	122,168	2,567,355	2,689,523	118,257	4,619,719	7,309,242		
Total expenses	422,168	4,659,474	5,081,642	118, 257	6,052,987	11, 134, 629		
Operating loss Other income:	(422,168)	(4,659,474)	(5,081,642)	(118, 257)	(6,052,987)	(11, 134, 629)		
Interest income	33,961	160,689	194,650	27,407	245,050	439,700		
Net loss before income taxes	(388,207) 800	(4,498,785) 800	(4,886,992) 1,600	(90,850) 200	(5,807,937) 200	(10,694,929) 1,800		
Net loss Return to series C preferred shareholders for beneficial	(389,007)	(4,499,585)	(4,888,592)	(91,050)	(5,808,137)	(10,696,729)		
conversion feature					(14,231,595)	(14,231,595)		
Loss available to common shareholders	\$ (389,007) ======	\$(4,499,585) =======	\$(4,888,592) =======	\$ (91,050) ======	\$(20,039,732) =======	\$(24,928,324) =======		
Basic and diluted loss per share	\$ (0.06) ======	\$ (0.48) ======		\$ (0.01) ======	\$ (2.10) ======			
Weighted-average shares used in computing basic and diluted loss per share	6,948,637 =======	9,322,441 ======		9,000,000	9,528,957 ======			

See accompanying notes to financial statements.

STATEMENTS OF STOCKHOLDERS' EQUITY (DEFICIT) FOR THE PERIOD MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31, 1998, THE YEAR ENDED DECEMBER 31, 1999, AND THE THREE MONTHS ENDED MARCH 31, 2000

	SERIES A CO	ED STOCK	COMMON STOCK		ADDITIONAL PAID-IN		
	SHARES	PAR VALUE	SHARES	PAR VALUE	CAPITAL	COMPENSATION	RECEIVABLE FOR STOCK
Balance May 4, 1998 (inception)		\$		\$	\$	\$	\$
Common stock issued on June 22,		Ψ		•	Ψ	Ψ	Ψ
1998 at \$.001 per share Series A convertible preferred stock issued between August 14, 1998 and October 28, 1998 at \$1.00 per share (net of issuance costs of			8,500,000	8,500			
\$19,490) Common stock issued on September 23, 1998 at \$.10 per share for	2,659,489	2,660			2,637,339		
notes receivable  Common stock issued on September 23, 1998 at \$.10 per share for			350,000	350	34,650		(35,000)
cash			150,000	150	14,850		
Net loss							
Balance December 31, 1998 Payment on note receivable	2,659,489	2,660	9,000,000	9,000	2,686,839		(35,000) 5,000
Common stock issued between April 1 and May 3, 1999 at \$.10 per share							
for notes receivable  Issuance of common stock pursuant			444,000	444	43,956		(44,400)
to exercise of stock options Issuance of warrants in connection			1,000	1	99		
with lease in August 1999 Deferred compensation with respect to options issuances during					33,810		
1999 Amortization of deferred					6,515,027	(6,515,027)	
compensation  Compensation expense with respect						1,534,847	
to non-employee option grants					88,019		
Net loss							
Balance December 31, 1999 Common stock issued between January 1 and March 31, 2000 at \$0.20 per share for notes receivable	2,659,489	2,660	9,445,000	9,445	9,367,750	(4,980,180)	(74, 400)
(unaudited)  Issuance of common stock pursuant to exercise of stock options			245,000	245	48,755		(49,000)
(unaudited)			28,230	28	3,014		
offering (unaudited) Deferred compensation with respect to option issuances					963,240		
(unaudited)					4,669,000	(4,669,000)	
compensation (unaudited) Charges related to stock purchase						1,200,810	
rights (unaudited) Beneficial conversion feature of					2,646,000		
series C preferred stock (unaudited)					14,231,595		
shareholders for beneficial conversion feature (unaudited)					(14,231,595)		
Net loss (unaudited)							
Balance March 31, 2000							***
(unaudited)	2,659,489 ======	\$2,660 =====	9,718,230 ======	\$9,718 =====	\$17,697,759 =======	\$(8,448,370) ======	\$(123,400) ======

DEFICIT
ACCUMULATED
DURING
DEVELOPMENT
STAGE

STOCKHOLDERS'
EQUITY
(DEFICIT)

Balance -- May 4, 1998
(inception)......\$ -- \$ -Common stock issued on June 22,

1998 at \$.001 per share Series A convertible preferred stock issued between August 14, 1998 and October 28, 1998 at \$1.00 per share		8,500
(net of issuance costs of \$19,490)		2,639,999
notes receivable Common stock issued on September 23, 1998 at \$.10 per share for		
cash Net loss	(389,007)	15,000 (389,007)
Balance December 31, 1998 Payment on note receivable Common stock issued between April 1 and May 3, 1999 at \$.10 per share	(389,007)	
for notes receivable		
Issuance of common stock pursuant to exercise of stock options Issuance of warrants in connection		100
with lease in August 1999 Deferred compensation with respect to options issuances during		33,810
1999 Amortization of deferred		
compensation		1,534,847
to non-employee option grants Net loss	(4,499,585)	88,019 (4,499,585)
Balance December 31, 1999 Common stock issued between January 1 and March 31, 2000 at \$0.20 per share for notes receivable	(4,888,592)	(563, 317)
(unaudited) Issuance of common stock pursuant to exercise of stock options		
(unaudited)		3,042
offering (unaudited)  Deferred compensation with respect to option issuances		963,240
(unaudited) Amortization of deferred		
compensation (unaudited) Charges related to stock purchase		1,200,810
rights (unaudited) Beneficial conversion feature of series C preferred stock		2,646,000
(unaudited)		14,231,595
conversion feature (unaudited) Net loss (unaudited)	(5,808,137)	(14,231,595) (5,808,137)
Balance March 31, 2000 (unaudited)	\$(10,696,729) ========	\$(1,558,362) =======

See accompanying notes to financial statements.

## STATEMENTS OF CASH FLOWS

	(INCEPTION) (INCEPT: THROUGH YEAR ENDED THROUG DECEMBER 31, DECEMBER 31, DECEMBER		MAY 4, 1998 (INCEPTION) THROUGH DECEMBER 31,	THREE END MARCH	MAY 4, 1997 (INCEPTION) THROUGH MARCH 31,	
	1998	1999	1999	1999	2000	2000
				(UNAUD	DITED)	(UNAUDITED)
Cash flows from operating activities:  Net loss	\$ (389,007)	\$(4,499,585)	\$(4,888,592)	\$ (91,050)	\$(5,808,137)	\$(10,696,729)
Depreciation and amortization Amortization of deferred	518	4,244	4,762	549	6,454	11,216
compensation Noncash expense for options and		1,534,847	1,534,847	17,083	1,200,810	2,735,657
warrants issued		121,829	121,829		2,646,000	2,767,829
Interest receivable Prepaid expensesAccounts payable	(3,138) (35,496) 108,108	(12,224) (5,891) 162,479	(15,362) (41,387) 270,587	(171) (27,951) (100,988)	(16,733) (30,263) 187,076	(32,095) (71,650) 457,663
Net cash used in operating activities	(319,015)	(2,694,301)	(3,013,316)	(202,528)	(1,814,793)	(4,828,109)
Cash flows used in investing activities purchase of property and equipment	(10,972)	(38,545)	(49,517)		(83,212)	(132,729)
Cash flows from financing activities: Proceeds from issuance of series B redeemable convertible preferred stock (net of issuance costs of \$296,096) Proceeds from issuance of series C redeemable convertible preferred stock (net of cash issuance costs of		9,733,903	9,733,903			9,733,903
\$25, 255)					15,194,835	15, 194, 835
Deferred financing costsStock subscription received  Proceeds from issuance of series A		5,000	5,000	5,000	(460,179) 	(460,179) 5,000
convertible preferred stock (net of issuance costs of \$19,490) Proceeds from issuance of common stock	2,639,999 23,500	 100	2,639,999 23,600	33,810	3,042	2,639,999 26,642
Net cash provided by financing activities	2,663,499	9,739,003	12,402,502	38,810	14,737,698	27,140,200
Net increase (decrease) in cash and cash equivalents	2,333,512	7,006,157	9,339,669	(163,718)	12,839,693	22,179,362
period		2,333,512		2,333,512	9,339,669	
Cash and cash equivalents at end of period	\$2,333,512 =======	\$ 9,339,669	\$ 9,339,669	\$2,169,794	\$22,179,362 =======	\$ 22,179,362 ========
Supplemental cash flow information: Cash paid for income taxes	\$ ========	\$ 1,600 =======	\$ 1,600 =======	=		=====

See accompanying notes to financial statements.

#### 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.

#### Interim Financial Statements

The financial information as of March 31, 2000 and for the three months ended March 31, 1999 and 2000 and the period from May 4, 1998 (inception) through March 31, 2000 is unaudited. This interim financial information has been prepared on substantially the same basis as the audited financial statements and in the opinion of management, contains all adjustments, consisting only of normal recurring adjustments, necessary for the fair presentation of the financial information set forth therein.

#### 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

#### NOTES TO FINANCIAL STATEMENTS (CONTINUED)

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.

#### 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 and series C redeemable, convertible preferred stock has a carrying amount that approximates fair value as the redemption amount equals the carrying amount (see note 7 regarding series C redeemable convertible preferred stock).

#### 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 fair value of the common stock for financial reporting purposes of stock options granted to employees.

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

#### NOTES TO FINANCIAL STATEMENTS (CONTINUED)

Instruments that Are Issued to Other than Employees for Acquiring, or in Conjunction with Selling, Goods or Services.

The compensation expense related to all grants is amortized over the vesting period of the related stock options in accordance with Financial Accounting Standards Board Interpretation No. 28 (FIN 28), as that methodology most closely approximates the way in which our options are earned by the option holder.

#### 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, 2,809,489 and 9,580,094 shares of common stock as of December 31, 1998 and 1999 and 2,809,489 and 13,206,882 shares of common stock as of March 31, 1999 and 2000, 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 11,108,912 shares of series A convertible preferred stock and B and C redeemable convertible preferred stock outstanding as of March 31, 2000 into shares of common stock, at a conversion rate of 1 common share for each preferred share of series A convertible preferred stock and each share of series B and C redeemable convertible preferred stock, upon the closing of our initial public offering.

#### NOTES TO FINANCIAL STATEMENTS (CONTINUED)

#### (2) PROPERTY AND EQUIPMENT

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

	1998	1999
Machinery and equipmentFixtures	\$ 7,195 3,777	\$14,703 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.

On February 25, 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.

#### 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 into common 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 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.

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.

#### NOTES TO FINANCIAL STATEMENTS (CONTINUED)

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 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 of 5 years. This fair value is being amortized to rent expense over the lease term.

#### NOTES TO FINANCIAL STATEMENTS (CONTINUED)

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.

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 0.10 0.10	1,361,200 (1,000) (65,000)	\$ 0.12 0.10 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.

#### NOTES TO FINANCIAL STATEMENTS (CONTINUED)

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	\$ 4,499,585
Adjusted pro forma net loss	389,007	4,505,402
Net loss per share basic and diluted as reported	0.06	0.48
Adjusted pro forma	0.06	0.48

The per share weighted-average fair value of stock options granted during 1999 was \$4.90 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

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

	OPTIONS OUTSTANDING			OPTIONS EX	ŒRCISABLE
		WEIGHTED- AVERAGE			
		REMAINING	WEIGHTED-	NUMBER	WEIGHTED-
	NUMBER	CONTRACTUAL	AVERAGE	0F	AVERAGE
EXERCISE	0F	LIFE	EXERCISE	VESTED	EXERCISE
PRICES	OPTIONS	(YEARS)	PRICE	OPTIONS	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 \$2,283,565 and \$4,231,462, respectively. No options were granted in 1998.

For employees, deferred compensation represents the difference between the exercise price of the option and the 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.

#### NOTES TO FINANCIAL STATEMENTS (CONTINUED)

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 \$187,621 and \$1,347,226, respectively.

#### (4) INCOME TAXES

Income tax expense 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
	====	====	====

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:

	=======	=========
	\$ 800	\$ 800
State taxes	800	800
Permanent differences	-,	1,146
Current NOLs for which no benefit was realized	,	, ,
		, , ,
Computed "expected" tax expense (benefit)	\$(131.990)	\$(1,529,587)
	1998	1999

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:	<b>4.</b> 44. 075	<b>.</b>
Intangible assetsIssuance of options and warrants	\$ 11,275 	\$ 8,817 634,542
Net operating loss carryforward	141,451	1,323,944
State taxes	272	571
Research and development credit	13,000	120,247
Gross deferred tax assets	165,998	2,088,121
Valuation allowance	(165,998)	(2,088,121)
Net deferred tax assets	\$	\$
	=======	========

#### NOTES TO FINANCIAL STATEMENTS (CONTINUED)

We have recorded a valuation allowance of \$165,998 and \$2,088,121 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 \$165,998 and \$1,922,123, respectively.

As of December 31, 1999, we have operating loss carryforwards (expiring through 2019 for federal purposes and 2006 for state purposes) of approximately \$3,324,000 and \$3,323,000 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 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
	, 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) FIRST QUARTER 2000 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 approximately \$14.2 million, 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.

### NOTES TO FINANCIAL STATEMENTS (CONTINUED)

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. The fair value of these warrants of \$963,240 was estimated using a Black-Scholes model and the following assumptions: estimated volatility of 60%, a risk-free interest rate of 4.59%, no dividend yield, and an expected life equal to the contractual term of 5 years. This fair value was recognized as an increase to additional paid-in capital in the three months ended March 31, 2000.

We determined that our series C preferred stock was issued with a beneficial conversion feature. The beneficial conversion feature has been recognized by allocating a portion of the preferred stock proceeds equal to the intrinsic value of that feature, limited to the net proceeds received (approximately \$14.2 million), to additional paid-in capital. The intrinsic value is calculated at the date of issue as the difference between the conversion price of the preferred stock and the fair value of our common stock, into which the preferred stock is convertible, multiplied by the number of common shares into which the preferred stock is convertible, limited to the net proceeds received. As our series C preferred stock is convertible into common stock at the option of the holder, at the issuance date of the preferred stock the entire \$14.2 million discount resulting from the allocation of proceeds to the beneficial conversion feature has been treated as a dividend and recognized as a return to the preferred stockholders for purposes of computing basic and diluted loss per share in the three months ended March 31, 2000.

#### **Board Resolutions**

In February 2000 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 February 1, 2000, our Board of Directors approved an amendment to our certificate of incorporation increasing the total number of shares authorized to 34,150,000 shares, 22,000,000 of which are common stock and 12,150,000 of which are preferred stock.

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.

#### 2000 Employee Stock Purchase Plan

Our 2000 Employee Stock Purchase Plan was adopted by our board of directors in April 2000 and is subject to shareholder 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) 1,000,000 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, overlapping 24-month offering periods. Each offering period includes four six month 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

### NOTES TO FINANCIAL STATEMENTS (CONTINUED)

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 May 1, 2002.

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 15% 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 six month purchase period is 7,500 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:

"Pain Therapeutics, Inc. is developing a new generation of opioid painkillers. Our strategic goal is to build a specialty pharmaceutical franchise 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 Our new oral morphine painkiller for patients with moderate to severe pain

#### PTT-501

o Our new injectable morphine painkiller for patients with moderate to severe pain

#### PTT-601

o Our new tramadol painkiller for patients with moderate pain

#### PTI-701

o Our new hydrocodone/acetaminophen painkiller for patients with moderate pain

The following words appear at the bottom of the page:

The clinical development process involves several phases of human clinical trials. Phase I trials involve the introduction of the test drug into healthy humans to analyze various effects, including pain relief, safety and dosage tolerance. Phase II and Phase III trials evaluate dosage and assess pain relief in an expanded population at geographically dispersed clinical study sites. Phase III trials must be completed prior to seeking approval of the test drug by the Food and Drug Administration through the submission of a New Drug Application or NDA.

#### 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 1999 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.

Edgar comment

5,000,000 Shares

Common Stock

THOMAS WEISEL PARTNERS LLC

CIBC WORLD MARKETS

TUCKER ANTHONY CLEARY GULL

Neither we nor any of the underwriters have authorized anyone to provide information different from that contained in this prospectus. When you make a decision about whether to invest in our common stock, you should not rely upon any information other than the information in this prospectus. Neither the delivery of this prospectus nor the sale of our common stock means that information contained in this prospectus is correct after the date of this prospectus. This prospectus is not an offer to sell or solicitation of an offer to buy these shares of common stock in any circumstances under which the offer or solicitation is unlawful.

Until , 2000 (25 days after commencement of this offering), all dealers that buy, sell or trade these shares of common stock, whether or not participating in this offering, may be required to deliver a prospectus. This is an addition to the dealers' obligation to deliver a prospectus when acting as underwriters and with respect to their unsold allotments or subscriptions.

#### 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, the NASD filing fee and the Nasdaq National Market listing fee.

SEC registration fee	\$	19,800
NASD filing fee		8,000
Nasdaq National Market listing fee		95,000
Printing and engraving costs		200,000
Legal fees and expenses		425,000
Accounting fees and expenses		300,000
Blue Sky fees and expenses		1,500
Transfer Agent and Registrar fees		10,000
Miscellaneous expenses		40,700
Total	\$1	,100,000
	==	=======

#### 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

#### 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.
- (9) In March 2000, we sold an aggregate of 26,042 shares of common stock at a price of \$0.10 per share for an aggregate purchase price of \$2,604.20.
- (10)In March 2000, we sold an aggregate of 2,188 shares of common stock at a price of \$0.20 per share for an aggregate purchase price of \$437.60.

#### 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 3,041,200 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 1,218,230 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 \$146,541.80.

#### 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	٥f	Underwriting	Agraamant
<b></b>	LOI III	UΙ	Under writiting	Agreement

- 3.1\* Form of Amended and Restated Certificate of Incorporation of the Registrant to be in effect upon closing of this offering
- Form of Bylaws of the Registrant to be in effect upon closing of this offering 3.2\*
- 4.1 Form of stock certificate
- Opinion of Wilson Sonsini Goodrich & Rosati, Professional 5.1 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. Lease Agreement dated August 25, 1998 between the Registrant
- 10.4\* and Britannia Pointe Grand Limited Partnership
- 10.5 1998 Stock Plan, as amended, and form of agreements thereunder between the Registrant and certain securityholders
- 2000 Employee Stock Purchase Plan 10.6

#### **EXHIBIT** NUMBER

- 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
- Employment Agreement dated July 1, 1998 between the 10.8\* Registrant and Mr. Barbier
- 10.9\* Employment Offer Letter dated December 3, 1999 between the
- Registrant and Mr. Jennings Employment Offer Letter dated November 23, 1999 between the 10.10\*
- Registrant and Mr. Johnson
- Employment Offer Letter dated March 29, 1999 between the 10.11\* Registrant and Dr. Sherman
- Consent of KPMG LLP, Independent Certified Public 23.1
- Accountants
- Consent\_of Counsel (see Exhibit 5.1) 23.2
- Power of Attorney (included on p. II-5 of the original 24.1\*
  - filina)
- 27.1 Financial Data Schedule
- 27.2 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.
- \* Previously filed.
- \*\* 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 20th day of June, 2000.

PAIN THERAPEUTICS, INC.

By: /s/ REMI BARBIER

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

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)	June 20,	2000
/s/ DAVID L. JOHNSON* David L. Johnson	Vice President, Finance and Chief Financial Officer (Principal Financial and Accounting Officer)	June 20,	2000
/s/ GERT CASPRITZ, PH.D.*	Director	June 20,	2000
Gert Caspritz, Ph.D.  /s/ NADAV FRIEDMANN, M.D., PH.D.*  Nadav Friedmann, M.D., Ph.D.	Director	June 20,	2000
/s/ WILFRED R. KONNEKER, PH.D.*	Director	June 20,	2000
Wilfred R. Konneker, Ph.D.  /s/ MICHAEL J. O'DONNELL*  Michael J. O'Donnell	Director	June 20,	2000
/s/ SANFORD R. ROBERTSON* Sanford R. Robertson	Director	June 20,	2000
*By: /s/ REMI BARBIER Remi Barbier Attorney-In-Fact	Attorney-In-Fact	June 20,	2000

### EXHIBIT INDEX

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	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 (included on page II-5 of the original
	filing)
27.1	Financial Data Schedule
27.2	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.

27.1 27.2

<sup>\*</sup> Previously filed.

 $<sup>\</sup>ensuremath{^{*\,*}}$  To be filed by amendment.

1

5,000,000 SHARES

PAIN THERAPEUTICS, INC.

COMMON STOCK

UNDERWRITING AGREEMENT

DATED \_\_\_\_\_

#### UNDERWRITING AGREEMENT

[Date]

Thomas Weisel Partners LLC CIBC World Markets Corp. Tucker Anthony Incorporated As Representatives of the several Underwriters c/o Thomas Weisel Partners LLC One Montgomery Street, Suite 3700 San Francisco, California 94104

Ladies and Gentlemen:

INTRODUCTORY. Pain Therapeutics, Inc., a Delaware corporation (the "Company"), proposes to issue and sell to the several underwriters named in Schedule A (the "Underwriters") an aggregate of 5,000,000 shares (the "Firm Shares") of its Common Stock, par value \$0.001 per share (the "Common Shares"). In addition, the Company has granted to the Underwriters an option to purchase up to an additional 750,000 Common Shares (the "Option Shares") as provided in Section 2. The Firm Shares and, if and to the extent such option is exercised, the Option Shares are collectively called the "Shares." Thomas Weisel Partners LLC ("Thomas Weisel Partners"), CIBC World Markets Corp. and Tucker Anthony Incorporated have agreed to act as representatives of the several Underwriters (in such capacity, the "Representatives") in connection with the offering and sale of the Shares. As a part of the offering contemplated by this Agreement, Thomas Weisel Partners has agreed to reserve out of the Shares set forth opposite its name on the Schedule A to this Agreement, up to 250,000 shares, for sale to the Company's employees, officers, and directors and other parties associated with the Company (collectively, "Participants"), as set forth in the Prospectus under the heading "Underwriting" (the "Directed Share Program"). The Shares to be sold by Thomas Weisel Partners pursuant to the Directed Share Program (the "Directed Shares") will be sold by Thomas Weisel Partners pursuant to this Agreement at the public offering price. Any Directed Shares not orally confirmed for purchase by any Participants as of the end of the first business day after the date on which this Agreement is executed will be offered to the public by Thomas Weisel Partners as set forth in the Prospectus.

The Company has prepared and filed with the Securities and Exchange Commission (the "Commission") a registration statement on Form S-1 (File No. 333-32370), which contains a form of prospectus, subject to completion, to be used in connection with the public offering and sale of the Shares. Each such prospectus, subject to completion, used in connection with such public offering is called a "preliminary prospectus." Such registration statement, as amended, including the financial statements, exhibits and schedules thereto, in the form in which it was declared effective by the Commission under the Securities Act of 1933, as amended, and the rules and regulations promulgated thereunder (collectively, the "Securities Act"), including any information deemed to be a part thereof at the time of effectiveness

pursuant to Rule 430A under the Securities Act, is called the "Registration Statement." Any registration statement filed by the Company pursuant to Rule 462(b) under the Securities Act is called the "Rule 462(b) Registration Statement," and from and after the date and time of filing of the Rule 462(b) Registration Statement the term "Registration Statement" shall include the Rule 462(b) Registration Statement. Such prospectus, in the form first used by the Underwriters to confirm sales of the Shares, is called the "Prospectus," which term shall be deemed to include the "electronic Prospectus" provided by the Company for use in connection with the offering of the Shares as contemplated by Section 3(e) of this Agreement. All references in this Agreement to the Registration Statement, the Rule 462(b) Registration Statement, a preliminary prospectus, the Prospectus, or any amendments or supplements to any of the foregoing, shall include any copy thereof filed with the Commission pursuant to its Electronic Data Gathering, Analysis and Retrieval System ("EDGAR").

 $\label{the company hereby confirms its agreements with the Underwriters as follows: \\$ 

#### SECTION 1. REPRESENTATIONS AND WARRANTIES.

 $\label{thm:company} \mbox{ The Company hereby represents, warrants and covenants to each $$\operatorname{Underwriter}$ as follows:$ 

(a) Compliance with Registration Requirements. The Registration Statement and any Rule 462(b) Registration Statement have been declared effective by the Commission under the Securities Act. The Company has complied to the Commission's satisfaction with all requests of the Commission for additional or supplemental information. No stop order suspending the effectiveness of the Registration Statement or any Rule 462(b) Registration Statement is in effect and no proceedings for such purpose have been instituted or are pending or, to the best knowledge of the Company, are contemplated or threatened by the Commission.

Each preliminary prospectus and the Prospectus when filed complied in all material respects with the Securities Act and, if filed by electronic transmission pursuant to EDGAR (except as may be permitted by Regulation S-T under the Securities Act), was identical to the copy thereof delivered to the Underwriters for use in connection with the offer and sale of the Shares. Each of the Registration Statement, any Rule 462(b) Registration Statement and any post-effective amendment thereto, at the time it became effective and at all subsequent times, complied and will comply in all material respects with the Securities Act and did not and will not contain any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading. Each preliminary prospectus, as of its date, and the Prospectus, as amended or supplemented, as of its date and at all subsequent times through the 30th day after the date hereof, did not and will not contain any untrue statement of a material fact or omit to state a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading. The representations and warranties set forth in the two immediately preceding sentences do not apply to statements in or omissions from the Registration Statement, any Rule 462(b) Registration Statement, or any post-effective amendment thereto, or the Prospectus, or any amendments or supplements thereto, made in reliance upon and in conformity with information relating to any Underwriter furnished to the Company in writing by the Representatives expressly for use therein. There are no contracts or other documents required to be described in the Prospectus or to be filed as exhibits to the Registration Statement which have not been described or filed as required.

- (b) Offering Materials Furnished to Underwriters. The Company has delivered to the Representatives one complete conformed copy of the Registration Statement and of each consent and certificate of experts filed as a part thereof, and conformed copies of the Registration Statement (without exhibits) and preliminary prospectuses and the Prospectus, as amended or supplemented, in such quantities and at such places as the Representatives have reasonably requested for each of the Underwriters.
- (c) Distribution of Offering Material By the Company. The Company has not distributed and will not distribute, prior to the later of the Second Closing Date (as defined below) and the completion of the Underwriters' distribution of the Shares, any offering material in connection with the offering and sale of the Shares other than a preliminary prospectus, the Prospectus or the Registration Statement.
- (d) The Underwriting Agreement. This Agreement has been duly authorized, executed and delivered by, and is a valid and binding agreement of, the Company, enforceable in accordance with its terms, except as rights to indemnification hereunder may be limited by applicable law and except as the enforcement hereof may be limited by bankruptcy, insolvency, reorganization, moratorium or other similar laws relating to or affecting the rights and remedies of creditors or by general equitable principles.
- (e) Authorization of the Shares. The Shares to be purchased by the Underwriters from the Company have been duly authorized for issuance and sale pursuant to this Agreement and, when issued and delivered by the Company pursuant to this Agreement, will be validly issued, fully paid and nonassessable.
- (f) No Applicable Registration or Other Similar Rights. There are no persons with registration or other similar rights to have any equity or debt securities registered for sale under the Registration Statement or included in the offering contemplated by this Agreement, except for such rights as have been duly waived.
- (g) No Material Adverse Change. Subsequent to the respective dates as of which information is given in the Prospectus: (i) there has been no material adverse change, or any development that could reasonably be expected to result in a material adverse change, in the condition, financial or otherwise, or in the earnings, business, operations or prospects, whether or not arising from transactions in the ordinary course of business, of the Company (any such change or effect, where the context so requires, is called a "Material Adverse Change" or a "Material Adverse Effect"); (ii) the Company has not incurred any material liability or obligation, indirect, direct or contingent, not in the ordinary course of business nor entered into any material transaction or agreement not in the ordinary course of business; and (iii) there has been no dividend or distribution of any kind declared, paid or made by the Company on any class of capital stock or repurchase or redemption by the Company of any class of capital stock.
- (h) Independent Accountants. KPMG LLP who have expressed their opinion with respect to the financial statements (which term as used in this Agreement includes the related notes thereto) and supporting schedules filed with the Commission as a part of the Registration Statement and included in the Prospectus, are independent public or certified public accountants as required by the Securities Act.
- (i) Preparation of the Financial Statements. The financial statements filed with the Commission as a part of the Registration Statement and included in the Prospectus present fairly the financial position of the Company as of and at the dates indicated and the results of its

operations and cash flows for the periods specified. The supporting schedules included in the Registration Statement present fairly the information required to be stated therein. Such financial statements and supporting schedules have been prepared in conformity with generally accepted accounting principles applied on a consistent basis throughout the periods involved, except as may be expressly stated in the related notes thereto. No other financial statements or supporting schedules are required to be included in the Registration Statement. The financial data set forth in the Prospectus under the captions "Summary--Summary Selected Financial Data," "Selected Financial Data" and "Capitalization" fairly present the information set forth therein on a basis consistent with that of the audited financial statements contained in the Registration Statement. The pro forma financial information included under the caption "Prospectus Summary--Summary Financial Data" and "Capitalization" and elsewhere in the Prospectus and in the Registration Statement present fairly the information contained therein, have been prepared in accordance with the Commission's rules and guidelines with respect to pro forma financial statements and have been properly presented on the bases described therein, and the assumptions used in the preparation thereof are reasonable and the adjustments used therein are appropriate to give effect to the transactions and circumstances referred to therein. No other pro forma financial information is required to be included in the Registration Statement Pursuant to Regulation

- (j) Company's Accounting System. The Company maintains a system of accounting controls sufficient to provide reasonable assurances that (i) transactions are executed in accordance with management's general or specific authorization; (ii) transactions are recorded as necessary to permit preparation of financial statements in conformity with generally accepted accounting principles and to maintain accountability for assets; (iii) access to assets is permitted only in accordance with management's general or specific authorization; and (iv) the recorded accountability for assets is compared with existing assets at reasonable intervals and appropriate action is taken with respect to any differences.
- (k) Subsidiaries of the Company. The Company has no subsidiaries and does not own or control, directly or indirectly, any corporation, association or other entity.
- (1) Incorporation and Good Standing of the Company. The Company has been duly organized and is validly existing as a corporation in good standing under the laws of the State of Delaware with full corporate power and authority to own its properties and conduct its business as described in the prospectus, and is duly qualified to do business as a foreign corporation and is in good standing under the laws of each jurisdiction which requires such qualification.
- (m) Capitalization and Other Capital Stock Matters. The authorized, issued and outstanding capital stock of the Company is as set forth in the Prospectus under the caption "Capitalization" (other than for subsequent issuances, if any, pursuant to employee benefit plans described in the Prospectus or upon exercise of outstanding options or warrants described in the Prospectus). The Common Shares (including the Shares) conform in all material respects to the description thereof contained in the Prospectus. All of the issued and outstanding Common Shares have been duly authorized and validly issued, are fully paid and nonassessable and have been issued in compliance with federal and state securities laws. None of the outstanding Common Shares were issued in violation of any preemptive rights, rights of first refusal or other similar rights to subscribe for or purchase securities of the Company. There are no authorized or outstanding options, warrants, preemptive rights, rights of first refusal or other rights to purchase, or equity or debt securities convertible into or exchangeable or exercisable for, any capital stock of the Company other than those accurately described in the Prospectus. The description of the Company's stock option, stock bonus and other stock plans or arrangements,

and the options or other rights granted thereunder, set forth in the Prospectus accurately and fairly presents the information required to be shown with respect to such plans, arrangements, options and rights.

- (n) Stock Exchange Listing. The Shares have been approved for inclusion on the Nasdaq National Market, subject only to official notice of issuance.
- (o) No Consents, Approvals or Authorizations Required. No consent, approval, authorization, filing with or order of any court or governmental agency or regulatory body is required in connection with the transactions contemplated herein, except such as have been obtained or made under the Securities Act and such as may be required (i) under the blue sky laws of any jurisdiction in connection with the purchase and distribution of the Shares by the Underwriters in the manner contemplated here and in the Prospectus, (ii) by the National Association of Securities Dealers, Inc. (together with its regulatory subsidiary, NASD Regulation, Inc., the "NASD") and (iii) by the federal and provincial laws of Canada.
- (p) Non-Contravention of Existing Instruments Agreements. Neither the issue and sale of the Shares nor the consummation of any other of the transactions herein contemplated nor the fulfillment of the terms hereof will conflict with, result in a breach or violation or imposition of any lien, charge or encumbrance upon any property or assets of the Company pursuant to, (i) the charter or by-laws of the Company, (ii) the terms of any indenture, contract, lease, mortgage, deed of trust, note agreement, loan agreement or other agreement, obligation, condition, covenant or instrument to which the Company is a party or bound or to which its property is subject or (iii) any statute, law, rule, regulation, judgment, order or decree applicable to the Company of any court, regulatory body, administrative agency, governmental body, arbitrator or other authority having jurisdiction over the Company or any of its properties.
- (q) No Defaults or Violations. The Company is not in violation or default of (i) any provision of its charter or by-laws, (ii) the terms of any indenture, contract, lease, mortgage, deed of trust, note agreement, loan agreement or other agreement, obligation, condition, covenant or instrument to which it is a party or bound or to which its property is subject or (iii) any statute, law, rule, regulation, judgment, order or decree of any court, regulatory body, administrative agency, governmental body, arbitrator or other authority having jurisdiction over the Company or any of its properties, except any such violation or default which would not, singly or in the aggregate, result in a Material Adverse Change except as otherwise disclosed in the Prospectus.
- (r) No Actions, Suits or Proceedings. No action, suit or proceeding by or before any court or governmental agency, authority or body or any arbitrator involving the Company or its property is pending or, to the best knowledge of the Company, threatened that (i) could reasonably be expected to have a Material Adverse Effect on the performance of this Agreement or the consummation of any of the transactions contemplated hereby or (ii) could reasonably be expected to result in a Material Adverse Effect.
- (s) All Necessary Permits, Etc. Except as otherwise disclosed in the Prospectus, The Company possesses such valid and current certificates, authorizations or permits issued by the appropriate state, federal or foreign regulatory agencies or bodies necessary to conduct its business, and the Company has not received any notice of proceedings relating to the revocation or modification of, or non-compliance with, any such certificate, authorization or permit which, singly or in the aggregate, if the subject of an unfavorable decision, ruling or finding, could result in a Material Adverse Change.

- (t) License Agreement. The License Agreement, dated May 5, 1998 by and between the Company and Albert Einstein College of Medicine has been duly authorized by all necessary corporate action on the part of the Company and has been duly executed and delivered by the Company and, assuming due authorization, execution and delivery by Albert Einstein College of Medicine, is a valid and binding agreement of Albert Einstein College of Medicine, enforceable in accordance with its terms.
- (u) Title to Properties. The Company has good and marketable title to all the properties and assets reflected as owned in the financial statements referred to in Section 1(i) above (or elsewhere in the Prospectus), in each case free and clear of any security interests, mortgages, liens, encumbrances, equities, claims and other defects, except such as do not materially and adversely affect the value of such property and do not materially interfere with the use made or proposed to be made of such property by the Company. The real property, improvements, equipment and personal property held under lease by the Company are held under valid and enforceable leases, with such exceptions as are not material and do not materially interfere with the use made or proposed to be made of such real property, improvements, equipment or personal property by the Company.
- (v) Tax Law Compliance. The Company has filed all necessary federal, state and foreign income and franchise tax returns and has paid all taxes required to be paid by it and, if due and payable, any related or similar assessment, fine or penalty levied against any it. The Company has made adequate charges, accruals and reserves in the applicable financial statements referred to in Section 1(i) above in respect of all federal, state and foreign income and franchise taxes for all periods as to which the tax liability of the Company has not been finally determined. The Company is not aware of any tax deficiency that has been or might be asserted or threatened against the Company that could result in a Material Adverse Change.
- (w) Intellectual Property Rights. The Company owns or possesses adequate rights to use all patents, patent rights or licenses, inventions, collaborative research agreements, trade secrets, know-how, trademarks, service marks, trade names and copyrights which are necessary to conduct its businesses as described in the Registration Statement and Prospectus. The expiration of any patents, patent rights, trade secrets, trademarks, service marks, trade names or copyrights would not result in a Material Adverse Change that is not otherwise disclosed in the Prospectus. The Company has not received any notice of, and has no knowledge of, any infringement of or conflict with asserted rights of the Company by others with respect to any patent, patent rights, inventions, trade secrets, know-how, trademarks, service marks, trade names or copyrights; and the Company has not received any notice of, and has no knowledge of, any infringement of or conflict with asserted rights of others with respect to any patent, patent rights, inventions, trade secrets, know-how, trademarks, service marks, trade names or copyrights which, singly or in the aggregate, if the subject of an unfavorable decision, ruling or finding, might have a Material Adverse Change. There is no claim being made against the Company regarding patents, patent rights or licenses, inventions, collaborative research, trade secrets, know-how, trademarks, service marks, trade names or copyrights. The Company does not in the conduct of its business as now or proposed to be conducted as described in the Prospectus infringe or conflict with any right or patent of any third party, or any discovery, invention, product or process which is the subject of a patent application filed by any third party, known to the Company, which such infringement or conflict is reasonably likely to result in a Material Adverse Change.
- (x) Year 2000. There are no Year 2000 issues related to the Company that(i) are of a character required to be described or referred to in theRegistration Statement or Prospectus by

the Securities Act which have not been accurately described in the Registration Statement or Prospectus or (ii) might reasonably be expected to result in any Material Adverse Change or that might materially affect their properties, assets or rights.

- (y) No Transfer Taxes or Other Fees. There are no transfer taxes or other similar fees or charges under Federal law or the laws of any state, or any political subdivision thereof, required to be paid in connection with the execution and delivery of this Agreement or the issuance and sale by the Company of the shares.
- (z) Company Not an "Investment Company". The Company has been advised of the rules and requirements under the Investment Company Act of 1940, as amended (the "Investment Company Act"). The Company is not, and after receipt of payment for the Shares will not be, an "investment company" or an entity "controlled" by an "investment company" within the meaning of the Investment Company Act and will conduct its business in a manner so that it will not become subject to the Investment Company Act.
- (aa) Insurance. Except as otherwise disclosed in the Prospectus, the Company is insured by recognized, financially sound and reputable institutions with policies in such amounts and with such deductibles and covering such risks as are generally deemed adequate and customary for its business including, but not limited to, policies covering real and personal property owned or leased by the Company against theft, damage, destruction, acts of vandalism and earthquakes, general liability and Directors and Officers liability. The Company has no reason to believe that it will not be able (i) to renew its existing insurance coverage as and when such policies expire or (ii) to obtain comparable coverage from similar institutions as may be necessary or appropriate to conduct its business as now conducted and at a cost that would not result in a Material Adverse Change. The Company has not been denied any insurance coverage which it has sought or for which it has applied.
- (bb) Labor Matters. To the best of Company's knowledge, no labor disturbance by the employees of the Company exists or is imminent; and the Company is not aware of any existing or imminent labor disturbance by the employees of any of its principal suppliers or clinical investigators that might be expected to result in a Material Adverse Change.
- (cc) No Price Stabilization or Manipulation. The Company has not taken and will not take, directly or indirectly, any action designed to or that might be reasonably expected to cause or result in stabilization or manipulation of the price of the Common Stock to facilitate the sale or resale of the Shares.
- (dd) Lock-Up Agreements. Each officer and director of the company and each beneficial owner of one or more percent of the outstanding issued share capital of the Company has agreed to sign an agreement substantially in the form attached hereto as Exhibit A (the "Lock-up Agreements"). The Company has provided to counsel for the Underwriters a complete and accurate list of all securityholders of the Company and the number and type of securities held by each securityholder. The Company has provided to counsel for the Underwriters true, accurate and complete copies of all of the Lock-up Agreements presently in effect or effected hereby. The Company hereby represents and warrants and agrees that during the 180 days following the date of the Prospectus (the "Lock-Up Period"), the Company will not (i) release any of its officers, directors or other securityholders from any lock-up agreements currently existing or hereafter effected or (ii) consent to the removal of any transfer-restrictive legends from any certificate representing any Common Shares, in each case without the prior written consent of Thomas Weisel Partners.

- (ee) Related Party Transactions. There are no business relationships or related-party transactions involving the Company or any other person required to be described in the Prospectus which have not been described as required.
- (ff) No Unlawful Contributions or Other Payments. Neither the Company nor, to the best of the Company's knowledge, any employee or agent of the Company, has made any contribution or other payment to (i) any official of, or candidate for, any federal, state or foreign office in violation of any law or of the character required to be disclosed in the Prospectus or (ii) any clinical researcher in violation of any federal, state or foreign law or any rule or policy of the Food and Drug Administration.
- (gg) Environmental Laws. (i) the Company is in compliance with all rules, laws and regulations relating to the use, treatment, storage and disposal of toxic substances and protection of health or the environment ("Environmental Laws") which are applicable to its business, except where the failure to comply would not result in a Material Adverse Change, (ii) the Company has received no notice from any governmental authority or third party of an asserted claim under Environmental Laws, which claim is required to be disclosed in the Registration Statement and the Prospectus, (iii) the Company is not currently aware that it will be required to make future material capital expenditures to comply with Environmental Laws and (iv) no property which is owned, leased or occupied by the Company has been designated as a Superfund site pursuant to the Comprehensive Response, Compensation, and Liability Act of 1980, as amended (42 U.S.C. Section 9601, et seq.), or otherwise designated as a contaminated site under applicable state or local law.
- (hh) Periodic Review of Costs of Environmental Compliance. In the ordinary course of its business, the Company conducts a periodic review of the effect of Environmental Laws on the business, operations and properties of the Company, in the course of which it identifies and evaluates associated costs and liabilities (including, without limitation, any capital or operating expenditures required for clean-up, closure of properties or compliance with Environmental Laws or any permit, license or approval, any related constraints on operating activities and any potential liabilities to third parties). On the basis of such review and the amount of its established reserves, the Company has reasonably concluded that such associated costs and liabilities would not, individually or in the aggregate, result in a Material Adverse Change.
- (ii) ERISA Compliance. The Company and any "employee benefit plan" (as defined under the Employee Retirement Income Security Act of 1974, as amended, and the regulations and published interpretations thereunder (collectively, "ERISA")) established or maintained by the Company or its "ERISA Affiliates" (as defined below) are in compliance in all material respects with ERISA. "ERISA Affiliate" means, with respect to the Company, any member of any group of organizations described in Sections 414(b),(c),(m) or (o) of the Internal Revenue Code of 1986, as amended, and the regulations and published interpretations thereunder (the "Code") of which the Company is a member. No "reportable event" (as defined under ERISA) has occurred or is reasonably expected to occur with respect to any "employee benefit plan" established or maintained by the Company or any of its ERISA Affiliates. No "employee benefit plan" established or maintained by the Company or any of its ERISA Affiliates, if such "employee benefit plan" were terminated, would have any "amount of unfunded benefit liabilities" (as defined under ERISA). Neither the Company nor any of its ERISA Affiliates has incurred or reasonably expects to incur any liability under (i) Title IV of ERISA with respect to termination of, or withdrawal from, any "employee benefit plan" or (ii) Sections 412, 4971, 4975 or 4980B of the Code. Each "employee benefit plan" or (ii) Sections 412, 4971, 4975 or 4980B of the Code. Each "employee benefit plan" established or maintained by the Company or any of its ERISA Affiliates that is intended to be qualified under Section 401(a) of the Code is

so qualified and nothing has occurred, whether by action or failure to act, which would cause the loss of such qualification.

- (jj) Consents Required in Connection with the Directed Share Program. No consent, approval, authorization or order of, or qualification with, any governmental body or agency, other than those obtained, is required in connection with the offering of the Directed Shares in any jurisdiction where the Directed Shares are being offered.
- (kk) No Improper Influence in Connection with the Directed Share Program. The Company has not offered, or caused Thomas Weisel Partners to offer, Shares to any person pursuant to the Directed Share Program with the specific intent to unlawfully influence (i) a customer or supplier of the Company to alter the customer's or supplier's level or type of business with the Company or (ii) a trade journalist or publication to write or publish favorable information about the Company or its products.

Any certificate signed by an officer of the Company and delivered to the Representatives or to counsel for the Underwriters shall be deemed to be a representation and warranty by the Company to each Underwriter as to the matters set forth therein.

#### SECTION 2. PURCHASE, SALE AND DELIVERY OF THE SHARES.

- (a) The Firm Shares. The Company agrees to issue and sell to the several Underwriters the Firm Shares upon the terms herein set forth. On the basis of the representations, warranties and agreements herein contained, and upon the terms but subject to the conditions herein set forth, the Underwriters agree, severally and not jointly, to purchase from the Company the respective number of Firm Shares set forth opposite their names on Schedule A. The purchase price per Firm Share to be paid by the several Underwriters to the Company shall be \$[\_\_\_] per share.
- (b) The First Closing Date. Delivery of the Firm Shares to be purchased by the Underwriters and payment therefor shall be made by the Company and the Representatives at 6:00 a.m. San Francisco time, at the offices of Wilson Sonsini Goodrich & Rosati, Professional Corporation, 650 Page Mill Road, Palo Alto, California (or at such other place and time as may be agreed upon among the Representatives and the Company), (i) on the third (3rd) full business day following the first day that Shares are traded, or (ii) if this Agreement is executed and delivered after 1:30 P.M., San Francisco time, the fourth (4th) full business day following the day that this Agreement is executed and delivered or (iii) at such other time and date not later that seven (7) full business days following the first day that Shares are traded as the Representatives and the Company may determine (or at such time and date to which payment and delivery shall have been postponed pursuant to Section 8 hereof), such time and date of payment and delivery being herein called the "Closing Date"; provided, however, that if the Company has not made available to the Representatives copies of the Prospectus within the time provided in Section 2(g) and 3(e) hereof, the Representatives may, in their sole discretion, postpone the Closing Date until no later that two (2) full business days following delivery of copies of the Prospectus to the Representatives.
- (c) The Option Shares; the Second Closing Date. In addition, on the basis of the representations, warranties and agreements herein contained, and upon the terms but subject to the conditions herein set forth, the Company hereby grants an option to the several Underwriters to purchase, severally and not jointly, up to an aggregate of 750,000 Option Shares from the Company at the purchase price per share to be paid by the Underwriters for the Firm Shares.

The option granted hereunder is for use by the Underwriters solely in covering any over-allotments in connection with the sale and distribution of the Firm Shares. The option granted hereunder may be exercised at any time upon notice by the Representatives to the Company, which notice may be given at any time within 30 days from the date of this Agreement. The time and date of delivery of the Option Shares, if subsequent to the First Closing Date, is called the "Second Closing Date" and shall be determined by the Representatives and shall not be earlier than three nor later than five full business days after delivery of such notice of exercise. If any Option Shares are to be purchased, each Underwriter agrees, severally and not jointly, to purchase the number of Option Shares (subject to such adjustments to eliminate fractional shares as the Representatives may determine) that bears the same proportion to the total number of Option Shares to be purchased as the number of Firm Shares set forth on Schedule A opposite the name of such Underwriter bears to the total number of Firm Shares. The Representatives may cancel the option at any time prior to its expiration by giving written notice of such cancellation to the Company.

- (d) Public Offering of the Shares. The Representatives hereby advise the Company that the Underwriters intend to offer for sale to the public, as described in the Prospectus, their respective portions of the Shares as soon after this Agreement has been executed and the Registration Statement has been declared effective as the Representatives, in their sole judgment, have determined is advisable and practicable.
- (e) Payment for the Shares. Payment for the Shares shall be made at the First Closing Date (and, if applicable, at the Second Closing Date) by wire transfer in immediately available-funds to the order of the Company.

It is understood that the Representatives have been authorized, for their own accounts and the accounts of the several Underwriters, to accept delivery of and receipt for, and make payment of the purchase price for, the Firm Shares and any Option Shares the Underwriters have agreed to purchase. Thomas Weisel Partners, individually and not as a Representative of the Underwriters, may (but shall not be obligated to) make payment for any Shares to be purchased by any Underwriter whose funds shall not have been received by the Representatives by the First Closing Date or the Second Closing Date, as the case may be, for the account of such Underwriter, but any such payment shall not relieve such Underwriter from any of its obligations under this Agreement.

- (f) Delivery of the Shares. The Company shall deliver, or cause to be delivered, a credit representing the Firm Shares to an account or accounts at The Depository Trust Company, as designated by the Representatives for the accounts of the Representatives and the several Underwriters at the First Closing Date, against the irrevocable release of a wire transfer of immediately available funds for the amount of the purchase price therefor. The Company shall also deliver, or cause to be delivered a credit representing the Option Shares the Underwriters have agreed to purchase at the First Closing Date (or the Second Closing Date, as the case may be), to an account or accounts at The Depository Trust Company as designated by the Representatives for the accounts of the Representatives and the several Underwriters, against the irrevocable release of a wire transfer of immediately available funds for the amount of the purchase price therefor. Time shall be of the essence, and delivery at the time and place specified in this Agreement is a further condition to the obligations of the Underwriters.
- (g) Delivery of Prospectus to the Underwriters. Not later than 12:00 noon on the second business day following the date the Shares are released by the Underwriters for sale to the

public, the Company shall deliver or cause to be delivered copies of the Prospectus in such quantities and at such places as the Representatives shall request.

# SECTION 3. COVENANTS OF THE COMPANY.

The Company further covenants and agrees with each Underwriter as  $\ensuremath{\mathsf{follows}}\xspace$  :

- (a) Registration Statement Matters. The Company will (i) use its best efforts to cause a registration statement on Form 8-A (the "Form 8-A Registration Statement") as required by the Securities Exchange Act of 1934, as amended (the "Exchange Act"), to become effective simultaneously with the Registration Statement, (ii) use its best efforts to cause the Registration Statement to become effective or, if the procedure in Rule 430A of the Securities Act is followed, to prepare and timely file with the Commission under Rule 424(b) under the Securities Act a Prospectus in a form approved by the Representatives containing information previously omitted at the time of effectiveness of the Registration Statement in reliance on Rule 430A of the Securities Act and (iii) not file any amendment to the Registration Statement or supplement to the Prospectus of which the Representatives shall not previously have been advised and furnished with a copy or to which the Representatives shall have reasonably objected in writing or which is not in compliance with the Securities Act. If the Company elects to rely on Rule 462(b) under the Securities Act, the Company shall file a Rule 462(b) Registration Statement with the Commission in compliance with Rule 462(b) under the Securities Act prior to the time confirmations are sent or given, as specified by Rule 462(b)(2) under the Securities Act, and shall pay the applicable fees in accordance with Rule 111 under the Securities Act.
- (b) Securities Act Compliance. The Company will advise the Representatives promptly (i) when the Registration Statement or any post-effective amendment thereto shall have become effective, (ii) of receipt of any comments from the Commission, (iii) of any request of the Commission for amendment of the Registration Statement or for supplement to the Prospectus or for any additional information and (iv) of the issuance by the Commission of any stop order suspending the effectiveness of the Registration Statement or the use of the Prospectus or of the institution of any proceedings for that purpose. The Company will use its best efforts to prevent the issuance of any such stop order preventing or suspending the use of the Prospectus and to obtain as soon as possible the lifting thereof, if issued.
- (c) Blue Sky Compliance. The Company will cooperate with the Representatives and counsel for the Underwriters in endeavoring to qualify the Shares for sale under the securities laws of such jurisdictions (both national and foreign) as the Representatives may reasonably have designated in writing and will make such applications, file such documents, and furnish such information as may be reasonably required for that purpose, provided the Company shall not be required to qualify as a foreign corporation or to file a general consent to service of process in any jurisdiction where it is not now so qualified or required to file such a consent. The Company will, from time to time, prepare and file such statements, reports and other documents, as are or may be required to continue such qualifications in effect for so long a period as the Representatives may reasonably request for distribution of the Shares.
- (d) Amendments and Supplements to the Prospectus and Other Securities Act Matters. The Company will comply with the Securities Act and the Exchange Act, and the rules and regulations of the Commission thereunder, so as to permit the completion of the distribution of the Shares as contemplated in this Agreement and the Prospectus. If during the period in which a prospectus is required by law to be delivered by an Underwriter or dealer, any event shall occur as a result of which, in the judgment of the Company or in the reasonable opinion of

the Representatives or counsel for the Underwriters, it becomes necessary to amend or supplement the Prospectus in order to make the statements therein, in the light of the circumstances existing at the time the Prospectus is delivered to a purchaser, not misleading, or, if it is necessary at any time to amend or supplement the Prospectus to comply with any law, the Company promptly will prepare and file with the Commission, and furnish at its own expense to the Underwriters and to dealers, an appropriate amendment to the Registration Statement or supplement to the Prospectus so that the Prospectus as so amended or supplemented will not, in the light of the circumstances when it is so delivered, be misleading, or so that the Prospectus will comply with the law.

- (e) Copies of the Prospectus and any Amendments and Supplements Thereto; Electronic Prospectus. The Company agrees to furnish the Representatives, without charge, during the period beginning on the date hereof and ending on the later of the First Closing Date or such date, as in the opinion of counsel for the Underwriters, the Prospectus is no longer required by law to be delivered in connection with sales by an Underwriter or dealer (the "Prospectus Delivery Period"), as many copies of the Prospectus and any amendments and supplements thereto as the Representatives may request. The Company shall also cause to be prepared and delivered to any Underwriter upon request, at the Company's expense, within one business day from the filing of the Prospectus with the Commission (and again within one business day after the filing of any amendment or supplement thereto with the Commission), an "electronic Prospectus" to be used in connection with the offering and sale of the Common Shares. As used herein, the term "electronic Prospectus" means a form of Prospectus, and any amendment or supplement thereto, that meets each of the following conditions: (i) it shall be encoded in a format, satisfactory to the Representatives, that may be transmitted electronically over the internet or via other online distribution to offerees and purchasers of the Common Shares; and (ii) it shall disclose the same information as the paper Prospectus (or any amendment or supplement thereto), except to the extent that graphic and image material contained in the paper Prospectus (or such amendment or supplement) cannot be presented in such electronic format, in which case such graphic and image material shall be replaced in the electronic Prospectus with a fair and accurate narrative description or tabular representation of such material, as appropriate. The Company hereby consents to distribution of the electronic Prospectus (including posting of the electronic Prospectus on the internet) by any of the Underwriters or their affiliates.
- (f) Insurance. The Company shall (i) obtain Directors and Officers liability insurance in the minimum amount of \$10 million which shall apply to the offering contemplated hereby and (ii) cause Thomas Weisel Partners LLC to be added to such policy such that up to \$500,000 of its expenses pursuant to Section 7(a) shall be paid directly by such insurer and (iii) shall cause Thomas Weisel Partners LLC to be added as an additional insured to such policy in respect of the offering contemplated hereby.
- (g) Notice of Subsequent Events. If at any time during the ninety (90) day period after the Registration Statement becomes effective, any rumor, publication or event relating to or affecting the Company shall occur as a result of which in your opinion the market price of the Company Shares has been or is likely to be materially affected (regardless of whether such rumor, publication or event necessitates a supplement to or amendment of the Prospectus), the Company will, after written notice from you advising the Company to the effect set forth above, forthwith prepare, consult with you concerning the substance of and disseminate a press release or other public statement, reasonably satisfactory to you, responding to or commenting on such rumor, publication or event.

- (h) Use of Proceeds. The Company shall apply the net proceeds from the sale of the Shares sold by it in the manner described under the caption "Use of Proceeds" in the Prospectus.
- (i) Transfer Agent. The Company shall engage and maintain, at its expense, a registrar and transfer agent for the Company Shares.
- (j) Earnings Statement. As soon as practicable, the Company will make generally available to its security holders and to the Representatives an earnings statement (which need not be audited) covering a period of at least twelve months beginning after the effective date of the Registration Statement that satisfies the provisions of Section 11(a) of the Securities Act.
- (k) Periodic Reporting Obligations. During the Prospectus Delivery Period the Company shall file, on a timely basis, with the Commission and the Nasdaq National Market all reports and documents required to be filed under the Exchange Act in the manner and within the time periods required by the Exchange Act and the Nasdaq National Market.
- (1) Agreement Not to Offer or Sell Additional Securities. The Company will not offer, sell or contract to sell, or otherwise dispose of or enter into any transaction which is designed to, or could be expected to, result in the disposition (whether by actual disposition or effective economic disposition due to cash settlement or otherwise by the Company or any affiliate of the Company or any person in privity with the Company or any affiliate of the Company directly or indirectly, or announce the offering of, any other Common Shares or any securities convertible into, or exchangeable for, Common Shares; provided, however, that the Company may (i) issue and sell Common Shares pursuant to any director or employee stock option plan, stock ownership plan or dividend reinvestment plan of the Company in effect at the date of the Prospectus and described in the Prospectus so long as none of those shares may be transferred and the Company shall enter stop transfer instructions with its transfer agent and registrar against the transfer of any such Common Shares and (ii) the Company may issue Common Shares issuable upon the conversion of securities or the exercise of warrants outstanding at the date of the Prospectus and described in the Prospectus. These restrictions terminate after the close of trading of the Shares on the final day of the Lock-Up Period.
- (m) Future Reports to the Representatives. During the period of five years hereafter the Company will furnish to the Representatives (i) as soon as practicable after the end of each fiscal year, copies of the Annual Report of the Company containing the balance sheet of the Company as of the close of such fiscal year and statements of income, stockholders' equity and cash flows for the year then ended and the opinion thereon of the Company's independent public or certified public accountants; (ii) as soon as practicable after the filing thereof, copies of each proxy statement, Annual Report on Form 10-K, Quarterly Report on Form 10-Q, Current Report on Form 8-K or other report filed by the Company with the Commission, the NASD or any securities exchange; and (iii) as soon as available, copies of any report or communication of the Company mailed generally to holders of its capital stock.
- (n) Directed Share Program. The Company (i) will indemnify Thomas Weisel Partners for any losses incurred in connection with the Directed Share Program, (ii) will comply with all applicable securities and other applicable laws, rules and regulations in each jurisdiction in which the Directed Shares are offered in connection with the Directed Share Program, and (iii) will pay all reasonable fees and disbursements of counsel incurred by the Underwriters in connection with the Directed Share Program and any stamp duties, similar taxes or duties or other taxes, if any, incurred by the underwriters in connection with the Directed Share Program.

### SECTION 4. CONDITIONS OF THE OBLIGATIONS OF THE UNDERWRITERS.

The obligations of the several Underwriters to purchase and pay for the Shares as provided herein on the First Closing Date and, with respect to the Option Shares, the Second Closing Date, shall be subject to the accuracy of the representations and warranties on the part of the Company set forth in Section 1 hereof as of the date hereof and as of the First Closing Date as though then made and, with respect to the Option Shares, as of the Second Closing Date as though then made, to the timely performance by the Company of its covenants and other obligations hereunder, and to each of the following additional conditions:

- (a) Compliance with Registration Requirements; No Stop Order; No Objection from the NASD. The Registration Statement shall have become effective prior to the execution of this Agreement, or at such later date as shall be consented to in writing by you; and no stop order suspending the effectiveness thereof shall have been issued and no proceedings for that purpose shall have been initiated or, to the knowledge of the Company or any Underwriter, threatened by the Commission, and any request of the Commission for additional information (to be included in the Registration Statement or the Prospectus or otherwise) shall have been complied with to the satisfaction of Underwriters' Counsel; and the NASD shall have raised no objection to the fairness and reasonableness of the underwriting terms and arrangements.
- (b) Corporate Proceedings. All corporate proceedings and other legal matters in connection with this Agreement, the form of Registration Statement and the Prospectus, and the registration, authorization, issue, sale and delivery of the Shares, shall have been reasonably satisfactory to Underwriters' Counsel, and such counsel shall have been furnished with such papers and information as they may reasonably have requested to enable them to pass upon the matters referred to in this Section.
- (c) No Material Adverse Change. Subsequent to the execution and delivery of this Agreement and prior to the First Closing Date, or the Second Closing Date, as the case may be, there shall not have been any Material Adverse Change in the condition (financial or otherwise), earnings, operations, business or business prospects of the Company from that set forth in the Registration Statement or Prospectus, which, in your sole judgment, is material and adverse and that makes it, in your sole judgment, impracticable or inadvisable to proceed with the public offering of the Shares as contemplated by the Prospectus.
- (d) Opinion of Counsel for the Company. You shall have received on the First Closing Date, or the Second Closing Date, as the case may be, an opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation counsel for the Company substantially in the form of Exhibit B attached hereto, dated the First Closing Date, or the Second Closing Date, addressed to the Underwriters and with reproduced copies or signed counterparts thereof for each of the Underwriters.

Counsel rendering the opinion contained in Exhibit B may rely as to questions of law not involving the laws of the United States or the States of California or Delaware upon opinions of local counsel, and as to questions of fact upon representations or certificates of officers of the Company and of government officials, in which case their opinion is to state that they are so relying and that they have no knowledge of any material misstatement or inaccuracy in any such opinion, representation or certificate. Copies of any opinion, representation or certificate so relied upon shall be delivered to you, as Representatives of the Underwriters, and to Underwriters' Counsel.

- (e) Opinion of Intellectual Property Counsel . You shall have received on the First Closing Date, or the Second Closing Date, as the case may be, an opinion of Amster, Rothstein & Ebenstein, intellectual property counsel for Albert Einstein College of Medicine, substantially in the form of Exhibit C attached hereto.
- (f) Opinion of FDA Regulatory Counsel for the Company. You shall have received on the First Closing Date, or the Second Closing Date, as the case may be, an opinion of Wilson Sonsini Goodrich & Rosati, Professional Corporation, FDA regulatory counsel for the Company substantially in the form of Exhibit D attached hereto.
- (g) Opinion of Counsel for the Underwriters. You shall have received on the First Closing Date or the Second Closing Date, as the case may be, an opinion of O'Melveny & Myers LLP, counsel for the Underwriters, in form and substance reasonably satisfactory to the Representatives, with respect to the sufficiency of all corporate proceedings and other legal matters relating to this Agreement and the transactions contemplated hereby as the Representatives may reasonably require. The Company shall have furnished to such counsel such documents as they may have requested for the purpose of enabling them to pass upon such matters.
- (h) Accountants' Comfort Letter. You shall have received on the First Closing Date and on the Second Closing Date, as the case may be, a letter from KPMG LLP addressed to the Underwriters, dated the First Closing Date or the Second Closing Date, as the case may be, confirming that they are independent certified public accountants with respect to the Company within the meaning of the Act and the applicable published Rules and Regulations and based upon the procedures described in such letter delivered to you concurrently with the execution of this Agreement (herein called the "Original Letter"), but carried out to a date not more than four (4) business days prior to the First Closing Date or the Second Closing Date, as the case may be, (i) confirming, to the extent true, that the statements and conclusions set forth in the Original Letter are accurate as of the First Closing Date or the Second Closing Date, as the case may be, and (ii) setting forth any revisions and additions to the statements and conclusions set forth in the Original Letter which are necessary to reflect any changes in the facts described in the Original Letter since the date of such letter, or to reflect the availability of more recent financial statements, data or information. The letter shall not disclose any change in the condition (financial or otherwise), earnings, operations, business or business prospects of the Company from that set forth in the Registration Statement or Prospectus, which, in your sole judgment, is material and adverse and that makes it, in your sole judgment, impracticable or inadvisable to proceed with the public offering of the Shares as contemplated by the Prospectus. The Original Letter from KPMG LLP shall be addressed to or for the use of the Underwriters in form and substance satisfactory to the Underwriters and shall (i) represent, to the extent true, that they are independent certified public accountants with respect to the Company within the meaning of the Act and the applicable published Rules and Regulations, (ii) refer to their opinion with respect to their examination of the balance sheet of the Company as of December 31, 1999 and related statements of operations, shareholders' equity, and cash flows for the twelve (12) months ended December 31, 1999, (iii) state that KPMG LLP has performed the procedures set out in Statement on Auditing Standards ("SAS") No. 71 for a review of interim financial information and providing the report of KPMG LLP as described in SAS No. 71 on the financial statements for the one-quarter period ended March 31, 2000 (the "Quarterly Financial Statements"), (iv) state that in the course of such review, nothing came to their attention that leads them to believe that any material modifications need to be made to any of the Quarterly Financial Statements in order for them to be in compliance with generally accepted accounting principles consistently applied across the periods presented, (v) state that KPMG LLP has performed the

procedures set forth in Statement on Standards for Attestation Engagements No. 8 on the information included in the Prospectus under the caption "Management's Discussion and Analysis of Financial Conditions and Results of Operations" and describe or attach their report thereon (as described by SAS No. 86) and (vi) address any other matters agreed upon by KPMG LLP and you.

- (i) Officers' Certificate. You shall have received on the First Closing Date and the Second Closing Date, as the case may be, a certificate of the Company, dated the First Closing Date or the Second Closing Date, as the case may be, signed by the Chief Executive Officer and Chief Financial Officer of the Company, to the effect that, and you shall be satisfied that:
  - (i) The representations and warranties of the Company in this Agreement are true and correct, as if made on and as of the First Closing Date or the Second Closing Date, as the case may be, and the Company has complied with all the agreements and satisfied all the conditions on its part to be performed or satisfied at or prior to the First Closing Date or the Second Closing Date, as the case may be;
  - (ii) No stop order suspending the effectiveness of the Registration Statement has been issued and no proceedings for that purpose have been instituted or are pending or threatened under the Act;
  - (iii) When the Registration Statement became effective and at all times subsequent thereto up to the delivery of such certificate, (a) the Registration Statement and the Prospectus, and any amendments or supplements thereto, contained all material information required to be included therein by the Securities Act and in all material respects conformed to the requirements of the Securities Act, (b) the Registration Statement and the Prospectus, and any amendments or supplements thereto, did not and does not include any untrue statement of a material fact or omit to state a material fact required to be stated therein or necessary to make the statements therein not misleading; and (c) since the effective date of the Registration Statement, there has occurred no event required to be set forth in an amended or supplemented Prospectus which has not been so set forth; and
  - (iv) Subsequent to the respective dates as of which information is given in the Registration Statement and Prospectus, there has not been (a) any material adverse change in the condition (financial or otherwise), earnings, operations, business or business prospects of the Company, (b) any transaction that is material to the Company, except transactions entered into in the ordinary course of business, (c) any obligation, direct or contingent, that is material to the Company, incurred by the Company, except obligations incurred in the ordinary course of business, (d) any change in the capital stock or outstanding indebtedness of the Company that is material to the Company, (e) any dividend or distribution of any kind declared, paid or made on the capital stock of the Company, or (f) any loss or damage (whether or not insured) to the property of the Company which has been sustained or will have been sustained which has a material adverse effect on the condition (financial or otherwise), earnings, operations, business or business prospects of the Company.
- (j) Lock-up Agreement from Certain Stockholders of the Company. The Company shall have obtained and delivered to you an agreement substantially in the form of Exhibit A attached hereto from each officer and director of the Company and each beneficial owner of one or more percent of the outstanding issued share capital of the Company.

- (k) Stock Exchange Listing. The Shares shall have been approved for inclusion on the Nasdaq National Market, subject only to official notice of issuance.
- (1) Compliance with Prospectus Delivery Requirements. The Company shall have complied with the provisions of Sections 2(g) and 3(e) hereof with respect to the furnishing of Prospectuses.
- (m) Additional Documents. On or before each of the First Closing Date and the Second Closing Date, as the case may be, the Representatives and counsel for the Underwriters shall have received such information, documents and opinions as they may reasonably require for the purposes of enabling them to pass upon the issuance and sale of the Shares as contemplated herein, or in order to evidence the accuracy of any of the representations and warranties, or the satisfaction of any of the conditions or agreements, herein contained.

If any condition specified in this Section 4 is not satisfied when and as required to be satisfied, this Agreement may be terminated by the Representatives by notice to the Company at any time on or prior to the First Closing Date and, with respect to the Option Shares, at any time prior to the Second Closing Date, which termination shall be without liability on the part of any party to any other party, except that Section 5 (Payment of Expenses), Section 6 (Reimbursement of Underwriters' Expenses), Section 7 (Indemnification and Contribution) and Section 10 (Representations and Indemnities to Survive Delivery) shall at all times be effective and shall survive such termination.

# SECTION 5. PAYMENT OF EXPENSES.

The Company agrees to pay all costs, fees and expenses incurred in connection with the performance of its obligations hereunder and in connection with the transactions contemplated hereby, including without limitation (i) all expenses incident to the issuance and delivery of the Shares (including all printing and engraving costs), (ii) all fees and expenses of the registrar and transfer agent of the Common Shares, (iii) all necessary issue, transfer and other stamp taxes in connection with the issuance and sale of the Shares to the Underwriters, (iv) all fees and expenses of the Company's counsel and independent public or certified public accountants, (v) all costs and expenses incurred in connection with the preparation, printing, filing, shipping and distribution of the Registration Statement (including financial statements, exhibits, schedules, consents and certificates of experts), each preliminary prospectus and the Prospectus, and all amendments and supplements thereto, and this Agreement, (vi) all costs and expenses incurred by Underwriters counsel in connection with the Directed Share Program, (vii) all filing fees, attorneys' fees and expenses incurred by the Company or the Underwriters in connection with qualifying or registering (or obtaining exemptions from the qualification or registration of) all or any part of the Shares for offer and sale under the state securities or blue sky laws or the provincial securities laws of Canada or any other country, and, if requested by the Representatives, preparing and printing a "Blue Sky Survey," an "International Blue Sky Survey" or other memorandum, and any supplements thereto, advising the Underwriters of such qualifications, registrations and exemptions, (viii) the filing fees incident to, and the reasonable fees and expenses of counsel for the Underwriters in connection with, the NASD review and approval of the Underwriters' participation in the offering and distribution of the Common Shares, (ix) the fees and expenses associated with including the Shares on the Nasdaq National Market, (x) all costs and expenses incident to the travel and accommodation of the Company's employees on the "roadshow," and (xi) all other fees, costs and expenses referred to in Item 13 of Part II of the Registration Statement. Except as provided in this Section 5, Section 6, and

Section 7 hereof, the Underwriters shall pay their own expenses, including the fees and disbursements of their counsel.

### SECTION 6. REIMBURSEMENT OF UNDERWRITERS' EXPENSES.

If this Agreement is terminated by the Representatives pursuant to Section 4, Section 8 or Section 9, or if the sale to the Underwriters of the Shares on the First Closing Date is not consummated because of any refusal, inability or failure on the part of the Company to perform any agreement herein or to comply with any provision hereof, the Company agrees to reimburse the Representatives and the other Underwriters (or such Underwriters as have terminated this Agreement with respect to themselves), severally, upon demand for all out-of-pocket expenses that shall have been reasonably incurred by the Representatives and the Underwriters in connection with the proposed purchase and the offering and sale of the Shares, including but not limited to fees and disbursements of counsel, printing expenses, travel and accommodation expenses, postage, facsimile and telephone charges.

# SECTION 7. INDEMNIFICATION AND CONTRIBUTION.

(a) Indemnification of the Underwriters. The Company agrees to indemnify and hold harmless each Underwriter, its officers and employees, and each person, if any, who controls any Underwriter within the meaning of the Securities Act and the Exchange Act against any loss, claim, damage, liability or expense, as incurred, to which such Underwriter or such controlling person may become subject, under the Securities Act, the Exchange Act or other federal or state statutory law or regulation, or at common law or otherwise (including in settlement of any litigation, if such settlement is effected with the written consent of the Company, which consent shall not be unreasonably withheld), insofar as such loss, claim, damage, liability or expense (or actions in respect thereof as contemplated below) arises out of or is based (i) upon any untrue statement or alleged untrue statement of a material fact contained in the Registration Statement, or any amendment thereto, including any information deemed to be a part thereof pursuant to Rule 430A under the Securities Act, or the omission or alleged omission therefrom of a material fact required to be stated therein or necessary to make the statements therein not misleading; or (ii) upon any untrue statement or alleged untrue statement of a material fact contained in any preliminary prospectus or the Prospectus (or any amendment or supplement thereto), or the omission or alleged omission therefrom of a material fact necessary in order to make the statements therein, in the light of the circumstances under which they were made, not misleading; or (iii) in whole or in part upon any inaccuracy in the representations and warranties of the Company contained herein; or (iv) in whole or in part upon any failure of the Company to perform its obligations hereunder or under law; or (v) any untrue statement or alleged untrue statement of any material fact contained in any audio or visual materials provided by the Company or based upon written information furnished by or on behalf of the Company including, without limitation, slides, videos, films or tape recordings, used in connection with the marketing of the Shares, and including, without limitation, statements communicated to securities analysts employed by the Underwriters; or (vi) any act or failure to act or any alleged act or failure to act by any Underwriter in connection with, or relating in any manner to, the Shares or the offering contemplated hereby, and which is included as part of or referred to in any loss, claim, damage, liability or action arising out of or based upon any matter covered by clause (i), (ii), (iii) (iv) or (v) above, provided that the Company shall not be liable under this clause (vi) to the extent that a court of competent jurisdiction shall have determined by a final judgment that such loss, claim, damage, liability or action resulted directly from any such acts or failures to act undertaken or omitted to be taken by such Underwriter through its bad faith or willful

misconduct; and to reimburse each Underwriter and each such controlling person for any and all expenses (including the fees and disbursements of counsel chosen by Thomas Weisel Partners) as such expenses are reasonably incurred by such Underwriter or such controlling person in connection with investigating, defending, settling, compromising or paying any such loss, claim, damage, liability, expense or action; provided, however, that the foregoing indemnity agreement shall not apply to any loss, claim, damage, liability or expense to the extent, but only to the extent, that such loss, claim, damage, liability or expense arises out of or is based upon any untrue statement or alleged untrue statement or omission or alleged omission made in reliance upon and in conformity with written information furnished to the Company by the Representatives expressly for use in the Registration Statement, any preliminary prospectus or the Prospectus (or any amendment or supplement thereto); and provided, further, that with respect to any preliminary prospectus, the foregoing indemnity agreement shall not inure to the benefit of any Underwriter from whom the person asserting any loss, claim, damage, liability or expense purchased Shares, or any person controlling such Underwriter, if copies of the Prospectus were timely delivered to the Underwriter pursuant to Section 2 and a copy of the Prospectus (as then amended or supplemented if the Company shall have furnished any amendments or supplements thereto) was not sent or given by or on behalf of such Underwriter to such person, if required by law so to have been delivered, and if the Prospectus (as so amended or supplemented) would have cured the defect giving rise to such loss, claim, damage, liability or expense. The indemnity agreement set forth in this Section 7(a) shall be in addition to any liabilities that the Company may otherwise have.

- (b) Indemnification of the Company, its Directors and Officers. Each Underwriter agrees, severally and not jointly, to indemnify and hold harmless the Company, each of its directors, each of its officers who signed the Registration Statement and each person, if any, who controls the Company within the meaning of the Securities Act or the Exchange Act, against any loss, claim, damage, liability or expense, as incurred, to which the Company, or any such director, officer or controlling person may become subject, under the Securities Act, the Exchange Act, or other federal or state statutory law or regulation, or at common law or otherwise (including in settlement of any litigation, if such settlement is effected with the written consent of such Underwriter), insofar as such loss, claim, damage, liability or expense (or actions in respect thereof as contemplated below) arises out of or is based upon any untrue or alleged untrue statement of a material fact contained in the Registration Statement, any preliminary prospectus or the Prospectus (or any amendment or supplement thereto), or arises out of or is based upon the omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading, in each case to the extent, but only to the extent, that such untrue statement or alleged untrue statement or omission or alleged omission was made in the Registration Statement, any preliminary prospectus, the Prospectus (or any amendment or supplement thereto), in reliance upon and in conformity with written information furnished to the Company by the Representatives expressly for use therein; and to reimburse the Company, or any such director, officer or controlling person for any legal and other expense reasonably incurred by the Company, or any such director, officer or controlling person in connection with investigating, defending, settling, compromising or paying any such loss, claim, damage, liability, expense or action. The indemnity agreement set forth in this Section 7(b) shall be in addition to any liabilities that each Underwriter may otherwise have.
- (c) Information Provided by the Underwriters. The Company and each person, if any, who controls the Company within the meaning of the Securities Act or the Exchange Act, hereby acknowledges that the only information that the Underwriters have furnished to the Company expressly for use in the Registration Statement, any preliminary prospectus or the

Prospectus (or any amendment or supplement thereto) are the statements set forth in the table in the first paragraph and the paragraphs titled "Dealers' Compensation" and "Discretionary Accounts" under the caption "Underwriting" in the Prospectus; and the Underwriters confirm that such statements are correct.

- (d) Notifications and Other Indemnification Procedures. Promptly after receipt by an indemnified party under this Section 7 of notice of the commencement of any action, such indemnified party will, if a claim in respect thereof is to be made against an indemnifying party under this Section 7, notify the indemnifying party in writing of the commencement thereof, but the omission so to notify the indemnifying party shall not relieve it from any liability hereunder to the extent it is not materially prejudiced as a proximate result of such failure and in any event shall not relieve it from any liability which it may have otherwise than on account of this indemnity agreement. In case any such action is brought against any indemnified party and such indemnified party seeks or intends to seek indemnity from an indemnifying party, the indemnifying party will be entitled to participate in, and, to the extent that it shall elect, jointly with all other indemnifying parties similarly notified, by written notice delivered to the indemnified party promptly after receiving the aforesaid notice from such indemnified party, to assume the defense thereof with counsel reasonably satisfactory to such indemnified party; provided, however, if the defendants in any such action include both the indemnified party and the indemnifying party and the indemnified party shall have reasonably concluded that a conflict may arise between the positions of the indemnifying party and the indemnified party in conducting the defense of any such action or that there may be legal defenses available to it and/or other indemnified parties which are different from or additional to those available to the indemnifying party, the indemnified party or parties shall have the right to select separate counsel to assume such legal defenses and to otherwise participate in the defense of such action on behalf of such indemnified party or parties. Upon receipt of notice from the indemnifying party to such indemnified party of such indemnifying party's election so to assume the defense of such action and approval by the indemnified party of counsel, the indemnifying party will not be liable to such indemnified party under this Section 7 for any legal or other expenses subsequently incurred by such indemnified party in connection with the defense thereof unless (i) the indemnified party shall have employed separate counsel in accordance with the proviso to the next preceding sentence (it being understood, however, that the indemnifying party shall not be liable for the expenses of more than one separate counsel (together with local counsel), approved by the indemnifying party (Thomas Weisel Partners in the case of Section 7(b) and Section 8), representing the indemnified parties who are parties to such action), (ii) the indemnifying party shall not have employed counsel satisfactory to the indemnified party to represent the indemnified party within a reasonable time after notice of commencement of the action, or (iii) the indemnifying party has authorized the employment of counsel for the indemnified party at the expense of the indemnifying party, in each of which cases the fees and expenses of counsel shall be at the expense of the indemnifying party.
- (e) Settlements. The indemnifying party under this Section 7 shall not be liable for any settlement of any proceeding effected without its written consent, which consent shall not be unreasonably withheld, but if settled with such consent or if there be a final judgment for the plaintiff, the indemnifying party agrees to indemnify the indemnified party against any loss, claim, damage, liability or expense by reason of such settlement or judgment. Notwithstanding the foregoing sentence, if at any time an indemnified party shall have requested an indemnifying party to reimburse the indemnified party for fees and expenses of counsel as contemplated by Section 7(d) hereof, the indemnifying party agrees that it shall be liable for any settlement of any proceeding effected without its written consent if (i) such settlement is entered into more than 60 days after receipt by such indemnifying party of the aforesaid request and (ii) such

indemnifying party shall not have reimbursed the indemnified party in accordance with such request prior to the date of such settlement. No indemnifying party shall, without the prior written consent of the indemnified party, effect any settlement, compromise or consent to the entry of judgment in any pending or threatened action, suit or proceeding in respect of which any indemnified party is or could have been a party and indemnity was or could have been sought hereunder by such indemnified party, unless such settlement, compromise or consent includes (i) an unconditional release of such indemnified party from all liability on claims that are the subject matter of such action, suit or proceeding and (ii) does not include a statement as to or an admission of fault, culpability or a failure to act by or on behalf of any indemnified party.

(f) Contribution. If the indemnification provided for in this Section 7 is unavailable to or insufficient to hold harmless an indemnified party under Section 7(a) or (b) above in respect of any losses, claims, damages or liabilities (or actions or proceedings in respect thereof) then each indemnifying party shall contribute to the aggregate amount paid or payable by such indemnified party in such proportion as is appropriate to reflect the relative benefits received by the Company on the one hand and the Underwriters on the other from the offering of the Shares. If, however, the allocation provided by the immediately preceding sentence is not permitted by applicable law then each indemnifying party shall contribute to such amount paid or payable by such indemnified party in such proportion as is appropriate to reflect not only such relative benefits but also the relative fault of the Company on the one hand and the Underwriters on the other in connection with the statements or omissions which resulted in such losses, claims, damages or liabilities, (or actions or proceedings in respect thereof), as well as any other relevant equitable considerations. The relative benefits received by the Company on the one hand, and the Underwriters on the other shall be deemed to be in the same proportion as the total net proceeds (before deducting expenses) received by the Company from the sale of the Shares sold by it in the offering bears to the total underwriting discounts and commissions received by the Underwriters in connection with the sale of such Shares, in each case as described in the Prospectus. The relative fault shall be determined by reference to, among other things, whether the untrue or alleged untrue statement of a material fact or the omission or alleged omission to state a material fact relates to information supplied by the Company on the one hand or the Underwriters on the other and the parties' relative intent, knowledge, access to information and opportunity to correct or prevent such statement or omission.

The Company and the Underwriters agree that it would not be just and equitable if contributions pursuant to this Section 7(f) were determined by pro rata allocation (even if the Underwriters were treated as one entity for such purpose) or by any other method of allocation which does not take account of the equitable considerations referred to above in this Section 7(f). The amount paid or payable by an indemnified party as a result of the losses, claims, damages or liabilities (or actions or proceedings in respect thereof) referred to above in this Section 7(f) shall be deemed to include any legal or other expenses reasonably incurred by such indemnified party in connection with investigating or defending any such action or claim. Notwithstanding the provisions of this subsection (f), (i) no Underwriter shall be required to contribute any amount in excess of the underwriting discounts and commissions applicable to the Shares purchased by such Underwriter and (ii) no person guilty of fraudulent misrepresentation (within the meaning of Section 11(f) of the Securities Act) shall be entitled to contribution from any person who was not guilty of such fraudulent misrepresentation. The Underwriters' obligations in this Section 7(f) to contribute are several in proportion to their respective underwriting obligations and not joint.

(g) Timing of Any Payments of Indemnification. Any losses, claims, damages, liabilities or expenses for which an indemnified party is entitled to indemnification or

contribution under this Section 7 shall be paid by the indemnifying party to the indemnified party as such losses, claims, damages, liabilities or expenses are incurred, but in all cases, no later than forty-five (45) days of invoice to the indemnifying party.

- (h) Survival. The indemnity and contribution agreements contained in this Section 7 and the representation and warranties set forth in this Agreement shall remain operative and in full force and effect, regardless of (i) any investigation made by or on behalf of any Underwriter or any person controlling any Underwriter, the Company, its directors or officers or any persons controlling the Company, (ii) acceptance of any Shares and payment therefor hereunder, and (iii) any termination of this Agreement. A successor to any Underwriter, or to the Company, its directors or officers or any person controlling the Company, shall be entitled to the benefits of the indemnity, contribution and reimbursement agreements contained in this Section 7.
- (i) Acknowledgements of Parties. The parties to this Agreement hereby acknowledge that they are sophisticated business persons who were represented by counsel during the negotiations regarding the provisions hereof including, without limitation, the provisions of this Section 7, and are fully informed regarding said provisions. They further acknowledge that the provisions of this Section 7 fairly allocate the risks in light of the ability of the parties to investigate the Company and its business in order to assure that adequate disclosure is made in the Registration Statement and Prospectus as required by the Securities Act and the Exchange Act.
- (j) Indemnification for Directed Share Program. The Company agrees to indemnify and hold harmless Thomas Weisel Partners and its affiliates and each person, if any, who controls Thomas Weisel Partners or its affiliates within the meaning of either Section 15 of the Securities Act or Section 20 of the Exchange Act ("Thomas Weisel Partners Entities"), from and against any and all losses, claims, damages and liabilities (including, without limitation, any legal or other expenses reasonably incurred in connection with defending or investigating any such action or claim) (i) caused by any untrue statement or alleged untrue statement of a material fact contained in any material prepared by or with the consent of the Company for distribution to participants in connection with the Directed Share Program, or caused by any omission or alleged omission to state therein a material fact required to be stated therein or necessary to make the statements therein not misleading; (ii) the failure of any participant to pay for and accept delivery of Directed Shares that the participant has agreed to purchase; or (iii) related to, arising out of, or in connection with the Directed Share Program other than losses, claims, damages or liabilities (or expenses relating thereto) that are finally judicially determined to have resulted from the bad faith or willful misconduct of Thomas Weisel Partners Entities.

# SECTION 8. DEFAULT OF ONE OR MORE OF THE SEVERAL UNDERWRITERS.

If, on the First Closing Date or the Second Closing Date, as the case may be, any one or more of the several Underwriters shall fail or refuse to purchase Shares that it or they have agreed to purchase hereunder on such date, and the aggregate number of Common Shares which such defaulting Underwriter or Underwriters agreed but failed or refused to purchase does not exceed 10% of the aggregate number of the Shares to be purchased on such date, the other Underwriters shall be obligated, severally, in the proportions that the number of Firm Common Shares set forth opposite their respective names on Schedule A bears to the aggregate number of Firm Shares set forth opposite the names of all such non-defaulting Underwriters, or in such other proportions as may be specified by the Representatives with the consent of the non-defaulting Underwriters, to purchase the Shares which such defaulting Underwriter or Underwriters agreed but failed or refused to purchase on such date. If, on the First Closing Date

or the Second Closing Date, as the case may be, any one or more of the Underwriters shall fail or refuse to purchase Shares and the aggregate number of Shares with respect to which such default occurs exceeds 10% of the aggregate number of Shares to be purchased on such date, and arrangements satisfactory to the Representatives and the Company for the purchase of such Shares are not made within 48 hours after such default, this Agreement shall terminate without liability of any party to any other party except that the provisions of Section 5, and Section 7 shall at all times be effective and shall survive such termination. In any such case either the Representatives or the Company shall have the right to postpone the First Closing Date or the Second Closing Date, as the case may be, but in no event for longer than seven days in order that the required changes, if any, to the Registration Statement and the Prospectus or any other documents or arrangements may be effected.

As used in this Agreement, the term "Underwriter" shall be deemed to include any person substituted for a defaulting Underwriter under this Section 8. Any action taken under this Section 8 shall not relieve any defaulting Underwriter from liability in respect of any default of such Underwriter under this Agreement.

# SECTION 9. TERMINATION OF THIS AGREEMENT.

This Agreement may be terminated by the Representatives by notice given to the Company if (a) at any time after the execution and delivery of this Agreement and prior to the First Closing Date (i) trading or quotation in any of the Company's securities shall have been suspended or limited by the Commission or by the Nasdaq Stock Market, or trading in securities generally on either the Nasdaq Stock Market or the New York Stock Exchange shall have been suspended or limited, or minimum or maximum prices shall have been generally established on any of such stock exchanges by the Commission or the NASD; (ii) a general banking moratorium shall have been declared by any of federal, New York, Delaware or California authorities; (iii) there shall have occurred any outbreak or escalation of national or international hostilities or any crisis or calamity, or any change in the United States or international financial markets, or any substantial change or development involving a prospective change in United States' or international political, financial or economic conditions, as in the judgment of the Representatives is material and adverse and makes it impracticable or inadvisable to market the Common Shares in the manner and on the terms contemplated in the Prospectus or to enforce contracts for the sale of securities; (iv) in the judgment of the Representatives there shall have occurred any Material Adverse Change; or (v) the Company shall have sustained a loss by strike, fire, flood, earthquake, accident or other calamity of such character as in the judgment of the Representatives may interfere materially with the conduct of the business and operations of the Company regardless of whether or not such loss shall have been insured; or (b) in the case of any of the events specified 9(a)(i)-(v), such event singly or together with any other event, makes it, in your judgment, impracticable or inadvisable to market the Common Shares in the manner and on the terms contemplated in the Prospectus. Any termination pursuant to this Section 9 shall be without liability on the part of (x) the Company to any Underwriter, except that the Company shall be obligated to reimburse the expenses of the Representatives and the Underwriters pursuant to Sections 5 and 6 hereof, (y) any Underwriter to the Company or any person controlling the Company, or (z) of any party hereto to any other party except that the provisions of Section 7 shall at all times be effective and shall survive such termination.

# SECTION 10. REPRESENTATIONS AND INDEMNITIES TO SURVIVE DELIVERY.

The respective indemnities, agreements, representations, warranties and other statements of the Company or any person controlling the company, of its officers and of the several Underwriters set forth in or made pursuant to this Agreement will remain in full force and effect, regardless of any investigation made by or on behalf of any Underwriter or the Company or any of its or their partners, officers or directors or any controlling person, as the case may be, and will survive delivery of and payment for the Shares sold hereunder and any termination of this Agreement.

# SECTION 11. NOTICES.

 $\,$  All communications hereunder shall be in writing and shall be mailed, hand delivered or telecopied and confirmed to the parties hereto as follows:

# If to the Representatives:

Thomas Weisel Partners LLC One Montgomery Street, Suite 3700 San Francisco, California 94104 Attention: General Counsel

# with a copy to:

O'Melveny & Myers LLP Embarcadero Center West 275 Battery Street, Suite 2600 San Francisco, CA 94111-3305 Facsimile: (415) 984-8701 Attention: Peter T. Healy, Esq.

# If to the Company:

Pain Therapeutics, Inc. 250 East Grand Avenue, Suite 70 South San Francisco, CA 94080 Facsimile: (650) 624-8222 Attention: Remi Barbier

# with a copy to:

Wilson Sonsini Goodrich & Rosati, Professional Corporation 650 Page Mill Road

Palo Alto, California 94304 Facsimile: (650) 493-6811 Attention: Martin Waters, III

Any party hereto may change the address for receipt of communications by giving written notice to the others.

### SECTION 12. SUCCESSORS.

This Agreement will inure to the benefit of and be binding upon the parties hereto, including any substitute Underwriters pursuant to Section 9 hereof, and to the benefit of the employees, officers and directors and controlling persons referred to in Section 7, and to their respective successors, and personal representatives, and no other person will have any right or obligation hereunder. The term "successors" shall not include any purchaser of the Shares as such from any of the Underwriters merely by reason of such purchase.

# SECTION 13. PARTIAL UNENFORCEABILITY.

The invalidity or unenforceability of any Section, paragraph or provision of this Agreement shall not affect the validity or enforceability of any other Section, paragraph or provision hereof. If any Section, paragraph or provision of this Agreement is for any reason determined to be invalid or unenforceable, there shall be deemed to be made such minor changes (and only such minor changes) as are necessary to make it valid and enforceable.

# SECTION 14. SECTION 14. GOVERNING LAW PROVISIONS.

- (a) Governing Law. This agreement shall be governed by and construed in accordance with the internal laws of the state of New York applicable to agreements made and to be performed in such state.
- (b) Consent to Jurisdiction. Any legal suit, action or proceeding arising out of or based upon this Agreement or the transactions contemplated hereby ("Related Proceedings") may be instituted in the federal courts of the United States of America located in the City and County of San Francisco or the courts of the State of California in each case located in the City and County of San Francisco (collectively, the "Specified Courts"), and each party irrevocably submits to the exclusive jurisdiction (except for proceedings instituted in regard to the enforcement of a judgment of any such court (a "Related Judgment"), as to which such jurisdiction is non-exclusive) of such courts in any such suit, action or proceeding. Service of any process, summons, notice or document by mail to such party's address set forth above shall be effective service of process for any suit, action or other proceeding brought in any such court. The parties irrevocably and unconditionally waive any objection to the laying of venue of any suit, action or other proceeding in the Specified Courts and irrevocably and unconditionally waive and agree not to plead or claim in any such court that any such suit, action or other proceeding brought in any such court has been brought in an inconvenient forum.

# SECTION 15. GENERAL PROVISIONS.

This Agreement constitutes the entire agreement of the parties to this Agreement and supersedes all prior written or oral and all contemporaneous oral agreements, understandings and negotiations with respect to the subject matter hereof. This Agreement may be executed in two or more counterparts, each one of which shall be an original, with the same effect as if the signatures thereto and hereto were upon the same instrument. This Agreement may not be amended or modified unless in writing by all of the parties hereto, and no condition herein (express or implied) may be waived unless waived in writing by each party whom the condition is meant to benefit. Section headings herein are for the convenience of the parties only and shall not affect the construction or interpretation of this Agreement.

[The remainder of this page has been intentionally left blank.]

If the foregoing is in accordance with your understanding of our agreement, please sign and return to the Company the enclosed copies hereof, whereupon this instrument, along with all counterparts hereof, shall become a binding agreement in accordance with its terms.

Very truly yours,

PAIN THERAPEUTICS, INC.

By:

Remi Barbier
President

THOMAS WEISEL PARTNERS LLC CIBC WORLD MARKETS CORP. TUCKER ANTHONY INCORPORATED

On their behalf and on behalf of each of the several underwriters named in Schedule A hereto.

BY: THOMAS WEISEL PARTNERS LLC

By:
Authorized Signatory

# SCHEDULE A

# UNDERWRITERS

Underwriters	Number of Firm Shares To be Purchased
Thomas Weisel Partners LLC CIBC World Markets Corp. Tucker Anthony Incorporated.  [] [] [] [] [] [] [] [_	
[]	r——]
Total	[]

Schedule A

### EXHIBIT A

### LOCK-UP AGREEMENT

Re: Pain Therapeutics, Inc. (the "Company")

### Ladies & Gentlemen:

The undersigned is an owner of record or beneficially of certain shares of Common Stock of the Company ("Common Stock") or securities convertible into or exchangeable or exercisable for Common Stock. The Company proposes to carry out a public offering of Common Stock (the "Offering") for which you will act as the representatives (the "Representatives") of the underwriters. The undersigned recognizes that the Offering will be of benefit to the undersigned and will benefit the Company by, among other things, raising additional capital for its operations. The undersigned acknowledges that you and the other underwriters are relying on the representations and agreements of the undersigned contained in this letter in carrying out the Offering and in entering into underwriting arrangements with the Company with respect to the Offering.

In consideration of the foregoing, the undersigned hereby agrees that the undersigned will not offer to sell, contract to sell, or otherwise sell, dispose of, loan, pledge or grant any rights with respect to (collectively, a "Disposition") any shares of Common Stock, any options or warrants to purchase any shares of Common Stock or any securities convertible into or exchangeable for shares of Common Stock (collectively, "Securities") now owned or hereafter acquired directly by such person or with respect to which such person has or hereafter acquires the power of disposition, otherwise than (i) as a bona fide gift or gifts, provided the donee or donees thereof agree in writing to be bound by this restriction, (ii) as a distribution to partners or shareholders of such person, provided that the distributees thereof agree in writing to be bound by the terms of this restriction, (iii) with respect to sales or purchases of Common Stock acquired on the open market or (iv) with the prior written consent of Thomas Weisel Partners LLC. The foregoing restrictions will terminate after the close of trading of the Common Stock on the 180th day of (and including) the day the Common Stock commenced trading on the Nasdag National Market (the "Lock-Up" Period). The foregoing restriction has been expressly agreed to preclude the holder of the Securities from engaging in any hedging or other transaction which is designed to or reasonably expected to lead to or result in a Disposition of Securities during the Lock-up Period, even if such Securities would be disposed of by someone other than such holder. Such prohibited hedging or other transactions would include, without limitation, any short sale (whether or not against the box) or any purchase, sale or grant of any right (including, without limitation, any put or call option) with respect to any Securities or with respect to any security (other than a broad-based market basket or index) that included, relates to or derives any significant part of its value from Securities. The undersigned also agrees and consents to the entry of stop transfer instructions with the Company's transfer agent and registrar against the

transfer of shares of Common Stock or Securities held by the undersigned except in compliance with the foregoing restrictions.

With respect to the Offering only, the undersigned waives any registration rights relating to registration under the Securities Act of 1933, as amended, of any Common Stock owned either of record or beneficially by the undersigned, including any rights to receive notice of the Offering.

This agreement is irrevocable and will be binding on the undersigned and the respective successors, heirs, personal representatives, and assigns of the undersigned. In the event the Offering has not occurred on or before December 31, 2000, this Lock-Up Agreement shall be of no further force or effect

Date	ed:
	Printed Name of Holder
Bv.	
Бу	Signature
	Printed Name of Person Signing
(and	indicate capacity of person signing if signing as custodian, trustee, or on
	behalf of an entity)

#### EXHIBIT B

# MATTERS TO BE COVERED IN THE OPINION OF COMPANY COUNSEL

- (i) The Company has been duly incorporated and is validly existing as a corporation in good standing under the laws of the jurisdiction of its incorporation;
- (ii) The Company has the corporate power and authority to own, lease and operate its properties and to conduct its business as described in the Prospectus;
- (iii) The Company is duly qualified to do business as a foreign corporation and is in good standing in each jurisdiction, if any, in which the ownership or leasing of its properties or the conduct of its business requires such qualification, except where the failure to be so qualified or be in good standing would not have a Material Adverse Effect. To such counsel's knowledge, the Company does not own or control, directly or indirectly, any corporation, association or other entity.
- (iv) The authorized, issued and outstanding capital stock of the Company is as set forth in the Prospectus under the caption "Capitalization" as of the dates stated therein, the issued and outstanding shares of capital stock of the Company outstanding prior to the issuance of the Shares have been duly and validly issued and are fully paid and nonassessable, and will not have been issued in violation of or subject to any preemptive right arising under the certificate of incorporation or Delaware General Corporation Law, or, to such counsel's knowledge, any co-sale right, right of first refusal or other similar right, other than any registration rights described in Opinion (xix) hereof;
- (v) The Firm Shares or the Option Shares, as the case may be, to be issued by the Company pursuant to the terms of the Underwriting Agreement have been duly authorized and, upon issuance and delivery against payment therefor in accordance with the terms hereof, will be duly and validly issued and fully paid and nonassessable, and will not have been issued in violation of or subject to any preemptive right arising under the certificate of incorporation or Delaware General Corporation Law, or, any co-sale right, right of first refusal or other similar right, other than any registration rights described in Opinion (xix) hereof.
- (vi) The Company has the corporate power and authority to enter into this Agreement and to issue, sell and deliver to the Underwriters the Shares to be issued and sold by it hereunder;
- (vii) This Agreement has been duly authorized by all necessary corporate action on the part of the Company and has been duly executed and delivered by the Company and, assuming due authorization, execution and delivery by you, [and assuming that the laws of the State of New York are identical to the laws of the State of California] is a valid and binding agreement of the Company, enforceable in accordance with its terms, except as rights to indemnification hereunder may be limited by applicable law and except as enforceability may be limited by bankruptcy, insolvency, reorganization, moratorium or similar laws relating to or affecting creditors' rights generally or by general equitable principles (whether relief is sought in a proceeding at law or in equity);

- (viii) The Registration Statement has become effective under the Securities Act and the Shares have been validly registered under the Securities Act and the applicable rules and regulations of the Commission thereunder and, to such counsel's knowledge, no stop order suspending the effectiveness of the Registration Statement has been issued and no proceedings for that purpose have been instituted or are pending or threatened under the Securities Act;
- (ix) The 8-A Registration Statement complied as to form in all material respects with the requirements of the Exchange Act; the 8-A Registration Statement has become effective under the Exchange Act; and the Common Shares have been validly registered under the Exchange Act and the applicable rules and regulations of the Commission thereunder, and, to such counsel's knowledge, no stop order suspending the effectiveness of the Form 8-A Registration Statement has been issued and no proceedings for that purpose have been instituted or are pending or threatened under the Exchange Act;
- (x) The Registration Statement and the Prospectus, and each amendment or supplement thereto (other than the financial statements (including supporting schedules) and financial data derived therefrom as to which such counsel need express no opinion), as of the effective date of the Registration Statement, complied as to form in all material respects with the requirements of the Securities Act and the applicable Rules and Regulations;
- (xi) The information in the Prospectus under the captions "Risk Factors--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," "Risk Factors--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," "Management--Limitations on Directors' and Officers' Liability and Indemnification," "Management--Stock Plans," "Description of Capital Stock" and "Shares Eligible for Future Sale," to the extent that it constitutes matters of law or legal conclusions, has been reviewed by such counsel and is an accurate and fair summary of such matters and conclusions;
- (xii) The forms of certificates evidencing the Common Stock and filed as exhibits to the Registration Statement comply with Delaware law:
- (xiii) The description in the Registration Statement and the Prospectus of the charter and bylaws of the Company and of statutes are accurate and fairly present the information required to be presented by the Securities Act;
- (xiv) To such counsel's knowledge, there are no agreements, contracts, leases or documents to which the Company is a party of a character required to be described or referred to in the Registration Statement or Prospectus or to be filed as an exhibit to the Registration Statement which are not described or referred to therein or filed as required;
- (xv) The performance of this Agreement and the consummation of the transactions herein contemplated (other than performance of the Company's indemnification obligations hereunder, concerning which no opinion need be expressed) will not (a) result in any violation of the Company's charter or bylaws or (b) to such counsel's knowledge, result in a material breach or violation of any of the terms and provisions of, or constitute a default under, any bond, debenture, note or other evidence of

indebtedness, or any lease, contract, indenture, mortgage, deed of trust, loan agreement, joint venture or other agreement or instrument known to such counsel to which the Company is a party or by which its properties are bound, or any applicable statute, rule or regulation known to such counsel or, to such counsel's knowledge, any order, writ or decree of any court, government or governmental agency or body having jurisdiction over the Company or over any of its properties or operations;

(xvi) No consent, approval, authorization or order of or qualification with any court, government or governmental agency or body having jurisdiction over the Company or over any of its properties or operations is necessary in connection with the consummation by the Company of the transactions herein contemplated, except (i) such as have been obtained under the Securities Act, (ii) such as may be required under state or other securities or Blue Sky laws in connection with the purchase and the distribution of the Shares by the Underwriters, (iii) such as may be required by the NASD and (iv) such as may be required under the federal or provincial laws of Canada;

(xvii) To such counsel's knowledge, there are no legal or governmental proceedings pending or threatened against the Company of a character required to be disclosed in the Registration Statement or the Prospectus by the Securities Act, other than those described therein;

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

(xix) To such counsel's knowledge, except as set forth in the Registration Statement and Prospectus, no holders of Common Shares or other securities of the Company have registration rights with respect to securities of the Company and, except as set forth in the Registration Statement and Prospectus, all holders of securities of the Company having rights known to such counsel to registration of Common Shares or other securities, because of the filing of the Registration Statement by the Company, have, with respect to the offering contemplated thereby, waived such rights or such rights have expired by reason of lapse of time following notification of the Company's intent to file the Registration Statement or have included securities in the Registration Statement pursuant to the exercise of and in full satisfaction of such rights.

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

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

In addition, such counsel shall state that such counsel has participated in conferences with officials and other representatives of the Company, the Representatives, Underwriters' Counsel and the independent certified public accountants of the Company, at which such conferences the contents of the Registration Statement and Prospectus and related matters were discussed, and although they have not verified the accuracy or completeness of the statements contained in the Registration Statement or the Prospectus, nothing has come to the attention of such counsel which leads them to believe that, at the time the Registration Statement became effective and at all times subsequent thereto up to and on the First Closing Date or Second Closing Date, as the case may be, the Registration Statement and any amendment or supplement thereto (other than the financial statements including supporting schedules and other financial and statistical information derived therefrom, as to which such counsel need express no comment) contained any untrue statement of a material fact or omitted to state a material fact required to be stated therein or necessary to make the statements therein not misleading, or at the First Closing Date or the Second Closing Date, as the case may be, the Registration Statement, the Prospectus and any amendment or supplement thereto (except as aforesaid) contained any untrue statement of a material fact or omitted to state a material fact necessary to make the statements therein, in the light of the circumstances under which they were made, not misleading.

#### EXHIBIT C

# MATTERS TO BE COVERED IN THE OPINION OF INTELLECTUAL PROPERTY COUNSEL FOR THE COMPANY

Such counsel shall state that they are familiar with the technology used by the Company in its business and the manner of its use thereof and have read the Registration Statement and the Prospectus, including particularly the portions of the Registration Statement and the Prospectus referring to patents, trade secrets, trademarks, service marks or other proprietary information or materials and:

- (i) The information in the Prospectus under the captions "Risk Factors--If we are unable to protect our intellectual property our competitors could develop and market products with similar features that may reduce demand for our products," and the final three paragraphs of "Business--Technology Overview," and in the final sentence of the first paragraph under the caption "Business--Products in Development--PTI-601: tramadol" (regarding the expiration of certain patents) to the extent that it constitutes matters of law or legal conclusions, has been reviewed by such counsel and is an accurate and fair summary of such matters and conclusions;
- (ii) Such counsel knows of no material action, suit, claim or proceeding relating to patents, patent rights or licenses, trademarks or trademark rights, copyrights, collaborative research, licenses or royalty arrangements or agreements or trade secrets, know-how or proprietary techniques, including processes and substances, owned by, licensed by or affecting the business or operations of the Company which are pending or threatened against the Company or Albert Einstein College of Medicine ("AECOM") or any of their respective officers or directors;
- (iii) AECOM is listed in the records of the United States Patent and Trademark Office as the holder of record of the patents listed on a schedule to such opinion (the "Patents") and each of the applications listed on a schedule to such opinion (the "Applications"). AECOM has granted the Company an exclusive worldwide license to each of the Patents and Applications listed in such schedule. To the knowledge of such counsel, there are no claims of third parties to any ownership interest, license or lien with respect to any of the Patents or Applications, other than the U.S. Government to the extent indicated on such schedule. Such counsel is not aware of any material defect in form in the preparation or filing of the Applications. To the knowledge of such counsel, the Applications are being pursued by the Company or Albert Einstein College of Medicine (as applicable). To the knowledge of such counsel, except as indicated on such schedule, Albert Einstein College of Medicine (apart from the license to the Company) owns as its sole property the Patents and pending Applications;
- (iv) The license agreement between AECOM and Alan E. Kligerman, dated October 1, 1994, as amended, has been validly and effectively terminated and neither Alan E. Kligerman nor his successors or assigns retains any residual interest in any of the Patents or Applications. The license agreement between AECOM and the \_\_\_\_\_\_\_\_\_ dated August 30, 1996, as amended, has been validly and effectively terminated and neither the \_\_\_\_\_\_\_ nor its successors or assigns retains any residual interest in any of the Patents or Applications.

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

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

### EXHIBIT D

# MATTERS TO BE COVERED IN THE OPINION OF FDA REGULATORY COUNSEL FOR THE COMPANY

Such counsel shall state that they act as the Company's Food and Drug Administration ("FDA") counsel and in such capacity are familiar with the Company's submissions to and relations with the FDA. Such counsel shall further state that they have read the Registration Statement and the Prospectus, including particularly those portions of the Registration Statement and the Prospectus describing (a) the Company's FDA applications and the status thereof and (b) the Federal Food, Drug, and Cosmetic Act ("FDC Act"), the Public Health Service Act ("PHS Act") or the FDA regulations (such matters (a) and (b) collectively, the "FDA Regulatory Matters") and in their opinion:

- (i) The information in the Prospectus under the captions "Risk Factors--If we are unable to design, conduct and complete clinical trials successfully, we will not be able to obtain FDA approval of our product candidates," "--If we fail to obtain the necessary regulatory approvals, we will not be allowed to commercialize our drugs and we will not generate product revenues," and "Business--Government Regulation," insofar as such statements constitute legal conclusions under the FDC Act, the PHS Act or FDA regulations or summaries of FDA Regulatory Matters, has been reviewed by such counsel and is an accurate and fair summary of such matters and conclusions.
- (ii) Such counsel knows of no material action, suit, claim or proceeding relating to FDA Regulatory Matters which is pending or threatened against the Company or any of its officers or directors, nor is such counsel aware of any material violations of the FDC Act, the PHS Act or FDA regulations by the Company or any of its officers or directors.
- (iii) The Company has filed the Investigational New Drug ("IND") applications the FDA listed on Schedule 1 to such letter (collectively, the "US Applications"). The FDA has not denied any of the Company's US Applications, [other than as noted on Schedule 1]. [Apart from such denied US Applications,] such counsel is not aware of any material defect in form in the preparation or filing of the US Applications, other than as noted in Schedule 1. To the knowledge of such counsel, [apart from such denied US Applications,] the US Applications are being diligently pursued by the Company, [other than as noted in Schedule 1]. To the knowledge of such counsel, the Company is the sole owner of the US Applications, [other than as noted in Schedule 1].
- (iv) The FDA has issued to the Company the IND approval letters listed on Schedule 2 to such opinion, and none of such approvals has been modified, revoked or rescinded.
- (v) The Company has filed the applications with foreign regulators listed on Schedule 3 to such letter (collectively, the "Foreign Applications"). No foreign authority has denied any of the Company's Foreign Applications, [other than as noted on Schedule 3]. [Apart from such denied Foreign Applications,] such counsel is not aware of any material defect in form in the preparation or filing of the Foreign Applications, [other than as noted in Schedule 3]. To the knowledge of such counsel, [apart from such

denied Foreign Applications,] the Applications are being diligently pursued by the Company, [other than as noted in Schedule 3]. To the knowledge of such counsel, the Company is the sole owner of the Foreign Applications, [other than as noted in Schedule 3].

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

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

[PAIN THERAPEUTICS, INC. LOGO]

# PAIN THERAPEUTICS, INC.

# INCORPORATED UNDER THE LAWS OF THE STATE OF DELAWARE

COMMON STOCK

SEE REVERSE FOR CERTAIN DEFINITIONS CUSIP 695621 00 7

THIS CERTIFIES THAT

is the owner of

FULLY PAID AND NON-ASSESSABLE SHARES OF COMMON STOCK, PAR VALUE \$0.001 EACH, OF

(hereinafter called the "Corporation") transferable on the books of the Corporation by the holder hereof in person or by duly authorized attorney upon surrender of this certificate properly endorsed. This certificate and the shares represented hereby are issued and shall be held subject to all of the provisions of the Certificate of Incorporation and the By-Laws, as from time to time amended, of the Corporation (copies of which are on file at the office of the Transfer Agent), and the holder hereof, by acceptance of this certificate, consents to and agrees to be bound by all of said provisions. This certificate is not valid unless countersigned and registered by the Transfer Agent and Registrar.

WITNESS the facsimile seal of the Corporation and the facsimile signatures of its duly authorized officers.

Dated:

[PAIN THERAPEUTICS, INC. CORPORATE SEAL]

/s/ MICHAEL J. O'DONNELL

REMI BARBIER

**SECRETARY** 

PRESIDENT, CHIEF EXECUTIVE OFFICER AND CHAIRMAN OF THE BOARD OF DIRECTORS

COUNTERSIGNED AND REGISTERED:

CHASEMELLON SHAREHOLDER SERVICES, L.L.C.

BY TRANSFER AGENT AND REGISTRAR

AUTHORIZED SIGNATURE

THE COMPANY WILL FURNISH WITHOUT CHARGE TO EACH STOCKHOLDER WHO SO REQUESTS, A COPY OF THE DESIGNATIONS, POWERS, PREFERENCES AND RELATIVE, PARTICIPATING, OPTIONAL OR OTHER SPECIAL RIGHTS OF EACH CLASS OF STOCK OR SERIES THEREOF AND THE QUALIFICATIONS, LIMITATIONS OR RESTRICTIONS OF SUCH PREFERENCES AND/OR RIGHTS. ANY SUCH REQUESTS MAY BE ADDRESSED TO THE SECRETARY OF THE CORPORATION.

The following abbreviations, when used in the inscription on the face of this certificate, shall be construed as though they were written out in full according to applicable laws or regulations:

TEN ENTas t JT TENas j surv	enants in common enants by the entireties oint tenants with right of vivorship and not as tenants common	UNIF GIFT MIN ACT-	Custodian (Cust) under Uniform Gifts Act (State)	(Minor)
Additional abbre	viations may also be used the	ough not in the abov	e list.	
For Value Received,	hereby	sell, assign and tr	ansfer unto	
(PLEASE PRINT OR TYP ASSIGNEE)	EWRITE NAME AND ADDRESS, INCL	UDING ZIP OR POSTAL	CODE OF	
	Stock represented by the wit te and appoint			
Attorney to transfer	the said stock on the books l power of substitution in th	of the within named		
Dated				
	THE SIGNATURE TO THIS ASSI NAME AS WRITTEN UPON THE F E: PARTICULAR, WITHOUT ALTERA CHANGE WHATEVER	GNMENT MUST CORRESPORTED FACE OF THE CERTIFIC.	OND WITH THE ATE IN EVERY	
Signature(s) Guarant	eed:			
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KEEP THIS CERTIFICATE IN A SAFE PLACE. IF IT IS LOST, STOLEN, MUTILATED OR DESTROYED, THE CORPORATION WILL REQUIRE A BOND OF INDEMNITY AS A CONDITION TO THE ISSUANCE OF A REPLACEMENT CERTIFICATE.

June 20, 2000

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

RE: REGISTRATION ON FORM S-1

Ladies and Gentlemen:

We have examined the Registration Statement on Form S-1 filed by you with the Securities and Exchange Commission on March 11, 2000 (Registration No. 333-32370), as amended (the "Registration Statement"), in connection with the registration under the Securities Act of 1933, as amended, of up to 5,750,000 shares of your Common Stock, \$0.001 par value per share (the "Shares"). The Shares include an over-allotment option granted to the underwriters of the offering to purchase up to 750,000 shares. We understand that the Shares are to be sold to the underwriters of the offering for resale to the public as described in the Registration Statement. As your legal counsel, we have examined the proceedings taken, and are familiar with the proceedings proposed to be taken, by you in connection with the sale and issuance of the Shares to be sold by you. It is our opinion that upon completion of the proceedings being taken or contemplated by us, as your counsel, to be taken prior to the issuance of the Shares, including the proceedings being taken in order to permit such transaction to be carried out in accordance with applicable state securities laws, the Shares, when issued and sold in the manner described in the Registration Statement, will be legally issued, fully paid and non-assessable. We are members of the Bar of the State of California only and express no opinion as to any matter relating to the laws of any jurisdiction other than the laws of the State of California and the federal laws of the United States. Without limiting the foregoing, we express no opinion as to the securities laws of the State of Delaware. We consent to the use of this opinion as an exhibit to the Registration Statement and further consent to the use of our name wherever appearing in the Registration Statement, including the Prospectus constituting a part thereof, and any amendments thereto.

Very truly yours,

# PAIN THERAPEUTICS, INC.

# 1998 STOCK PLAN

(AMENDED AND RESTATED AS OF \_\_\_\_\_, 2000)

- 1. Purposes of the Plan. The purposes of this 1998 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.

- 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 of the Plan.
- (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 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 of the Plan.
  - (f) "Common Stock" means the common stock of the Company.
- $\mbox{\ensuremath{\mbox{(g)}}}$  "Company" means Pain Therapeutics, Inc., a Delaware Corporation.
- - (i) "Director" means a member of the Board.
- (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, then three (3) months following the 91st 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.
- (1) "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 on the day 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, the Fair Market Value of a Share of Common Stock shall be the mean between the high bid and low asked prices for the Common Stock on the day of determination, as reported in The Wall Street Journal or such other source as the Administrator deems reliable; or
- (iii) In the absence of an established market for the Common Stock, the Fair Market Value 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 and the regulations promulgated thereunder.
  - (o) "Inside Director" means a Director who is an Employee.
- (p) "Nonstatutory Stock Option" means an Option not intended to qualify as an Incentive Stock Option.
- (q) "Notice of Grant" means a written or electronic notice evidencing certain terms and conditions of an individual Option grant. The Notice of Grant is part of the Option Agreement.

- (r) "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.
  - (s) "Option" means a stock option granted pursuant to the Plan.
- (t) "Option Agreement" means an 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.
  - (u) "Optioned Stock" means the Common Stock subject to an Option.
- (v) "Optionee" means the holder of an outstanding Option granted under the Plan.
  - (w) "Outside Director" means a Director who is not an Employee.
- (x) "Parent" means a "parent corporation," whether now or hereafter existing, as defined in Section 424(e) of the Code.
  - (y) "Plan" means this 1998 Stock Plan, as amended.
- (z) "Rule 16b-3" means Rule 16b-3 of the Exchange Act or any successor to Rule 16b-3, as in effect when discretion is being exercised with respect to the Plan.
  - (aa) "Section 16(b) " means Section 16(b) of the Exchange Act.
- (bb) "Service Provider" means an Employee, Director or Consultant.  $% \begin{center} \begin{cen$
- (cc) "Share" means a share of the Common Stock, as adjusted in accordance with Section 13 of the Plan.
- (dd) "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 13 of the Plan, the maximum aggregate number of Shares that may be optioned and sold under the Plan is 3,200,000 Shares, plus (a) an increase of 1,500,000 shares to be added on the day immediately following the date the Common Stock is publicly traded pursuant to an effective registration statement filed under the Exchange Act, plus (b) an annual increase to be added on the first day of the Commany's fiscal year, beginning fiscal year 2001, equal to the lesser of (i) 2,000,000 Shares, (ii) 5% of the outstanding Shares of Common Stock on the last day of the immediately preceding fiscal year or (iii) an amount determined by the Board. The Shares may be authorized, but unissued, or reacquired Common Stock.

If an Option expires or becomes unexercisable without having been exercised in full, the unpurchased Shares which were subject thereto shall become available for future grant or sale under the Plan (unless the Plan has terminated); provided, however, that Shares that have actually been issued under the Plan upon exercise of an Option shall not

be returned to the Plan and shall not become available for future distribution under the Plan, except that if unvested Shares 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) Procedure.
- (i) Multiple Administrative Bodies. Different Committees with respect to different groups of Service Providers may administer the Plan.
- (ii) Section 162(m). To the extent that the Administrator determines it to be desirable to qualify Options granted hereunder as "performance-based compensation" within the meaning of Section 162(m) of the Code, the Plan shall be administered by a Committee of two or more "outside directors" within the meaning of Section 162(m) of the Code.
- (iii) Rule 16b-3. To the extent desirable to qualify transactions hereunder as exempt under Rule 16b-3, the transactions contemplated hereunder shall be structured to satisfy the requirements for exemption under Rule 16b-3.
- (iv) Other Administration. Other than as provided above, the Plan shall be administered by (A) the Board or (B) a Committee, which committee shall be constituted to satisfy Applicable Laws.
- (b) Powers of the Administrator. Subject to the provisions of the Plan, and in the case of a Committee, subject to the specific duties delegated by the Board to such Committee, the Administrator shall have the authority, in its discretion:
  - (i) to determine the Fair Market Value;
- $\mbox{\ \ (ii)}$  to select the Service Providers to whom Options may be granted hereunder;
- $\hbox{(iii) to determine the number of shares of Common Stock to be covered by each Option granted hereunder;}\\$
- $\mbox{(iv) to approve forms of agreement for use under the } \label{eq:plan}$
- (v) to determine the terms and conditions, not inconsistent with the terms of the Plan, of any Option granted hereunder. Such terms and conditions include, but are not limited to, the exercise price, the time or times when Options 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 the shares of Common Stock relating thereto, based in each case on such factors as the Administrator, in its sole discretion, shall determine;
- (vi) to construe and interpret the terms of the Plan and awards granted pursuant to the Plan;

(vii) 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 satisfying applicable foreign laws;

(viii) to modify or amend each Option (subject to Section 15(c) of the Plan), including the discretionary authority to extend the post-termination exercisability period of Options longer than is otherwise provided for in the Plan;

(ix) 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 that number of Shares having a Fair Market Value equal to the minimum 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 an Optionee 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;

(x) to authorize any person to execute on behalf of the Company any instrument required to effect the grant of an Option previously granted by the Administrator;

 $\hbox{(xi) to make all other determinations deemed}\\ \hbox{necessary or advisable for administering the Plan.}$ 

- (c) Effect of Administrator's Decision. The Administrator's decisions, determinations and interpretations shall be final and binding on all Optionees and any other holders of Options or Shares issued under the Plan.
- 5. Eligibility. Nonstatutory Stock Options may be granted to Service Providers. Incentive Stock Options may be granted only to Employees.

# 6. Limitations.

- (a) 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 Optione 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 6(a), 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.
- (b) Neither the Plan nor any Option shall confer upon an Optionee any right with respect to continuing the Optionee's relationship as a Service Provider with the Company, nor shall they interfere in any way with the Optionee's right or the Company's right to terminate such relationship at any time, with or without cause.
  - (c) The following limitations shall apply to grants of Options:

(i) No Service Provider shall be granted, in any fiscal year of the Company, Options to purchase more than 1,000,000 Shares.

(ii) In connection with his or her initial service, a Service Provider may be granted Options to purchase up to an additional 1,000,000 Shares, which shall not count against the limit set forth in subsection (i) above.

(iii) The foregoing limitations shall be adjusted proportionately in connection with any change in the Company's capitalization as described in Section 13.

- 7. Term of Plan. Subject to Section 19 of the 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 terminated earlier under Section 15 of the Plan.
- 8. Term of Option. The term of each Option shall be stated in the Option Agreement. In the case of an Incentive Stock Option, the term shall be ten (10) years from the date of grant or such shorter term as may be provided in the Option Agreement. Moreover, in the case of an Incentive Stock Option granted to an Optionee who, at the time the Incentive Stock Option is granted, owns stock representing more than ten percent (10%) of the total combined voting power of all classes of stock of the Company or any Parent or Subsidiary, the term of the Incentive Stock Option shall be five (5) years from the date of grant or such shorter term as may be provided in the Option Agreement.
  - 9. Option Exercise Price and Consideration.
- (a) Exercise Price. The per share exercise price for the Shares to be issued pursuant to exercise of an Option shall be determined by the Administrator, subject to the following:
  - (i) In the case of an Incentive Stock Option

(A) granted to an Employee who, at the time the Incentive Stock 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 per Share exercise price shall be no less than 110% of the Fair Market Value per Share on the date of grant.

(B) granted to any Employee other than an Employee described in paragraph (A) immediately above, 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, the per Share exercise price shall be determined by the Administrator. In the case of a Nonstatutory Stock Option intended to qualify as "performance-based compensation" within the meaning of Section 162(m) of the Code, the per Share exercise price shall be no less than 100% 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 of less than 100% of the Fair Market Value per Share on the date of grant pursuant to a merger or other corporate transaction.

- (b) Waiting Period and Exercise Dates. At the time an Option is granted, the Administrator shall fix the period within which the Option may be exercised and shall determine any conditions that must be satisfied before the Option may be exercised.
- (c) Form of Consideration. The Administrator shall determine the acceptable form of consideration for exercising an Option, including the method of payment. In the case of an Incentive Stock Option, the Administrator shall determine the acceptable form of consideration at the time of grant. Such consideration may consist entirely of:
  - (i) cash;
  - (ii) check;
  - (iii) promissory note;

(iv) other Shares which, in the case of Shares acquired directly or indirectly from the Company, (A) have been owned by the Optionee for more than six (6) months on the date of surrender, and (B) have a Fair Market Value on the date of surrender equal to the aggregate exercise price of the Shares as to which said Option shall be exercised;

 $\mbox{(v)}$  consideration received by the Company under a cashless exercise program implemented by the Company in connection with the Plan:

(vi) a reduction in the amount of any Company liability to the Optionee, including any liability attributable to the Optionee's participation in any Company-sponsored deferred compensation program or arrangement;

(vii) any combination of the foregoing methods of

payment; or

(viii) such other consideration and method of payment for the issuance of Shares to the extent permitted by Applicable Laws.

Notwithstanding the foregoing, the Administrator may permit an Option to be exercised by delivery of a full-recourse promissory note secured by the purchased shares. All other terms of such promissory note shall be determined by the Administrator in its sole discretion.

- 10. Exercise of Option.
- (a) Procedure for Exercise; Rights as a Stockholder. Any Option granted hereunder shall be exercisable according to the terms of the Plan and at such times and under such conditions as determined by the Administrator and set forth in the Option Agreement. Unless the Administrator provides otherwise, vesting of Options granted hereunder shall be suspended 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 Optioned Stock, 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 13 of the Plan.

Exercising an Option in any manner shall decrease 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, other than upon the Optionee's death or Disability, the Optionee may exercise his or her Option within such period of time as is specified in the Option Agreement 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 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 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 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 following Optionee's death within such period of time as is specified in the Option Agreement to the extent that the Option is vested on the date of death (but in no event may the option be exercised later than the expiration of the term of such Option as set forth in the Option Agreement) by the Optionee's designated beneficiary, provided such beneficiary has been desig-

nated prior to Optionee's death in a form acceptable by the Administrator. If no such beneficiary has been designated by the Optionee, then such Option may be exercised by the personal representative of the Optionee's estate or by the person(s) to whom the Option is transferred pursuant to the Optionee's will or in accordance with the laws of descent and distribution. In the absence of a specified time in the Option Agreement, the Option shall remain exercisable for twelve (12) months following Optionee's death. If, at the time of death, the Optionee is not vested as to his or her 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.

- 11. Formula Option Grants to Outside Directors. Outside Directors shall automatically be granted Options in accordance with the following provisions:
- (a) All Options granted pursuant to this Section shall be Nonstatutory Stock Options and, except as otherwise provided herein, shall be subject to the other terms and conditions of the Plan.
- (b) Each Outside Director shall be automatically granted an Option to purchase up to 20,000 Shares on the date of each Annual Stockholder's Meeting, beginning in fiscal year 2001, provided the individual continues to serve as an Outside Director through the date of such Annual Stockholder's Meeting.
- (c) Notwithstanding the provisions of subsections (b) hereof, any exercise of an Option granted before the Company has obtained stockholder approval of the Plan in accordance with Section 19 hereof shall be conditioned upon obtaining such stockholder approval of the Plan in accordance with Section 19 hereof.
- (d) The terms of each Option granted pursuant to this Section shall be as follows:
  - (i) the term of the Option shall be ten (10) years.
- $\,$  (ii) the Option shall be exercisable only while the Outside Director remains a Director of the Company.
- (iii) the exercise price per Share shall be 100% of the Fair Market Value per Share on the date of grant of the Option.
- (iv) subject to Section 13, the Option shall become exercisable as to 25% of the Shares subject to the Option on each anniversary of its date of grant, provided that the Optionee continues to serve as a Director on such dates.
- 12. Limited Transferability of Options. Unless determined otherwise by the Administrator, an Option 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. If the Administrator makes an Option transferable, such Option shall contain such additional terms and conditions as the Administrator deems appropriate.

13. Adjustments Upon Changes in Capitalization, Dissolution, 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 which have been authorized for issuance under the Plan but as to which no Options have yet been granted or which have been returned to the Plan upon cancellation or expiration of an Option, the number of Shares that may be added to the Plan pursuant to Section 3, the number of shares granted under Options pursuant to Section 11(b), and the number of shares of Common Stock covered by each outstanding Option as well as the price per share of Common Stock covered by each such outstanding Option, 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; provided, however, that 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.

(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 until ten (10) days prior to such transaction as to all of the Optioned Stock covered thereby, including Shares as to which the Option 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 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 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 shall be assumed or an equivalent option 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, the Optionee shall fully vest in and have the right to exercise the Option as to all of the Optioned Stock, including Shares as to which it would not otherwise be vested or exercisable. If an Option 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 shall be fully vested and exercisable for a period of fifteen (15) days from the date of such notice, and the Option shall terminate upon the expiration of such period. For the purposes of this paragraph, the Option shall be considered assumed if, following the merger or sale of assets, the option confers the right to purchase or receive, for each Share of Optioned Stock subject to the Option 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, for each Share of Optioned Stock subject to the Option, 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.

- 14. Date of Grant. The date of grant of an Option shall be, for all purposes, the date on which the Administrator makes the determination granting such Option, or such other later date as is determined by the Administrator. Notice of the determination shall be provided to each Optionee within a reasonable time after the date of such grant.
  - 15. 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 Company 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.
  - 16. 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 Company 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.
- 17. 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.

- 18. Reservation of Shares. The Company, during the term of this Plan, will at all times reserve and keep available such number of Shares as shall be sufficient to satisfy the requirements of the Plan.
- 19. 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 manner and to the degree required under Applicable Laws.

# PAIN THERAPEUTICS, INC.

# 2000 EMPLOYEE STOCK PURCHASE PLAN

The following constitute the provisions of the 2000 Employee Stock Purchase Plan of Pain Therapeutics, Inc.

1. Purpose. The purpose of the Plan is to provide employees of the Company and its Designated Subsidiaries with an opportunity to purchase Common Stock of the Company through accumulated payroll deductions. It is the intention of the Company to have the Plan qualify as an "Employee Stock Purchase Plan" under Section 423 of the Internal Revenue Code of 1986, as amended. The provisions of the Plan, accordingly, shall be construed so as to extend and limit participation in a manner consistent with the requirements of that section of the Code.

# 2. Definitions.

- (a) "Board" shall mean the Board of Directors of the Company or any committee thereof designated by the Board of Directors of the Company in accordance with Section 14 of the Plan.
- (b) "Code" shall mean the Internal Revenue Code of 1986, as amended.
  - (c) "Common Stock" shall mean the common stock of the Company.
- (d) "Company" shall mean Pain Therapeutics, Inc., a Delaware Corporation and any Designated Subsidiary of the Company.
- (e) "Compensation" shall mean all base straight time gross earnings but exclusive of payments for commissions, overtime, shift premium, incentive compensation, incentive payments, bonuses and other compensation.
- (f) "Designated Subsidiary" shall mean any Subsidiary that has been designated by the Board from time to time in its sole discretion as eligible to participate in the Plan.
- (g) "Employee" shall mean any individual who is an Employee of the Company for tax purposes whose customary employment with the Company is at least twenty (20) hours per week and more than five (5) months in any calendar year. For purposes of the Plan, the employment relationship shall be treated as continuing intact while the individual is on sick leave or other leave of absence approved by the Company. Where the period of leave exceeds 90 days and the individual's right to reemployment is not guaranteed either by statute or by contract, the employment relationship shall be deemed to have terminated on the 91st day of such leave.
- (h) "Enrollment Date" shall mean the first Trading Day of each Offering Period.

- (i) "Exercise Date" shall mean the first Trading Day on or after MAY 1ST AND NOVEMBER 1ST of each year.
- (j) "Fair Market Value" shall mean, 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 on the date of determination, as reported in The Wall Street Journal or such other source as the Board 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 of the closing bid and asked prices for the Common Stock on the date of determination, as reported in The Wall Street Journal or such other source as the Board deems reliable;
- (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 Board: or
- (iv) For purposes of the Enrollment Date of the first Offering Period under the Plan, the Fair Market Value shall be the initial price to the public as set forth in the final prospectus included within the registration statement in Form S-1 filed with the Securities and Exchange Commission for the initial public offering of the Company's Common Stock (the "Registration Statement").
- (k) "Offering Periods" shall mean the periods of approximately twenty-four (24) months during which an option granted pursuant to the Plan may be exercised, commencing on the first Trading Day on or after MAY 1ST AND NOVEMBER 1ST of each year and terminating on the first Trading Day on or after the MAY 1ST AND NOVEMBER 1ST Offering Period commencement date approximately twenty-four months later; provided, however, that the first Offering Period under the Plan shall commence with the first Trading Day on or after the date on which the Securities and Exchange Commission declares the Company's Registration Statement effective and ending on the first Trading Day on or after MAY 1, 2002. The duration and timing of Offering Periods may be changed pursuant to Section 4 of this Plan.
  - (1) "Plan" shall mean this 2000 Employee Stock Purchase Plan.
- (m) "Purchase Period" shall mean the approximately six month period commencing on one Exercise Date and ending with the next Exercise Date, except that the first Purchase Period of any Offering Period shall commence on the Enrollment Date and end with the next Exercise Date.
- (n) "Purchase Price" shall mean 85% of the Fair Market Value of a share of Common Stock on the Enrollment Date or on the Exercise Date, whichever is lower; provided however, that the Purchase Price may be adjusted by the Board pursuant to Section 20.

- (o) "Reserves" shall mean the number of shares of Common Stock covered by each option under the Plan which have not yet been exercised and the number of shares of Common Stock which have been authorized for issuance under the Plan but not yet placed under option.
- (p) "Subsidiary" shall mean a corporation, domestic or foreign, of which not less than 50% of the voting shares are held by the Company or a Subsidiary, whether or not such corporation now exists or is hereafter organized or acquired by the Company or a Subsidiary.
- (q) "Trading Day" shall mean a day on which national stock exchanges and the Nasdaq System are open for trading.

# 3. Eligibility.

- (a) Any Employee who shall be employed by the Company on a given Enrollment Date shall be eligible to participate in the Plan.
- (b) Any provisions of the Plan to the contrary notwithstanding, no Employee shall be granted an option under the Plan (i) to the extent that, immediately after the grant, such Employee (or any other person whose stock would be attributed to such Employee pursuant to Section 424(d) of the Code) would own capital stock of the Company and/or hold outstanding options to purchase such stock possessing five percent (5%) or more of the total combined voting power or value of all classes of the capital stock of the Company or of any Subsidiary, or (ii) to the extent that his or her rights to purchase stock under all employee stock purchase plans of the Company and its subsidiaries accrues at a rate which exceeds Twenty-Five Thousand Dollars (\$25,000) worth of stock (determined at the fair market value of the shares at the time such option is granted) for each calendar year in which such option is outstanding at any time.
- 4. Offering Periods. The Plan shall be implemented by consecutive, overlapping Offering Periods with a new Offering Period commencing on the first Trading Day on or after MAY 1ST AND NOVEMBER 1ST each year, or on such other date as the Board shall determine, and continuing thereafter until terminated in accordance with Section 20 hereof; provided, however, that the first Offering Period under the Plan shall commence with the first Trading Day on or after the date on which the Securities and Exchange Commission declares the Company's Registration Statement effective and ending on the first Trading Day on or after [MAY 1, 2002.] The Board shall have the power to change the duration of Offering Periods (including the commencement dates thereof) with respect to future offerings without stockholder approval if such change is announced at least five (5) days prior to the scheduled beginning of the first Offering Period to be affected thereafter.

# 5. Participation.

- (a) An eligible Employee may become a participant in the Plan by completing a subscription agreement authorizing payroll deductions in the form of Exhibit A to this Plan and filing it with the Company's payroll office prior to the applicable Enrollment Date.
- (b) Payroll deductions for a participant shall commence on the first payroll following the Enrollment Date and shall end on the last payroll in the Offering Period to which such authorization is applicable, unless sooner terminated by the participant as provided in Section 10 hereof.

## 6. Payroll Deductions.

- (a) At the time a participant files his or her subscription agreement, he or she shall elect to have payroll deductions made on each pay day during the Offering Period in an amount not exceeding fifteen percent (15%) of the Compensation which he or she receives on each pay day during the Offering Period; provided, however, that should a pay day occur on an Exercise Date, a participant shall have the payroll deductions made on such day applied to his or her account under the new Offering Period or Purchase Period, as the case may be.
- (b) All payroll deductions made for a participant shall be credited to his or her account under the Plan and shall be withheld in whole percentages only. A participant may not make any additional payments into such account.
- (c) A participant may discontinue his or her participation in the Plan as provided in Section 10 hereof, or may increase or decrease the rate of his or her payroll deductions during the Offering Period by completing or filing with the Company a new subscription agreement authorizing a change in payroll deduction rate. The Company may, in its discretion, limit the nature and/or number of participation rate changes during any Offering Period, and may establish such other conditions or limitations as it deems appropriate for Plan administration. The change in rate shall be effective with the first full payroll period following five (5) business days after the Company's receipt of the new subscription agreement unless the Company elects to process a given change in participation more quickly. A participant's subscription agreement shall remain in effect for successive Offering Periods unless terminated as provided in Section 10 hereof.
- (d) Notwithstanding the foregoing, to the extent necessary to comply with Section 423(b)(8) of the Code and Section 3(b) hereof, a participant's payroll deductions may be decreased to zero percent (0%) at any time during a Purchase Period. Payroll deductions shall recommence at the rate provided in such participant's subscription agreement at the beginning of the first Purchase Period which is scheduled to end in the following calendar year, unless terminated by the participant as provided in Section 10 hereof.
- (e) At the time the option is exercised, in whole or in part, or at the time some or all of the Company's Common Stock issued under the Plan is disposed of, the participant must make adequate provision for the Company's federal, state, or other tax withholding obligations, if any, which arise upon the exercise of the option or the disposition of the Common Stock. At any time, the Company may, but shall not be obligated to, withhold from the participant's compensation the amount necessary for the Company to meet applicable withholding obligations, including any withholding required to make available to the Company any tax deductions or benefits attributable to sale or early disposition of Common Stock by the Employee.
- 7. Grant of Option. On the Enrollment Date of each Offering Period, each eligible Employee participating in such Offering Period shall be granted an option to purchase on each Exercise Date during such Offering Period (at the applicable Purchase Price) up to a number of shares of the Company's Common Stock determined by dividing such Employee's payroll deductions accumulated prior to such Exercise Date and retained in the Participant's account as of the Exercise Date by the applicable Purchase Price; provided that in no event shall an Employee be permitted to purchase during each Purchase Period more than 7,500 shares of the Company's Common Stock

(subject to any adjustment pursuant to Section 19), and provided further that such purchase shall be subject to the limitations set forth in Sections 3(b) and 12 hereof. The Board may, for future Offering Periods, increase or decrease, in its absolute discretion, the maximum number of shares of the Company's Common Stock an Employee may purchase during each Purchase Period of such Offering Period. Exercise of the option shall occur as provided in Section 8 hereof, unless the participant has withdrawn pursuant to Section 10 hereof. The option shall expire on the last day of the Offering Period.

### 8. Exercise of Option.

- (a) Unless a participant withdraws from the Plan as provided in Section 10 hereof, his or her option for the purchase of shares shall be exercised automatically on the Exercise Date, and the maximum number of full shares subject to option shall be purchased for such participant at the applicable Purchase Price with the accumulated payroll deductions in his or her account. No fractional shares shall be purchased; any payroll deductions accumulated in a participant's account which are not sufficient to purchase a full share shall be retained in the participant's account for the subsequent Purchase Period or Offering Period, subject to earlier withdrawal by the participant as provided in Section 10 hereof. Any other monies left over in a participant's account after the Exercise Date shall be returned to the participant. During a participant's lifetime, a participant's option to purchase shares hereunder is exercisable only by him or her.
- (b) If the Board determines that, on a given Exercise Date, the  $\,$ number of shares with respect to which options are to be exercised may exceed (i) the number of shares of Common Stock that were available for sale under the Plan on the Enrollment Date of the applicable Offering Period, or (ii) the number of shares available for sale under the Plan on such Exercise Date, the Board may in its sole discretion (x) provide that the Company shall make a pro rata allocation of the shares of Common Stock available for purchase on such Enrollment Date or Exercise Date, as applicable, in as uniform a manner as shall be practicable and as it shall determine in its sole discretion to be equitable among all participants exercising options to purchase Common Stock on such Exercise Date, and continue all Offering Periods then in effect, or (y) provide that the Company shall make a pro rata allocation of the shares available for purchase on such Enrollment Date or Exercise Date, as applicable, in as uniform a manner as shall be practicable and as it shall determine in its sole discretion to be equitable among all participants exercising options to purchase Common Stock on such Exercise Date, and terminate any or all Offering Periods then in effect pursuant to Section 20 hereof. The Company may make pro rata allocation of the shares available on the Enrollment Date of any applicable Offering Period pursuant to the preceding sentence, notwithstanding any authorization of additional shares for issuance under the Plan by the Company's stockholders subsequent to such Enrollment Date.
- 9. Delivery. As promptly as practicable after each Exercise Date on which a purchase of shares occurs, the Company shall arrange the delivery to each participant, as appropriate, of a certificate representing the shares purchased upon exercise of his or her option.

#### 10. Withdrawal.

- (a) A participant may withdraw all but not less than all the payroll deductions credited to his or her account and not yet used to exercise his or her option under the Plan at any time by giving written notice to the Company in the form of Exhibit B to this Plan. All of the participant's payroll deductions credited to his or her account shall be paid to such participant promptly after receipt of notice of withdrawal and such participant's option for the Offering Period shall be automatically terminated, and no further payroll deductions for the purchase of shares shall be made for such Offering Period. If a participant withdraws from an Offering Period, payroll deductions shall not resume at the beginning of the succeeding Offering Period unless the participant delivers to the Company a new subscription agreement.
- (b) A participant's withdrawal from an Offering Period shall not have any effect upon his or her eligibility to participate in any similar plan which may hereafter be adopted by the Company or in succeeding Offering Periods which commence after the termination of the Offering Period from which the participant withdraws.

# 11. Termination of Employment.

Upon a participant's ceasing to be an Employee, for any reason, he or she shall be deemed to have elected to withdraw from the Plan and the payroll deductions credited to such participant's account during the Offering Period but not yet used to exercise the option shall be returned to such participant or, in the case of his or her death, to the person or persons entitled thereto under Section 15 hereof, and such participant's option shall be automatically terminated. The preceding sentence notwithstanding, a participant who receives payment in lieu of notice of termination of employment shall be treated as continuing to be an Employee for the participant's customary number of hours per week of employment during the period in which the participant is subject to such payment in lieu of notice.

12. Interest. No interest shall accrue on the payroll deductions of a participant in the Plan.

### 13. Stock.

- (a) Subject to adjustment upon changes in capitalization of the Company as provided in Section 19 hereof, the maximum number of shares of the Company's Common Stock which shall be made available for sale under the Plan shall be 500,000 shares, plus an annual increase to be added on the first day of the Company's fiscal year, beginning in 2001, equal to the lesser of (i) 500,000 shares, (ii) 1% of the outstanding shares of Common Stock on such date, or (iii) an amount determined by the Board.
- (b) The participant shall have no interest or voting right in shares covered by his option until such option has been exercised.
- (c) Shares to be delivered to a participant under the Plan shall be registered in the name of the participant or in the name of the participant and his or her spouse.

14. Administration. The Plan shall be administered by the Board or a committee of members of the Board appointed by the Board. The Board or its committee shall have full and exclusive discretionary authority to construe, interpret and apply the terms of the Plan, to determine eligibility and to adjudicate all disputed claims filed under the Plan. Every finding, decision and determination made by the Board or its committee shall, to the full extent permitted by law, be final and binding upon all parties.

# 15. Designation of Beneficiary.

- (a) A participant may file a written designation of a beneficiary who is to receive any shares and cash, if any, from the participant's account under the Plan in the event of such participant's death subsequent to an Exercise Date on which the option is exercised but prior to delivery to such participant of such shares and cash. In addition, a participant may file a written designation of a beneficiary who is to receive any cash from the participant's account under the Plan in the event of such participant's death prior to exercise of the option. If a participant is married and the designated beneficiary is not the spouse, spousal consent shall be required for such designation to be effective.
- (b) Such designation of beneficiary may be changed by the participant at any time by written notice. In the event of the death of a participant and in the absence of a beneficiary validly designated under the Plan who is living at the time of such participant's death, the Company shall deliver such shares and/or cash to the executor or administrator of the estate of the participant, or if no such executor or administrator has been appointed (to the knowledge of the Company), the Company, in its discretion, may deliver such shares and/or cash to the spouse or to any one or more dependents or relatives of the participant, or if no spouse, dependent or relative is known to the Company, then to such other person as the Company may designate.
- 16. Transferability. Neither payroll deductions credited to a participant's account nor any rights with regard to the exercise of an option or to receive shares under the Plan may be assigned, transferred, pledged or otherwise disposed of in any way (other than by will, the laws of descent and distribution or as provided in Section 15 hereof) by the participant. Any such attempt at assignment, transfer, pledge or other disposition shall be without effect, except that the Company may treat such act as an election to withdraw funds from an Offering Period in accordance with Section 10 hereof.
- 17. Use of Funds. All payroll deductions received or held by the Company under the Plan may be used by the Company for any corporate purpose, and the Company shall not be obligated to segregate such payroll deductions.
- 18. Reports. Individual accounts shall be maintained for each participant in the Plan. Statements of account shall be given to participating Employees at least annually, which statements shall set forth the amounts of payroll deductions, the Purchase Price, the number of shares purchased and the remaining cash balance, if any.

- Adjustments Upon Changes in Capitalization, Dissolution, Liquidation, Merger or Asset Sale.
- (a) Changes in Capitalization. Subject to any required action by the stockholders of the Company, the Reserves (including the number of shares automatically added annually to the Plan pursuant to Section 13(a)(i)), the maximum number of shares each participant may purchase each Purchase Period (pursuant to Section 7), as well as the price per share and the number of shares of Common Stock covered by each option under the Plan which has not yet been exercised 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 shares of Common Stock effected without receipt of consideration by the Company; provided, however, that 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.
- (b) Dissolution or Liquidation. In the event of the proposed dissolution or liquidation of the Company, the Offering Period then in progress shall be shortened by setting a new Exercise Date (the "New Exercise Date"), and shall terminate immediately prior to the consummation of such proposed dissolution or liquidation, unless provided otherwise by the Board. The New Exercise Date shall be before the date of the Company's proposed dissolution or liquidation. The Board shall notify each participant in writing, at least ten (10) business days prior to the New Exercise Date, that the Exercise Date for the participant's option has been changed to the New Exercise Date and that the participant's option shall be exercised automatically on the New Exercise Date, unless prior to such date the participant has withdrawn from the Offering Period as provided in Section 10 hereof.
- (c) Merger or Asset Sale. In the event of a proposed sale of all or substantially all of the assets of the Company, or the merger of the Company with or into another corporation, each outstanding option shall be assumed or an equivalent option 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, any Purchase Periods then in progress shall be shortened by setting a new Exercise Date (the "New Exercise Date") and any Offering Periods then in progress shall end on the New Exercise Date. The New Exercise Date shall be before the date of the Company's proposed sale or merger. The Board shall notify each participant in writing, at least ten (10) business days prior to the New Exercise Date, that the Exercise Date for the participant's option has been changed to the New Exercise Date and that the participant's option shall be exercised automatically on the New Exercise Date, unless prior to such date the participant has withdrawn from the Offering Period as provided in Section 10 hereof.

#### 20. Amendment or Termination.

- (a) The Board of Directors of the Company may at any time and for any reason terminate or amend the Plan. Except as provided in Section 19 hereof, no such termination can affect options previously granted, provided that an Offering Period may be terminated by the Board of Directors on any Exercise Date if the Board determines that the termination of the Offering Period or the Plan is in the best interests of the Company and its stockholders. Except as provided in Section 19 and this Section 20 hereof, no amendment may make any change in any option theretofore granted which adversely affects the rights of any participant. To the extent necessary to comply with Section 423 of the Code (or any successor rule or provision or any other applicable law, regulation or stock exchange rule), the Company shall obtain stockholder approval in such a manner and to such a degree as required.
- (b) Without stockholder consent and without regard to whether any participant rights may be considered to have been "adversely affected," the Board (or its committee) shall be entitled to change the Offering Periods, limit the frequency and/or number of changes in the amount withheld during an Offering Period, establish the exchange ratio applicable to amounts withheld in a currency other than U.S. dollars, permit payroll withholding in excess of the amount designated by a participant in order to adjust for delays or mistakes in the Company's processing of properly completed withholding elections, establish reasonable waiting and adjustment periods and/or accounting and crediting procedures to ensure that amounts applied toward the purchase of Common Stock for each participant properly correspond with amounts withheld from the participant's Compensation, and establish such other limitations or procedures as the Board (or its committee) determines in its sole discretion advisable which are consistent with the Plan.
- (c) In the event the Board determines that the ongoing operation of the Plan may result in unfavorable financial accounting consequences, the Board may, in its discretion and, to the extent necessary or desirable, modify or amend the Plan to reduce or eliminate such accounting consequence including, but not limited to:
- (i) altering the Purchase Price for any Offering Period including an Offering Period underway at the time of the change in Purchase Price;
- (ii) shortening any Offering Period so that Offering Period ends on a new Exercise Date, including an Offering Period underway at the time of the Board action; and

# (iii) allocating shares.

Such modifications or amendments shall not require stockholder approval or the consent of any Plan participants.

- 21. Notices. All notices or other communications by a participant to the Company under or in connection with the Plan shall be deemed to have been duly given when received in the form specified by the Company at the location, or by the person, designated by the Company for the receipt thereof.
- $\,$  22. Conditions Upon Issuance of Shares. Shares shall not be issued with respect to an option unless the exercise of such option and the issuance and delivery of such shares pursuant

thereto shall comply with all applicable provisions of law, domestic or foreign, including, without limitation, the Securities Act of 1933, as amended, the Securities Exchange Act of 1934, as amended, the rules and regulations promulgated thereunder, and the requirements of any stock exchange upon which the shares may then be listed, and shall be further subject to the approval of counsel for the Company with respect to such compliance.

As a condition to the exercise of an option, the Company 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 by any of the aforementioned applicable provisions of law.

- 23. Term of Plan. The Plan shall become effective upon the earlier to occur of its adoption by the Board of Directors or its approval by the stockholders of the Company. It shall continue in effect for a term of ten (10) years unless sooner terminated under Section 20 hereof.
- 24. Automatic Transfer to Low Price Offering Period. To the extent permitted by any applicable laws, regulations, or stock exchange rules if the Fair Market Value of the Common Stock on any Exercise Date in an Offering Period is lower than the Fair Market Value of the Common Stock on the Enrollment Date of such Offering Period, then all participants in such Offering Period shall be automatically withdrawn from such Offering Period immediately after the exercise of their option on such Exercise Date and automatically re-enrolled in the immediately following Offering Period.

#### EXHIBIT A

### PAIN THERAPEUTICS, INC. 2000 EMPLOYEE STOCK PURCHASE PLAN

# SUBSCRIPTION AGREEMENT

	Original Application	Enrollment Date:
	Change in Payroll Deduction Rate	
	Change of Beneficiary(ies)	
1.	hereby elects to participate in the Pain Therapeutics, Inc. 2000 Employee Stock Purchase Plan (the "Employee Stock Purchase Plan") and subscribes to purchase shares of the Company' Common Stock in accordance with this Subscription Agreement and the Employee Stock Purchase Plan.	
2.	I hereby authorize payroll deductions from ea of% of my Compensation on each payday ( Offering Period in accordance with the Employ	from 0 to 15%) during the

- (Please note that no fractional percentages are permitted.)

  3. I understand that said payroll deductions shall be accumulated for the purchase of shares of Common Stock at the applicable Purchase Price determined in accordance with the Employee Stock Purchase Plan. I understand that if I do not withdraw from an Offering Period, any accumulated payroll deductions will be used to automatically exercise my
- 4. I have received a copy of the complete Employee Stock Purchase Plan. I understand that my participation in the Employee Stock Purchase Plan is in all respects subject to the terms of the Plan. I understand that my ability to exercise the option under this Subscription Agreement is subject to stockholder approval of the Employee Stock Purchase Plan.
- 5. Shares purchased for me under the Employee Stock Purchase Plan should be issued in the name(s) of (Employee or Employee and Spouse only).
- 6. I understand that if I dispose of any shares received by me pursuant to the Plan within 2 years after the Enrollment Date (the first day of the Offering Period during which I purchased such shares) or one year after the Exercise Date, I will be treated for federal income tax purposes as having received ordinary income at the time of such disposition in an amount equal to the excess of the fair market value of the shares at the time such shares were purchased by me over the price which I paid for the shares. I hereby agree to notify the Company in writing within 30 days after the date of any disposition of my shares and I will make adequate provision for Federal, state or other tax withholding obligations, if any, which arise upon the disposition of the Common Stock. The Company may, but will not be obligated to, withhold

from my compensation the amount necessary to meet any applicable withholding obligation including any withholding necessary to make available to the Company any tax deductions or benefits attributable to sale or early disposition of Common Stock by me. If I dispose of such shares at any time after the expiration of the 2-year and 1-year holding periods, I understand that I will be treated for federal income  $\tan$ purposes as having received income only at the time of such disposition, and that such income will be taxed as ordinary income only to the extent of an amount equal to the lesser of (1) the excess of the fair market value of the shares at the time of such disposition over the purchase price which I paid for the shares, or (2) 15% of the fair market value of the shares on the first day of the Offering Period. The remainder of the gain, if any, recognized on such disposition will be taxed as capital gain.

- I hereby agree to be bound by the terms of the Employee Stock Purchase 7. Plan. The effectiveness of this Subscription Agreement is dependent upon my eligibility to participate in the Employee Stock Purchase Plan.
- 8. In the event of my death, I hereby designate the following as my beneficiary(ies) to receive all payments and shares due me under the Employee Stock Purchase Plan:

NAME: (Please print)

	(First)	(Middle)	(Last)
Relationship			
Employee's Social Security Number:	(Address	)	
Employee's Address:			
Employee's Address.			
I UNDERSTAND THAT THIS SUBSCI SUCCESSIVE OFFERING PERIODS			CT THROUGHOUT
Dated:			
		re of Employee	
	Spouse' than sp	s Signature (If benefi ouse)	ciary other

EXHIBIT B

# PAIN THERAPEUTICS, INC. 2000 EMPLOYEE STOCK PURCHASE PLAN

# NOTICE OF WITHDRAWAL

The undersigned participant in the Offering Period of the Pain
Therapeutics, Inc. 2000 Employee Stock Purchase Plan which began on
, (the "Enrollment Date") hereby notifies the Company that he
or she hereby withdraws from the Offering Period. He or she hereby directs the
Company to pay to the undersigned as promptly as practicable all the payroll
deductions credited to his or her account with respect to such Offering Period.
The undersigned understands and agrees that his or her option for such Offering
Period will be automatically terminated. The undersigned understands further
that no further payroll deductions will be made for the purchase of shares in
the current Offering Period and the undersigned shall be eligible to participate
in succeeding Offering Periods only by delivering to the Company a new
Subscription Agreement.

Name and Address of Participant:
Signature:
Date:

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EXHIBIT 23.1

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 June 19, 2000

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JAN-01-1999
DEC-31-1999
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